

Management of non-cavitated and cavitated caries in primary, permanent, and mixed dentition

An evidence review

March 2022



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Abbreviations

Abbreviation	Expanded term
ACP	amorphous calcium phosphate
AHRQ	Agency for Healthcare Research and Quality
AMSTAR 2	A MeaSurement Tool to Assess systematic Reviews
BBO	Brazilian Library in Dentistry
BisGMA	BPA glycidyl methacrylate
BPA	bisphenol A
CAD/CAM	computer-aided design/computer-aided manufacturing
CADTH	Canadian Agency for Drugs and Technologies in Health
CAPES	Coordenação de Aperfeiçoamento de Pessoas [or “Pessoal”?] de Nível Superior
Casa Pia	Casa Pia Study of Health Effects of Dental Amalgam in Children
CENTRAL	Cochrane Central Register of Controlled Trials
CI	confidence interval
CPP-ACP	casein phosphopeptide-amorphous calcium phosphate
DoPHER	Database of Promoting Health Effectiveness Reviews
EDTA	Ethylenediaminetetraacetic acid
FDI	FDI World Dental Federation
GIC	glass ionomer cement
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
HEMA	2-hydroxyethyl methacrylate
HRB	Health Research Board
I ²	Index measuring the percentage of inconsistency or heterogeneity
ICDAS	International Caries Detection and Assessment System
kg	kilogram
LILACS	Latin American and Caribbean Health Sciences Literature
MeSH	Medical Subject Headings
mL	millilitre
NaF	sodium fluoride
NECAT	The New England Children’s Amalgam Trial
ng	nanogram
NICE	National Institute for Health and Care Excellence
nm	nanometer
OR	odds ratio
PICO	population, intervention, comparator, and outcomes
ppm	parts per million

Abbreviation	Expanded term
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
RCT	randomised controlled trial
SDF	silver diamine fluoride
µg	microgram
UK	United Kingdom
USA	United States of America
USPHS	United States Public Health Service
VS	vector system: air- and/or sono-abrasion
WHO	World Health Organization

Glossary of terms

Intervention	Explanation
1.23% acidulated phosphate fluoride gel adhesives	A professionally applied topical agent with a low pH that is used in the prevention [and remineralization] of dental caries.¹ Dental procedures and techniques that do not depend on traditional mechanical factors for retention, but rather adhere to tooth substance. The success relies on adhesive techniques that establish some form of 'bond' or adhesion between the restorative material and underlying tooth substance.¹ Types of adhesives used in caries management: Self-etching: one-step self-etching and two-step self-etching adhesive systems. Etch-and-rinse: two-step etch-and-rinse and three-step etch-and-rinse adhesives. Alcohol-based or acetone-based adhesives. 2-hydroxyethyl methacrylate (HEMA)-free adhesive systems and HEMA-containing adhesive systems.
aesthetic preformed crowns	A type of crown or prosthetic restoration encompassing the entire prepared clinical crown. A preformed steel crown used for the restoration of primary teeth and first permanent molars.¹
air- and/or sono-abrasion	Drill-free technique that blasts the tooth surface with air and abrasive particles. This can be used to remove tooth decay, failing composite restorations, and superficial stains and discolorations, as well as prepare a tooth surface for bonding or enamel sealants. The technique is also used to prepare intaglio surfaces of indirect restorations before bonding or cementing.¹
amalgam	An alloy containing mercury as one of its main constituents. A combination of silver, tin, and copper mixed with mercury to generate reaction products that cause hardening and create dental amalgam restorations. In the case of this review, dental amalgam is referred to as amalgam in the findings as this is the review authors descriptor.
atraumatic restorative treatment	The removal of dental caries with only hand instruments and restoring the tooth by filling the resulting tooth preparation with an adhesive restorative material, typically a glass ionomer cement.¹
bisphenol A	Bisphenol A-glycidyl methacrylate is a complex, aromatic, rigid difunctional acrylic monomer that is employed as the principal component in composite resin and sealant. It is based on the reaction of one molecule of bisphenol-A with two molecules of glycidyl methacrylate. Because of its high molecular weight, it is extremely viscous and requires the addition of diluents such as triethylene glycol dimethacrylate to reduce the viscosity. Concerns about potential effects of residual bisphenol-A during production or from bisphenol A-glycidyl methacrylate decomposition have shifted the use toward urethane dimethacrylate or other substitutes in many compositions.¹
bulk-fill resin composites	Bulk-fill resin composites have been designed to simplify the restorative technique because they can be placed into posterior teeth cavities in a single increment of 4–5 mm. These materials offer greater translucency, allowing greater light dissipation through the material; incorporation of more reactive photoinitiators, which enable a greater depth of cure; and include monomers that act as modulators of the polymerization reaction, achieving low polymerization shrinkage. Two types of these materials are commercially available: base and full-body bulk-fill resin composites.⁹⁵
casein phosphopeptide-amorphous calcium phosphate	A natural milk product that facilitates remineralisation of enamel subsurface lesions, slows progression of caries, and decreases dentinal hypersensitivity.¹

Intervention	Explanation
cavity pretreatment	Pretreatment is the protocol required before beginning therapy in a caries cavity, in this review with chlorhexidine, ethanol wet-bonding, or quaternary ammonium compounds. ¹
chemomechanical caries removal	Chemomechanical caries removal is done using either a sodium hypochlorite-based agent, known as CariSolv, and an enzyme-based agent, known as Papacarie. ¹
chlorhexidine	Chlorhexidine is an anti-infective oral prescription rinse to prevent dental biofilm formation and subsequent gingivitis; periodontal disease, irrigation during periodontal procedures, and aseptic pre-rinse before dental procedures. The rinse is slowly released from tooth surfaces, dental biofilm, and oral mucosa and thought to rupture bacterial cell membrane, leading to rapid leakage of cell contents and cell death, reducing the number of microorganisms, but it is not effective in presence of blood. ¹
complete (non-selective) caries removal	Non-selective (complete) caries removal is complete excavation or total carious tissue removal. ¹¹²
compomers (polyacid-modified resin composite)	A poly-acid modified resin composite which has an ion-leachable glass filler and monomers which will polymerize to create a matrix onto which some acidic side chains are grafted. A composite resin that has polyacid, fluoride-releasing groups added. ¹
composite resin	Conventional composite resin fillings are a popular restoration alternative to amalgam fillings. They are made of a plastic substance called acrylic resin that is reinforced with powdered glass quartz, silica, or other ceramic particles. Some components (such as bisphenol A) of restorative composite resins are released in the oral environment initially during polymerization reaction and later due to degradation of the material. ¹ The HRB did not identify any standardised terminology for composite resin or resin composite and so we used the authors descriptors. Siloranes, and ormocer composites are other newer composites.
crown	A crown is a complete coverage restoration for a decayed tooth and are used extensively in everyday clinical practice, especially when tooth structure loss is more than 50%. They are made from a selection of materials: stainless steel crowns, gold, metal ceramic, all ceramic, and zirconia crowns. ¹⁰⁴
dental cavity liner	Calcium hydroxide is a white powder that is mixed with water or another medium and used as a base material in cavity liners and for pulp capping as well as an intracanal medicament. ¹
dentifrice	Dentifrice or toothpaste is a pharmaceutical compound used in conjunction with the toothbrush to clean and polish the teeth. Contains a mild abrasive, a detergent, a flavouring agent, a binder, and occasionally deodorants and various medicaments designed as caries preventives (e.g., fluoride or other antiseptics) . ¹ Some toothpastes are used to treat very early caries and contain very high levels of fluoride (e.g., 5000 ppm fluoride or 1.1% sodium fluoride). ¹
pulp capping	Pulp capping is the covering of an exposed dental pulp with a material that protects it from external influences and stimulates a reparative bridge below the capping material. indirect pulp treatment is a procedure for a tooth with a deep carious lesion and a diagnosis of reversible pulpitis, in which most but not quite all carious dentin is removed before placing the restoration. The goal is to restore the tooth to a healthy, functional state while avoiding any form of direct pulp therapy. Also called indirect pulp capping, stepwise caries excavation. ¹
direct restoration materials	Direct restoration materials relate to any restorative procedure performed directly on a tooth without the use of a die (e.g., composite resin, silver amalgam restorations, or a gold foil restoration). ¹ In Ireland, dental resin-

Intervention	Explanation
	based composite (RBC) is the term used to describe direct composite resin restorations, however we have used the terms used by the authors of the systematic reviews included in the overview of reviews.
enamel bevel	An enamel bevel is any abrupt incline between the two surfaces of a prepared tooth or between the cavity wall and the cavosurface margins in the prepared cavity. Bevels are the variations which are created during tooth preparation or cavity preparation to help in increased retention and to prevent marginal leakage. ¹
flowable resin composite or resin composite	Flowable composite is a light-cured composite of lower viscosity for flow onto the walls of tooth (cavity) preparations as the first increment before application of regular composite. Lowered viscosity can be engineered using less filler, more diluent monomer, and special additives. While these materials flow well, they do not necessarily wet tooth surfaces any better. There is mixed evidence as to their usefulness.
fluoride gels	Fluoride is a salt of hydrofluoric acid, commonly sodium, stannous (tin), or silver. It is an inorganic, monatomic anion of fluorine with the chemical formula of F ⁻ . Fluoride is the simplest anion of fluorine. Fluoride inhibits dental caries through uptake into enamel, so is used systemically for water fluoridation and topically in products like toothpaste, mouthwash, gel or varnish. ¹
glass ionomer cement	A glass ionomer cement is a material used to cementation of indirect restorations, to line deep tooth preparation walls, and to restore small intracoronal cavities. It is based on the reaction of silicate glass powder (calcium aluminofluorosilicate glass) with polyacrylic acid liquid. It has an advantage of releasing some fluoride over time. The viscosity of glass ionomer cement can range from high to low. Viscosity is a liquid's resistance or inability to flow. ¹
Hall Technique to apply crowns	For the purpose of simplifying the procedure and making it receptive to the patients, Dr Hall devised a technique of stainless steel crown placement in children that does not require local anesthesia, or caries removal or any sort of tooth preparation. This technique is based on the scientific evidence that caries progression gets arrested once an effective marginal seal is achieved. A properly placed stainless steel crown denies the cariogenic bacteria of an environment that is conducive for acidic demineralization of the inorganic and proteolytic disintegration of the organic component of the tooth structure. ⁸²
indirect restoration materials	Composite, ceramic, metal ceramic, and gold inlay, onlay, and/or overlay A composite resin inlay restoration fabricated in the laboratory and cemented into the preparation in the tooth. Its advantage is that it avoids composite resin shrinkage experienced with direct materials. Its disadvantage is that it must be fabricated indirectly. A ceromer ceramic is a composite material (i.e., ceramic optimized polymer) designed for semi-permanent indirect onlay and crown restorations that are lab processed with heat, light, and pressure. ¹
laser	Erbium laser is a family of lasers that has two distinct wavelengths, Er, Cr: YSGG (yttrium scandium gallium garnet) lasers and Er: YAG (yttrium aluminium garnet) lasers. The erbium wavelengths have a high affinity for hydroxyapatite and the highest absorption in water of any dental laser wavelengths. Consequently, these lasers may be used for treatment of dental hard tissue (enamel, dentin, cementum, and bone). In addition to hard tissue procedures, erbium lasers may also be used for soft tissue ablation because dental soft tissue also contains a high percentage of water. These procedures show an excellent healing response. Soft tissue applications with erbium lasers feature less haemostasis and coagulation abilities relative to the CO ₂ lasers. See also erbium (Er); laser. ¹

Intervention	Explanation
nanofilled/nanohybrid restorations	Nanofilled composites consist of nanometer-sized particles in the composite matrix, which are mostly clustered into larger secondary particles, and nanohybrid composites take the approach of combining nanometer and micrometer-sized fillers. ⁹⁴
microinvasive treatment	Infiltration and sealing are microinvasive treatments for arresting proximal non-cavitated carious lesions. ¹⁶⁰
minimally invasive treatment	minimally invasive dentistry is the adoption of detection, diagnosis, limited surgical intervention for excavation of decay, and restoration, with a view toward maximum preservation of tooth structure and adjunctive remineralisation therapy. The employment of minimally invasive techniques helps to preserve the tooth substance and neighbouring structures, as well as uses dental materials with the highest possible stability and biocompatibility. ¹
NovaMin	NovaMin is a bioactive glass that is used in dental care products for remineralization of teeth, hypersensitivity, gingivitis, bleeding, non-carious lesions, carious lesions, and whitening of the teeth... NovaMin consists of calcium sodium phosphosilicate, which is the active ingredient that enables it to bind to the surface of the tooth to initiate the process of remineralization on the enamel. This occurs instantly on contact with saliva or any aqueous media. ¹⁵²
ozone therapy	Ozone (O ₃) is a natural gaseous molecule made up of three oxygen atoms. Ozone therapy presents great advantages when used as a support for conventional treatments and is indicated for use in a wide range of dental specialties. Its properties include immunostimulant, analgesic, antihypnotic, detoxicating, antimicrobial, bioenergetic, and biosynthetic actions. It is being used for caries control as well as in treatment of periodontal and endodontic microbial-based lesions. ¹
pit-and-fissure sealants	A resin-based sealant that does not contain filler particles (as opposed to a filled sealant, which contains additional filler particles). It is generally less viscous and fills a pit or fissure more effectively. Unfilled sealants typically do not require additional occlusal adjustments. Resin-based sealants can be combined with 5% sodium fluoride varnish to manage early carious lesions.
resin-modified glass ionomer cement	A resin-modified glass ionomer cement is a version of a glass ionomer cement that includes monomers in its composition that make it light- or dual-cured as well. ¹
resin infiltration	Resin infiltration is a microinvasive technique for treating early caries. It slows/stops the carious lesion progression rate by creating a diffusion barrier inside the porous enamel lesion body. ¹⁶²
rubber dam	A dental or rubber dam is a thin sheet of nitrile (not natural rubber latex because of allergies) used to isolate a tooth or teeth and keep them dry during a dental procedure and to protect the patient from instruments and materials from being inhaled, swallowed or damaging the mouth.
sandwich technique sealing	A lining of glass ionomer or resin-modified glass ionomer. ¹ The reported sealing materials were classified into three types: resin sealant (which included adhesives and pit-and-fissure sealant), glass ionomer cement, and polyurethane tap. ¹⁶⁵
selective (incomplete or partial) caries removal	The selective carious tissue removal technique is less invasive, consisting of selective removal of carious tissue from the surrounding cavity walls, allowing the possibility of remineralising the affected dentine in the pulpal wall, after a definitive cavity sealing is executed in the same session. ¹¹²
selective enamel etching	Selective etching of enamel margins or selective phosphoric acid etching the process of treating the tooth enamel, generally with phosphoric acid, by removal of approximately 3–10 µm of enamel rod to provide retention for enamel sealant, restorative material, or orthodontic bracket. ¹

Intervention	Explanation
silver diamine fluoride	Silver diamine fluoride is a topical medicament of a metal ammine complex of silver fluoride. It is used to arrest and prevent dental caries and relieve dentinal hypersensitivity. However, it will stain most oxidizable surfaces black. Dentin and enamel without demineralisation will receive surface (pellicle) stains that can be removed by mechanical means (brushing; may need pumice polish), while demineralised tooth structure will stain more permanently black (allowing additionally for caries diagnosis). Skin and soft tissue will discolour within minutes to hours after contact and fade away (via surface shedding) within a few days. Some indications for use include xerostomia, multiple carious lesions or delay for caries treatment, behavioural management patients, anatomic niches (e.g., furcations, restoration margins, partially erupted molars), and patients with geographic or financial barriers to access. ¹
stepwise caries removal	Stepwise caries removal consists of the non-selective removal of carious tissue over two sessions. In the first session, all carious dentine is removed from the surrounding walls of the cavity, and then only the most necrotic and contaminated dentine is removed from the pulp wall, with a temporary sealing (lasting 2–6 months) then applied. After this period, the cavity is reopened, remineralisation is evaluated, the softened remaining carious tissue is completely removed, and the final restoration is performed. The purpose of this treatment is to reduce the risk of pulpal exposure by stimulating the deposition of tertiary dentine. ¹¹²

Executive summary

Purpose

The purpose of this overview of reviews is to provide evidence to assist with the development of clinical guidelines on the management of non-cavitated and cavitated caries. Cavitated caries include caries in both crown and root. This overview updates an existing evidence review that was completed in 2019.

Questions

The review questions are:

1. What is the evidence from systematic reviews regarding strategies to manage non-cavitated* or cavitated† carious lesions in primary teeth?
2. What is the evidence from systematic reviews regarding strategies to manage non-cavitated* or cavitated† carious lesions in permanent teeth?
3. What is the evidence from systematic reviews regarding strategies to manage non-cavitated* or cavitated† carious lesions in mixed dentition?

*Non-cavitated caries include demineralisation and white spot lesions.

†Cavitated caries include caries in both crown and root, but not involving pulp.

Methods

The literature searches for this overview of reviews included searches of three clinical databases, 11 systematic review resources, three search engines, and six resources for open access/grey/preprint material. Reference and citation chasing was carried out, as was searching for and following up review protocols and summaries. Initial searches retrieved 3,712 results and reference/citation/protocol chasing retrieved 18 papers. Screening of article titles and abstracts was carried out by four screeners, the results of which were screened a second time by the same screeners. Full-text screening was carried out by two researchers and an information specialist. In addition to the standard exclusion criteria used in the first stages of screening (exclude on study type, intervention, date, etc.), three criteria from the adapted AMSTAR 2 (A MeaSurement Tool to Assess systematic Reviews, version 2) algorithm were used – inadequate research question considering population, intervention, comparator, and outcomes (PICO); inadequate literature search; and inadequate risk of bias/quality assessment. Two reviewers used AMSTAR 2 to assess each full-text review. We used the Joanna Briggs Institute data extraction form for systematic reviews and research syntheses to extract data on the descriptive characteristics and findings of each included systematic review. We extracted and documented in tabular format the following data from each included review: citation details; objectives of the review; participants; setting; interventions and comparators; search information; primary study date range; number of primary studies; study design; risk of bias tool used; risk of bias assessment, including publication bias; analysis methods; outcomes assessed; results by outcome(s); and commentary on bias, heterogeneity, and use of GRADE (Grading of Recommendations, Assessment, Development and Evaluations). We then summarised the main findings and applied GRADE to each of these outcomes. We used Pieper et al.'s methodology to assess overlap of primary studies for each effectiveness outcome.

Findings

Of the initial 3,712 papers retrieved by database searches, 94 were included in the final synthesis, and of the 18 papers retrieved by reference/citation/protocol chasing, 12 were included in the final synthesis. One additional paper was included after screening the references of a previous review by Keane *et al.* on this topic, resulting in the inclusion of 107 papers (or 106 systematic reviews).

We present a more detailed summary in the Discussion section 5.1. and present pertinent highlights here in the executive summary. The presence or absence of community water fluoridation was not considered as part of the intervention effect in this review.

Primary dentition

Non-cavitated caries

We identified one systematic review on the topic of non-invasive treatment for non-cavitated caries in primary teeth. There was low-quality evidence that **fluoride varnishes** were superior to placebo or no intervention as a remineralisation agent. In addition, there was low-quality evidence that **CPP-ACP combined with fluoride toothpaste** had the same remineralising effect as fluoride toothpaste alone. Furthermore, there was low-quality evidence (one primary study) that fluoride varnish had the same effect as pit-and-fissure resin sealants, Nd:YAG laser, and chlorhexidine. Finally, there was low-quality evidence that **fluoride varnish alone** was inferior to fluoride varnish plus chlorhexidine or Nd:YAG laser. There was low-quality evidence from one systematic review that **resin-based sealants plus application of 5% sodium fluoride varnish** had the same arresting effect as fluoride varnish alone.

Cavitated caries

There is moderate-quality evidence from two systematic reviews that **38% silver diamine fluoride** was effective in arresting cavitated caries in primary teeth.

We identified four systematic reviews on the topic of direct restoration material for treating cavitated caries in primary teeth. Each of the reviews examined aspects of clinical performance for **glass ionomer cement and composite resin** compared with each other and with other restoration materials. Overall, clinical performances in restored primary teeth were similar for conventional glass ionomer cement and composite resin in one review (based on low-quality evidence) and lower for glass ionomer cement in two reviews (one based on moderate-quality evidence and one based on low-quality evidence). However, the clinical performance of **resin-modified glass ionomer cement** was similar to that of composite resin in three reviews (one based on moderate-quality evidence and two based on low-quality evidence). Of note, glass ionomer cement was more effective in preventing secondary caries on a variety of primary teeth surfaces in two reviews, based on moderate-quality evidence.

We identified two systematic reviews on the use of the **Hall Technique** to apply crowns on children's carious primary teeth, and both provided signals of successful outcomes, but the quality of the evidence in the reviews was low or very low.

We identified two systematic reviews on **comparing direct and indirect restoration materials** for restoring cavitated caries in primary teeth. The findings of both reviews were uncertain as to which restoration materials were superior, and these findings were based on low-quality evidence.

We identified one systematic review on the topic of adhesives that supports resin composite restoration of cavitated caries in primary teeth. There was low-quality evidence that failure of adhesive restorations in restored cavities of primary teeth was similar with and without the placement of a **liner**.

We identified four systematic reviews on the topic of restoration process or techniques that assist restoration of cavitated caries in primary teeth: three on the stages and amount of caries removed and one on the method of caries removal. **Selective caries removal**, compared with complete caries removal, was associated with higher restoration failure rates and reduced pulp exposure in two reviews— one based on low-quality evidence and the second based on moderate-quality evidence. The third review on the stages and amount of caries removal did not complete a direct comparison. The review comparing **chemomechanical caries removal** (Papacarie) with conventional mechanical caries removal provided some evidence of reduced pain and anxiety among children undergoing chemomechanical caries removal, but the dentist required a longer time-period to complete the chemomechanical caries removal procedure. These findings were based on low- or very low-quality evidence.

Permanent dentition

Non-cavitated caries

We identified four systematic reviews on the topic of non-invasive treatment for non-cavitated caries in permanent teeth. One covered non-invasive treatment of coronal caries and the other three covered non-invasive treatment of root caries. All three reviews (one with moderate-quality evidence, one with moderate and low-quality evidence, and one with low-quality evidence) found that **silver diamine fluoride** provided a higher caries arrest effect than comparators in root carious lesions in adults' permanent teeth. In addition, one of the three reviews reported low-quality evidence that **dentifrice (toothpaste) containing 5000 ppm fluoride and professionally applied chlorhexidine varnish** inactivated existing root carious lesions and/or reduced the initiation of root carious lesions. The fourth review evaluated **fluorides monotherapy** compared with the combined use of CPP-ACP and fluorides for coronal caries and found low-quality evidence that the combination of CPP-ACP and fluoride treatment was better at decreasing the size of early occlusal carious lesions than fluorides monotherapy. However, there was low-quality evidence that fluoride combined with CPP-ACP achieved the same results as fluorides monotherapy for early carious lesions on smooth surfaces.

Non-cavitated caries and cavitated caries

One systematic review compared non-invasive, microinvasive, and minimally invasive treatments with each other, with no active treatment or a placebo treatment, or with standard oral home care for treating pit-and-fissure lesions in permanent posterior teeth in adults. The authors found very low-quality evidence that **microinvasive and minimally invasive treatments** were potentially effective in avoiding retreatments of pit-and-fissure lesions in permanent posterior teeth. In addition, there was some very low-quality evidence that **non-invasive treatments** might also be effective in avoiding retreatments of pit-and-fissure lesions in permanent posterior teeth. Based on very low-quality evidence, microinvasively sealed lesions required re-sealing regularly, increasing the overall need for re-interventions compared especially with minimally invasive treatments.

Cavitated caries

Four systematic reviews examined different forms of **direct composite resin** restoration materials compared with each other and/or **glass ionomer cement**. These four systematic reviews (two with moderate-quality evidence and two with low-quality evidence) that compared newer forms of composite resin with conventional composite resin in patients with direct restorations in posterior permanent teeth found that their clinical performance was similar. Three reviews that compared amalgam with composite resin fillings for permanent posterior teeth found that resin composite had higher failure rates and higher secondary caries rates than amalgam (low- or very low-quality evidence). In addition, there was low- or very low-quality evidence that restoration fracture was the same for both amalgam and resin composite.

One review evaluated **restoration materials for root caries** and found insufficient and low-quality evidence to recommend any specific material for routine use in the restoration of root carious lesions; all had high failure rates.

We identified seven systematic reviews on the topic of **indirect restoration materials** for cavitated caries in permanent teeth. Six of the seven reviews examined indirect restorations and had overlaps between the interventions and comparators, yet no reviews had the exact same interventions or comparators. The six reviews covering indirect restoration examined survival as an outcome, and three identified complications. However, the time points at which survival was assessed were different. These six reviews revealed that the average survival rate at 3 years was over 94%, at 5 years was over 90%, and at 10–11 years was over 87%. The seventh review compared **ceramic crowns** made by a computer-aided design/computer-aided manufacturing system with those made by conventional manufacturing. There was low-quality evidence that the longevity of tooth-supported ceramic crowns made by the computer-aided design/computer-aided manufacturing system was lower than that of crowns made by conventional manufacturing.

We identified four systematic reviews comparing **direct and indirect restoration materials** for cavitated caries in permanent teeth. One review compared all direct and indirect restoration materials with each other, while the other three reviews compared direct and indirect resin composite restorations with each other. The three reviews on **resin composites** (one based on moderate-quality evidence and two based on low-quality evidence) found no difference with respect to the clinical performance of direct and indirect resin composite restorations in permanent teeth for most parameters. One of the three reviews found that there was low-quality evidence that direct restorations were statistically significantly less likely to experience marginal discolouration. The single review comparing all direct and indirect restoration materials in permanent teeth, using data from RCTs, found that the best annual failure rate for direct restorations was for **amalgam** (at 1.9%), and for indirect restorations the best rate was for **metal ceramic** (at 0.3%). However, these findings were based on very low-quality evidence. Based on very low-quality evidence, the highest annual failure rate for any method was for **zirconia-based ceramic** (at 5.1%). **Indirect composite resin** (3.5%) had a marginally higher failure rate than direct composite resin (2.7%). The failure rate for **gold** was 0.75%.

One systematic review evaluated dental cavity liners with **resin composite** posterior restorations in permanent teeth in children and adults and found low-quality evidence that the use of **liners** did not add any benefit to the routine resin-based restorations in permanent posterior teeth in adults in the studies examined. There was no evidence for permanent teeth in children aged under 15 years by 2019.

One systematic review evaluated adhesives used alongside posterior resin composite restorations in permanent teeth and found high-quality evidence that the type of **adhesive** strategy (etch-and-rinse or self-etch) did not seem to influence the risk and intensity of post-operative sensitivity in posterior resin composite restorations.

We identified four systematic reviews evaluating restoration processes or techniques for cavitated caries in permanent teeth. Each of these four reviews evaluated a different technique. The first review evaluated the risk or benefit of **selective caries removal** for the treatment of dentinal caries in permanent teeth compared with non-selective (complete) or stepwise caries removal and found very low-quality evidence that selective removal resulted in greater success of maintaining pulp vitality compared with both non-selective (complete) and stepwise excavation. The second review evaluated the efficacy of **atraumatic restorative treatment** compared with conventional restorative treatment for restoring root carious lesions in older adults and found moderate-quality evidence that there was no significant difference in the failure rates of restorations using atraumatic restorative treatment compared with those

using conventional restorative treatment. The third review evaluated whether the survival rates of **indirect restorations** cemented with **self-adhesive resin** (cement) in permanent teeth were influenced by the presence or absence of selective **enamel etching** and found moderate-quality evidence of no statistically significant difference in the clinical longevity of indirect restorations cemented with self-adhesive resin cement in permanent teeth, with or without selective enamel etching. The fourth review evaluated the effects of **direct pulp capping using laser treatment** compared with pulpectomy or pulpotomy in patients who required such treatment for their deep carious lesions and estimated the success of restorations. There was low-quality evidence that the success rate of pulp capping using laser treatment (89.9%) was statistically significantly higher than that of control groups (67.2%) who had pulpectomy or pulpotomy.

Mixed dentition

Non-cavitated caries

We identified seven systematic reviews on the topic of non-invasive treatment for non-cavitated caries in primary and permanent teeth. One review evaluated the remineralisation potential of **NovaMin** and found low-quality evidence based on one trial that there was no statistically significant difference between the NovaMin group and the control group (Crest toothpaste) in remineralising capacity. Three reviews examined the remineralisation ability of **CPP-ACP**, but there was no overlap of primary studies across the three systematic reviews. The authors found that CPP-ACP was as effective for remineralisation as fluoride (moderate- or low-quality evidence), and it was better than no intervention in two reviews (moderate- or low-quality evidence). Four reviews evaluated the remineralisation and arresting potential of applied fluoride products. Three reviews (two based on low-quality evidence and one based on moderate-quality evidence) reported that **fluoride varnish** was an effective remineralising agent for targeting early caries in primary teeth, and two of the three reviews reported a similar finding for permanent teeth. One review, based on very low-quality evidence, found that **silver diamine fluoride** was more effective than controls for remineralising and arresting the progression of active caries in both primary and permanent teeth in children and adolescents. There was low-quality evidence, based on a review with one trial, that **slow-release fluoride devices** (glass beads) helped reduce dental decay.

We identified eight systematic reviews on the topic of **microinvasive treatment** for non-cavitated caries in primary and permanent teeth. Five examined **infiltration and sealing** and three examined **infiltration only**. There was consistent evidence reported in eight systematic reviews that resin infiltration is effective for reducing and/or arresting the progression of non-cavitated proximal carious lesions in primary and permanent teeth (moderate- or low-quality evidence). Five reviews reported that sealing demonstrated effectiveness for reducing and/or arresting the progression of non-cavitated proximal carious lesions in primary and permanent teeth (moderate- or low-quality evidence).

Non-cavitated caries and cavitated caries

We identified three systematic reviews on the topic of non-invasive treatment for non-cavitated caries and cavitated caries in primary and permanent teeth – one covering **ozone therapy** and two covering **silver diamine fluoride**. One review reported low and very low-quality evidence that ozone therapy was more effective for reducing lesion progression and severity compared with no ozone (compressed air) or no treatment. The same review reported that ozone therapy was as effective as fluoride varnish, and it was less effective than chlorhexidine digluconate. Two reviews (one with moderate-quality evidence and one with very low-quality evidence) reported that 38% and/or 30% concentrations of silver diamine fluoride arrested caries in primary teeth. The two reviews reported differing findings for permanent teeth: one review concluded there was not enough evidence to assess the effectiveness in permanent molars

(no evidence) whereas the other review reported that silver diamine fluoride was not more effective than comparators (very low-quality evidence).

We identified one systematic review on the topic of microinvasive and invasive treatment for non-cavitated caries and cavitated caries in primary and permanent teeth that evaluated the survival rate of **atraumatic restorative treatment with glass ionomer restorations** and **atraumatic restorative treatment with sealants** in primary and permanent posterior teeth. There was very low-quality evidence that the survival rates of single-surface and multiple-surface atraumatic restorative treatment restorations in primary posterior teeth over the first 2 years were 94.3% and 65.4%, respectively. Additionally, there was very low-quality evidence that single-surface atraumatic restorative treatment restorations in permanent posterior teeth over the first 3 years had a survival rate of 87.1%, and multiple-surface atraumatic restorative treatment restorations in permanent posterior teeth over the first 5 years had a survival rate of 77.0%. Based on very low-quality evidence, the weighted average annual failure rates of completely lost atraumatic restorative treatment sealants in permanent posterior teeth over the first 3 and 4 years were 10.7% and 9.6%, respectively. The average annual failure percentages for dentine carious lesions in previously sealed pits and fissures using atraumatic restorative treatment sealants in permanent posterior teeth were 0.9% at 3 years and 1.9% at 5 years, again based on very low-quality evidence.

We identified one systematic review on the topic of non-invasive and microinvasive treatment for non-cavitated caries and cavitated caries in primary and permanent teeth. Urquhart *et al.* compared non-restorative treatments with other active intervention(s), or with no treatment or a placebo, for the arrest or reversal of non-cavitated and cavitated carious lesions in primary and permanent teeth in children and adults. There was a series of findings from this large-scale systematic review:

- There was low-quality evidence that the combination of **sealants with 5% sodium fluoride varnish** for arrest or reversal of non-cavitated carious lesions on occlusal lesions in primary and permanent teeth is superior to most other treatments.
- There was very low-quality evidence that the combination of **resin infiltration and 5% sodium fluoride varnish** was better than no treatment for non-cavitated carious lesions on approximal surfaces in primary and permanent teeth.
- There was very low-quality evidence that **sealants or resin infiltration** were more effective than no treatment intervention for arrest or reversal of non-cavitated carious lesions on approximal surfaces in primary and permanent teeth.
- There was low-quality evidence that **30% silver diamine fluoride** solution, applied annually, is better than 30% silver diamine fluoride solution applied once per week for 3 weeks or 5% sodium fluoride varnish applied once per week for 3 weeks on any coronal surface for arrest or reversal of carious lesions.
- There was low-quality evidence that **38% silver diamine fluoride** solution, applied biannually, was better than 38% silver diamine fluoride solution applied annually or 12% silver diamine fluoride solution applied annually on any coronal surface for arrest or reversal of carious lesions.
- There was low-quality evidence that **5% sodium fluoride varnish** was more effective than some other non-invasive treatments or no treatment for arresting or reversing carious lesions on any coronal surface of primary and permanent teeth.
- There was low-quality evidence that the use of **1.23% acidulated phosphate fluoride gel** on facial/lingual lesions for arresting or reversing such lesions was more effective than oral health education, although only at longer follow-up times.

- There was low-quality evidence to suggest that **5000 ppm fluoride (1.1% sodium fluoride) toothpaste or gel** was more effective than no intervention for arresting or reversing non-cavitated and cavitated carious lesions on root surfaces in permanent teeth.

We identified two systematic reviews on the topic of microinvasive and restorative treatment for non-cavitated caries and cavitated caries in primary and permanent teeth, and these reviews dealt with safety. Both covered the release of **bisphenol A** into the body after the use of composite resin restorations and/or dental sealants. One review included studies that measured bisphenol A in urine only while the other review included studies that measured bisphenol A in saliva and blood as well as in urine. There was low-quality evidence in both reviews that there is bisphenol A exposure in humans from resin-based dental sealants and restorations, but its consequences were not yet known (no evidence). On the other hand, one primary study, in an evaluation of resin use followed immediately by mouthwash, demonstrated an abrupt decrease in bisphenol A levels. The authors do not mention the age cut-off for rinsing with mouthwash.

Cavitated caries

We identified two systematic reviews on the topic of direct restoration materials for cavitated caries in mixed dentition, i.e. both primary and permanent teeth. Each of the reviews evaluated the clinical performance of different restoration materials, so overlap of primary studies in the two systematic reviews was not an issue. One review examined the performance of **bulk-fill direct resin composites**, and based on low-quality evidence, reported that there were no significant differences in the clinical performance of bulk-fill resin composites compared with that of conventional resin composites, regardless of the type of restoration, type of tooth restored, or technique used. The second review examined **high-viscosity glass ionomer cement** covered with a resinous coating and found low-quality evidence of no difference in survival between high-viscosity glass ionomer cement and resin composite or other glass ionomer cements.

Two systematic reviews examined the usefulness of cavity pretreatment for cavitated caries in primary and permanent teeth. The two reviews reported that **cavity pretreatment with chlorhexidine** (two reviews), **ethanol wet-bonding** (one review), or **quaternary ammonium compounds** (one review), compared with no treatment, placebo, or alternative pretreatments, did not increase restoration survival; these findings were based on low- or moderate-quality evidence.

Two reviews evaluated the effectiveness of **cavity liners** for cavitated caries in primary and permanent teeth, and both examined different outcomes. For primary teeth, one review that evaluated liners (calcium hydroxide) found very low-quality evidence indicating better clinical success (lower failure rates) using liners for deep carious lesion treatments than using glass ionomer cement, and low-quality evidence of no difference in success compared with inert materials or adhesive systems. For permanent teeth, there was low-quality evidence from the other review that evaluated liners, based on bacterial counts, that calcium hydroxide liners did not increase the clinical success of carious lesion treatments.

One systematic review compared the survival of **combinations of adhesive and restorative materials** placed in load-bearing posterior cavitated lesions with each other in permanent and primary teeth. There was low-quality evidence that **conventional and bulk-fill resin composites** seem suitable for load-bearing lesions. Of note, bulk fills had not all been placed in bulk but in increments in included studies, which possibly improved this material class's performance. There was low-quality evidence that **etch-and-rinse adhesives** might be preferable in permanent teeth, whereas **self-etch** systems might be suitable for primary teeth.

We identified 11 systematic reviews on the topic of restoration processes or techniques for cavitated caries in primary and permanent teeth. Nine reviews evaluated methods of caries removal using one of the following methods: **chemomechanical methods, laser, or air- and/or sono-abrasion**, and compared the chosen method with the **traditional drill method**. Six of the nine reviews evaluating chemomechanical methods of caries removal measured procedure time, and all six reported that the alternative treatment methods had longer treatment times compared with the conventional method. The quality of evidence for the six reviews varied: two were based on moderate-quality evidence, one was based on low-quality evidence, and three were based on very low-quality evidence. Only three reviews (one based on moderate-quality evidence, one based on low-quality evidence, and one based on very low-quality evidence) examined the adequacy of caries removal using alternative methods compared with the conventional method, and all three reported no difference. One review estimated bacterial counts in the excavated cavity and reported reductions with all methods (very low-quality evidence). Seven reviews (two based on moderate-quality evidence, three based on low-quality evidence, and two based on very low-quality evidence) evaluated pain, and six of the seven reviews reported that the pain experienced was lower for the alternative methods compared with the conventional method. However, the pain experience during atraumatic restorative treatment and conventional drilling was reported to be similar. Four reviews (one based on moderate-quality evidence, one based on low-quality evidence, and two based on very low-quality evidence) documented the need for anaesthesia and reported a reduced need among patients receiving the alternative method of caries removal. One review (based on moderate-quality evidence) reported better experiences for patients receiving the alternative caries removal method. Two reviews (one based on low-quality evidence and one based on very low-quality evidence) reported that laser treatment was associated with an unpleasant smell and taste, which therefore reduced acceptance. The remaining review (based on very low-quality evidence) reported no difference between intervention and comparator with respect to fear and anxiety. Five reviews (one based on moderate-quality evidence, two based on low-quality evidence, and two based on very low-quality evidence) reported similar restoration survival rates. However, one of these reviews reported lower survival for high-viscosity glass ionomer cement placed using atraumatic restorative treatment compared with placement using the conventional method. One review, based on very low-quality evidence, measured microleakage, and reported that the incidence of microleakage was not statistically significantly higher after employing a traditional bur compared with the Er,Cr:YSGG laser on either the dentine or the whole marginal line.

Two reviews compared the effects of **different stages and amounts of caries** removal in primary and permanent teeth, and one review found no statistically significant differences with respect to risk of complications, pain, time required for excavation, and/or number of bacteria remaining. However, these findings were based on low-quality evidence. Another review compared **selective and stepwise removal** with complete (non-selective) caries removal and found significantly reduced pulpal exposure and no significant differences with respect to risk of post-operative pulpal symptoms, overall failure, and caries progression; however, the authors reported that the evidence was inconclusive and low quality.

Conclusions

There are effective alternatives to manage early carious lesions and avoid invasive restorative procedures through non-invasive (fluoride-based and other products), and microinvasive (sealants and resin infiltration) treatments. In addition, there are viable alternatives to using dental amalgam to restore cavitated caries through either direct or indirect restorations. The promising direct alternates to dental amalgam are resin-modified glass ionomer cement, compomers, and different composite resins. In addition, there are promising indirect alternates including ceramics and resin composites. Crowns

fabricated from gold, metal ceramic, all ceramic, or zirconia are other alternates in specific situations. Some of these alternatives are not quite as successful as dental amalgam and some are more successful. There are also improved support materials and techniques available to dentists to enhance the effectiveness of interventions and acceptability of their treatments. The techniques include methods (such as selective caries removal as well as chemical or laser caries removal methods) to maximise the conservation of dentine and reduce pain experienced by the patient. The support materials include using the most appropriate adhesive for the specific intervention.

The evidence base provided in this overview of reviews is based on the best available reviews; however, the description 'best' indicates a body of research that is of mainly low-quality evidence, and the quality of research requires improvement particularly in the design and conduct of RCTs. It is important to note that when we say that the evidence for an intervention is low or very low quality, it generally means that the research base upon which to evaluate the intervention is inadequate, rather than that the intervention itself is inadequate. There were few cases where the intervention was not useful (such as dental liners to support restorations of permanent teeth and silver-reinforced glass ionomer cement as a restorative material). The research base in Ireland for evidence on restoration materials, techniques and processes could be improved by partnerships with international state-funded trial networks to increase the power of the trials and by employing best practice research techniques to minimise bias. In addition, Ireland could add to restoration survival data by establishing data collection at sentinel sites.

Another important issue raised in several clinical guideline documents was the consideration, during the decision-making process, of patients' expectations, clinicians' expertise, and the individual clinical scenario alongside the best evidence. In addition, informed consent by patients was a requirement.

1 Introduction

1.1 Mercury regulation

The European Union (EU) has introduced Regulation (EU) 2017/852² to implement the 2013 United Nations Minamata Convention on Mercury,³ which aims to protect human health and the environment from mercury pollution. This is an environmental regulation rather than a health regulation, and its purpose is to reduce the amount of mercury used in many industries and professional sectors, including dentistry (Article 10).² The use of mercury in dental amalgam is a key component of this agreement and has a fundamental impact on the delivery of dental restorative treatments in Ireland. This EU Regulation is binding in its entirety and is directly applicable in all Member States. The then Department of Communications, Climate Action and Environment published S.I. No. 533/2018 – European Union (Mercury) Regulations 2018⁴ to implement Regulation (EU) 2017/852² and the United Nations Minamata Convention on Mercury.³ Since July 2018, the EU Regulation has introduced a ban on amalgam use in dentistry in children under 15 years of age, and in pregnant or breastfeeding women, except where deemed strictly necessary by the dental practitioner based on the specific medical needs of the patient.²

1.2 National plan for mercury

In July 2019, the Irish Government submitted a plan to the EU² detailing Ireland's approaches to the phase-down of amalgam up to 2030.⁵ In general, the advice and guidance in Ireland to support the public and dental professionals in choosing alternatives to dental amalgam is not sufficiently clear for either dental professionals or members of the public. Of note, the type of alternative restoration will differ according to tooth type (permanent or deciduous, function, and position), age cohort (child, adolescent, adult, or older person), for pregnant and breastfeeding women, place of care, and if dealing with allergies. Evidence for alternative approaches to dental amalgam restorations is crucial, while clarity on the advantages and disadvantages of alternative materials is not easily available. This evidence base will be used to inform the implementation of National Oral Health Policy 'packages of care' and to help inform clinical guidelines for dentists working in Ireland. The emphasis in the Policy is on prevention, minimal intervention, and, where possible, the use of a non-amalgam material for restorations (fillings). The preferred option in both children and adults will always be to select an alternative to dental amalgam for environmental reasons. In order to enable this, a variety of other choices needs to be available. Currently, the discussion substantially focuses on a binary decision between resin composite and dental amalgam, which may encourage excessive use of amalgam intervention because of its low cost, ease of use, and longevity in comparison with resin composites. Exploration of a variety of options is essential in order to ensure that this excessive use of dental amalgam does not inadvertently occur, and to give both dental professionals and the public greater choice.

1.3 Ireland's oral health policy

*Smile agus Sláinte: National Oral Health Policy*⁶ was published in April 2019 and considers Regulation (EU) 2017/852 on mercury² by providing for the phase-down of dental amalgam, in line with international policy on reducing mercury use. Two population cohorts – children under 15 years of age and pregnant and breastfeeding women – are initial target groups for the phase-down of amalgam use. The reduction in the use of traditional filling materials requires an overt change in the delivery of oral healthcare services, which to date have emphasised dental amalgam restoration as a central intervention. However, reduction in the use of dental amalgam involves more than just the substitution of amalgam fillings with

an alternative restorative material in the future; prevention, non-intervention, and minimal intervention will be the preferred actions. Both prevention and intervention in children and younger age groups are based on packages of oral healthcare which include prevention and some intervention. Keeping the younger age groups amalgam-free will be especially important, since once dental amalgam is used, it means that mercury will be released into the environment when that filling is replaced over the course of the individual's lifetime. The concern is that without clear guidance, the exceptions will be more common than should be expected. Adults will also have packages of care for preventive items through the new National Oral Health Policy. For adults who need more than one filling, additional dental restorations will be paid for through a fee-per-item system.

Smile agus Sláinte: National Oral Health Policy supports the phase-down of dental amalgam through its emphasis on health promotion, prevention, and the expansion of primary oral healthcare services for members of the public of all ages.⁶ In parallel, it supports education and broadening skills for dental professionals. The services proposed in the Policy will support the preferred use of alternative materials and restorations, rather than dental amalgam, throughout the life course. In the new system of service provision, amalgam will only be used in exceptional cases. Other means of enabling mercury reduction in dentistry will also be considered, such as supporting appropriate waste disposal mechanisms in dental practices.

1.4 Dental Council code of practice on amalgam

The Dental Council, established under the provisions of the Dentists Act, 1985,⁷ promotes high standards of professional education and professional conduct among dentists practising in Ireland. With respect to Regulation (EU) 2017/852² and amalgam, the Dental Council has drawn up a code of practice booklet for the dentistry profession.⁸ It quotes Article 10 of the Regulation and outlines that dentists must comply with this article:

“Article 10 of the regulations sets out the parameters for the use of dental amalgam:

1. From 1 January 2019, dental amalgam shall only be used in pre-dosed encapsulated form. The use of mercury in bulk form by dental practitioners shall be prohibited.
2. From 1 July 2018, dental amalgam shall not be used for dental treatment of deciduous teeth, of children under 15 years, and of pregnant or breastfeeding women, except when deemed strictly necessary by the dental practitioner based on the specific medical needs of the patient.
3. From 1 July 2019, each Member State set out a national plan concerning the measures it intends to implement to phase down the use of dental amalgam. Member States' national plans are publicly available on the Internet.
4. From 1 January 2019, operators of dental facilities in which dental amalgam is used or dental amalgam fillings or teeth containing such fillings are removed shall ensure that their facilities are equipped with amalgam separators for the retention and collection of amalgam particles, including those contained in used water.
5. Capsules and amalgam separators complying with European standards, or with other national or international standards that provide an equivalent level of quality and retention, shall be presumed to satisfy the requirements set out in paragraphs 1 and 4.
6. Dental practitioners shall ensure that their amalgam waste, including amalgam residues, particles and fillings, and teeth, or parts thereof, contaminated by dental amalgam, is handled and collected by an authorised waste management establishment or undertaking.”^{8(p2-3)}

The code of practice goes on to state that dentists “have an ethical as well as a legal obligation to comply with these regulations”, that dentists will “ensure that valid and explicit consent has been obtained to treat a patient using dental amalgam if it is being used for the treatment of deciduous teeth in children under the age of 15, or of [permanent teeth] in pregnant or breastfeeding women”, and, in the cases where it is clinically necessary to use dental amalgam, that dentists will be required to “record the specific clinical reasons why”.^{8(p3)}

1.5 Caries

Walsh *et al.*⁹ summarised existing literature and reports that tooth mineral is lost and gained in a continuous process of demineralisation and remineralisation. Caries (dental decay) is a disease of the hard tissues of the teeth caused by an imbalance in this process over time, where there is net demineralisation of tooth structure by organic acids formed from the interactions between cariogenic bacteria in dental plaque and fermentable carbohydrates (mainly sugars). The dental caries formation process is influenced by the susceptibility of the tooth surface, the bacterial profile, the quantity of saliva, and the presence of fluoride, which promotes remineralisation and inhibits demineralisation of the tooth structure.

Caries in permanent teeth was the most prevalent condition among all those evaluated in the Global Burden of Disease Study 2016, affecting 2.4 billion people; the estimated number of cases with caries in deciduous teeth was 486 million children worldwide.¹⁰

1.6 Dental amalgam

Dental amalgams are metallic alloys.¹¹ For more than 150 years, they have been predictable and inexpensive restorative materials for addressing permanent damage caused by caries.¹¹ Amalgams have been used for posterior coronal restorations¹¹ and were previously used for root-end fillings during surgical root canal procedures, although this report does not focus on this now outdated indication.¹² Their use and success rate have been documented, and amalgams are readily available, inexpensive, and easy to handle.¹¹

However, dental amalgams are declining in use in dentistry, mainly due to their unaesthetic appearance and environmental concerns about their mercury content,¹¹ despite some noted advantages, especially with respect to secondary caries risk.¹³

1.6.1 Dental amalgam compared with resin composites

Dental amalgam and resin composites are the most commonly used products for restoring permanent molar and premolar cavities.¹¹ Dental amalgam has been gradually replaced by resin composite as the preferred material to restore posterior teeth. This is thought to have been due to concerns relating to amalgam’s lack of adhesive properties (which are required for defect-oriented, minimally invasive preparation), its aesthetics, and its potential environmental effects.¹⁴ Composite materials have been increasingly used for the restoration of posterior teeth since the late 1980s as a tooth-coloured alternative to amalgam.¹⁴ They may be placed using either direct or indirect techniques.¹⁴ Surveys and retrospective studies developed by groups of practice-based researchers differ in their conclusions about which was the material most commonly used in restorative dentistry in 2010.¹¹ Some indicate that the usage of composite resins has surpassed the usage of amalgam over the since around 2010, but amalgam is still widely used in many countries.¹⁵ Based on the market volume and materials sold, it is estimated that more than 520 million direct dental restorations are placed around the world each year.¹⁵ Of these, about 261 million are estimated to be direct composite resin restorations, followed by 236 million dental amalgam restorations.¹⁵ However, the geographical distribution of these types of restorations

demonstrates strong regional differences. By 2012, in Scandinavian countries, almost no dental amalgam restorations were placed, whereas in central Europe and the United States of America (USA), more teeth were restored with composite than with amalgam, and in southern and eastern European countries, more teeth were restored with amalgam than with composite.¹⁵ Dental amalgam use has been found to be decreasing in Australia, the United Kingdom (UK), and the USA.¹⁴ There is low-quality evidence that dental amalgam posterior restorations in permanent teeth last longer than composite resin restorations and are associated with a lower incidence of secondary caries.^{11 13}

1.6.2 Need to replace the use of dental amalgam

As already mentioned, Regulation (EU) 2017/852 has introduced a ban on dental amalgam use in children under 15 years of age, and in pregnant or breastfeeding women, except where deemed strictly necessary by the dental practitioner based on the specific medical needs of the patient.² *Smile agus Sláinte: National Oral Health Policy*⁶ takes Regulation (EU) 2017/852 on mercury² into account by providing for the phase-down of dental amalgam, in line with international policy on reducing mercury use. *Smile agus Sláinte: National Oral Health Policy*⁶ supports the phase-down of amalgam.⁶ In parallel, it supports education and broadening skills for dental professionals. The services proposed in the Policy support the preferred use of alternative materials and restorations, rather than dental amalgam, throughout the life course. Section 1.7 covers non-mercury-containing options for replacing dental amalgam for occlusoproximal posterior restorations, and Section 1.8 presents options to deal with cervical restorations.

1.7 Non-mercury restoration materials

Due to time limitations, this section of the Introduction relies heavily on the background presented in high-quality peer-reviewed systematic reviews, such as Cochrane reviews.

1.7.1 Resin composites

Rasines Alcaraz *et al.* report that dental resin composites are considered the most likely substitutes or alternatives to dental amalgam for posterior coronal restorations and were developed in response to people's demands for tooth-coloured restorations.¹¹ Dental resin composites are particle-reinforced resins that require specially manufactured adhesives and procedures in order to ensure that the resins adhere to the surface of the tooth.¹¹ The indications for the use of resin composites have expanded from the anterior restoration of tooth crowns to posterior restorations, and even to stress-bearing posterior restorations, as dental amalgam substitutes or dental amalgam alternatives.¹¹ Early composite restorations in posterior teeth were more likely to fail compared with dental amalgam restorations.¹¹ This was due to polymerisation shrinkage, rapid loss of anatomic form, poor wear, and poor colour stability.¹⁴ They also lacked stiffness and adhesion to tooth structures.¹⁴ The higher sensitivity in the manufacturing technique, in addition to limitations such as contraction during polymerisation and the possibility of forming marginal gaps, can be critical factors for the durability of composites.¹³ More recently, improved resin composites, techniques, and instruments have been developed in order to address these limitations.¹⁴ The field of composite dental restoratives has also continued to advance resin formulation, filler loading and modification, and curing methodologies and mechanisms in recent years.¹¹ A systematic review by Downer, published in 1999, examined literature on the longevity of routine dental restorations in permanent teeth.¹⁶ This review found that the most frequently reported median survival time (between 6 and 10 years) of resin composite restorations was comparable with that of dental amalgam restorations. Studies have also shown a low annual failure average for composite resins in occlusal and occlusoproximal restorations, varying from 1% to 3%.¹³ The principal reasons for failure of restorations placed using contemporaneously available direct resin composites were secondary caries, fractures, marginal deterioration, discolouration, and wear.¹⁴ Factors that influence clinical outcomes of resin

composite restorations are the type of resin composite itself, the number of composite layers, the type of enamel or dentine conditioning, the operative technique used to bevel the enamel, and absolute compared with relative isolation.¹⁵

1.7.2 Glass ionomers

Glass ionomers have been used in dentistry since their invention in 1969.¹⁷ The terminology of this type of compound varies, and while the term 'glass ionomer' is widely used and accepted, the name used by the International Organization for Standardization is 'glass polyalkenoate cement'.¹⁸ Glass ionomers are versatile compounds, useful as restoration, sealing, lining, or luting materials. Glass ionomers are known as acid-base reaction cements and are composed of a polymeric water-soluble acid, a basic ion-leachable glass (usually a fluoroaluminosilicate), and water.¹⁸ They have three main clinical applications: as luting and bonding cements, as restorative cements, and as lining or base cements.¹⁸ They may also be used as fissure sealants and in atraumatic restorative treatment.

The true bonding between materials and dentine/enamel permits wide use of Class V restorations that have high adhesion requirements. Glass ionomers are also used for Class II and Class III restorations in deciduous or primary teeth, for luting of crowns, and as bases or liners.

The powder of a number of glass components mixes with the liquid of polyalkenoic acid to form a paste; then the acid-base reaction starts, and stiffens the paste. Initially, the mechanical properties did not suit the clinical requirements adequately, but over time, these have gradually improved.

One of the most significant advantages of glass ionomers is the sustained release of fluoride. This release is known to increase under acidic conditions. Glass ionomers can also buffer acidity, which may reduce tooth decay.¹⁸ The adhesive properties of glass ionomers are another considerable advantage of these compounds. The use of polyacrylic acid or similar polymers is believed to promote adhesion. This adhesion increases retentions of the cement within the tooth and also minimises leakage at the margins, preventing access of bacteria to the area under the cement restoration.¹⁸

In a recent systematic review, Mustafa *et al.* assessed the evidence in laboratory-based studies regarding the transition between glass ionomer cement and the tooth, described as an 'interphase'.¹⁹ The authors found that the glass ionomer-tooth interphase qualities develop over time. They reported that good attachment is evident even when surface preparation is compromised, and the attachment area is resistant to acidic dissolution. The primary studies reviewed by Mustafa *et al.* found that the glass ionomer-tooth interphases were generally intact at the time of the research. The authors reported that glass ionomer "bonds to the tooth structure and forms an acid-resistant attachment zone that might enhance caries inhibition. Due to fluoride release and ease of use, glass ionomer cement provides a cost-effective treatment, ideal for low-income or high-caries populations."^{19(p2180)}

A major limitation of glass ionomers is their mechanical properties – mainly flexural strength and wear resistance. Newer types of glass ionomers are resin-modified glass ionomers, which were introduced in the 1980s. These are a combination of conventional glass ionomer cement and light-cure resins to improve some characteristics of conventional glass ionomers such as increased strength, lower solubility, and less sensitivity to moisture. However, the fluoride release of resin-modified glass ionomer is lower, and the biocompatibility is not as good as that of conventional glass ionomers. The latest generation of glass ionomers employ has resin coating to overcome the limited wear resistance and increase their flexural strength. Moreover, these glass ionomers, also described as glass hybrids, have an improved cross-linking of particles and acids and generally improved mechanical properties. Notably, even these materials do not reach the mechanical strength of composites.²⁰⁻²²

The attention to glass ionomer restorative materials for primary dentition has increased;²³ for example, in Sweden, glass ionomer restoration using hand instruments is the first choice for primary dentition.²⁴ Its advantages are greater maintenance of the intact tooth structure and good adhesion to the remaining tooth structure compared with composite resin. These characteristics allow the use of more conservative restorative techniques, limiting the cavity preparation mainly to the removal of decayed tissue, thereby preserving the intact tooth structures.²³ Dias *et al.*²³ concluded that the materials analysed (glass ionomer cement and composite resin) both had similar clinical performance in terms of the percentage of failures, marginal adaptation, marginal discolouration, and anatomical form in Class II restorations in primary teeth. However, regarding the occurrence of secondary carious lesions, glass ionomer cement had superior clinical performance, and this effect was more evident for the resin-modified glass ionomer cement used with rubber dam isolation.

There are reviews demonstrating the suitability of glass ionomers to restore cervical cavities in permanent dentition. A 2016 network meta-analysis, which compared a range of composites and glass ionomers, found that resin-enforced glass ionomers have preferable survival and success rates for cervical lesions based on low-quality evidence.²⁵ This finding was confirmed by a 2018 systematic review which compared the retention and colour match of glass ionomer cement restorations with resin-based composite restorations in non-carious cervical lesions in the permanent teeth of adults, and there is moderate-quality evidence that glass ionomer restorations showed superior retention rates compared with resin-based composite restorations at follow-ups of between 1 and 5 years.²⁶

Data on permanent teeth and the usage of glass ionomers for cavities in posterior load-bearing teeth are sparse. A recent systematic review and meta-analysis did not identify any randomised controlled trials (RCTs) fitting their inclusion criteria of glass ionomers for cavities in posterior load-bearing teeth. Another review included two studies, one comparing glass ionomers and composites and one comparing glass ionomers against dental amalgam, and based on network meta-analysis, found that glass ionomers showed a lower probability of being the best material for this purpose due to their higher risk of failure overtime.²⁷

1.7.3 Compomers

Dental compomers are used in dentistry as restorative materials. They were introduced in the early 1990s as a hybrid of two other dental materials: dental composites and glass ionomer cement. Compomers are poly-acid modified resin composite which has an ion-leachable glass filler and monomers which will polymerize to create a matrix onto which some acidic side chains are grafted. A composite resin that has polyacid, fluoride-releasing groups added.¹ They are used for restorations in low-stress-bearing areas.

1.7.4 Indirect restorations

In dentistry, inlays, onlays, and overlays are a form of indirect restoration. This means that they are made outside of the mouth by a dental technician as a single, solid piece that fits the specific size and shape of the cavity. They are usually fabricated using gold or ceramics. Due to its tooth-like colour, ceramic provides better aesthetic value for the patient. In more recent years, inlays and onlays have increasingly been made out of ceramic materials. The restoration is then cemented in place in the mouth. This is an alternative to a direct restoration. New chairside devices allow for inlays and onlays to be created and fitted within a single appointment.

Inlays, onlays, and overlays are used in molars or premolars when the tooth has experienced too much damage to support a basic filling, but not so much damage that a crown is necessary. The key comparison between them is the amount and part of the tooth that they cover. An inlay will incorporate the pits and fissures of a tooth, mainly encompassing the chewing surface between the cusps. An onlay will involve

one or more cusps being covered, whereas an overlay covers all cusps. If all cusps and the entire surface of the tooth are covered, this is then known as a crown.

There is adequate evidence that ceramic onlays on posterior teeth, acting as an indirect dental restorative material, provide acceptable survival rates over both the medium (2–5 years and 5–9 years) and long term (6 years or over and 10 or over years), and all ceramic materials tested performed well.^{28,29} There is very low-quality evidence that ceramic inlays and overlays produce acceptably high restoration survival rates of more than 90% over a 10-year follow-up period.²⁹

1.7.5 Atraumatic restorative treatment

Atraumatic restorative treatment, according to Dorri *et al.*, “is a minimally invasive approach, which involves removal of decayed tissue using hand instruments alone, usually without use of anaesthesia and electrically driven equipment, and restoration of the dental cavity with an adhesive material such as glass ionomer cement, composite resins, resin-modified glass ionomer cement or compomers”.^{30(p6)} Atraumatic restorative treatment is used in many low- and middle-income countries, as well as in the Netherlands, Sweden, the UK, and the USA.²⁴

1.8 Interventions to prevent early non-cavitated carious lesions from becoming cavitated caries

Interventions to prevent cavitated caries are also legitimate supportive strategies to phase down or phase out the use of dental amalgam under Ireland’s recently published *Smile agus Sláinte: National Oral Health Policy*.⁶ Such interventions fall under two main groups: first, the prevention of cavitated caries (dietary control; antibacterial strategies, including oral hygiene; fluoride technologies; and pit-and-fissure sealants), and second, the early treatment of conditions that signal early dental carious lesions (with symptoms of demineralisation such as white spots; that is, non-cavitated carious lesions). In this review, we cover the management of non-cavitated lesions (lesion arrest, secondary prevention), but not primary prevention interventions.

1.8.1 Early treatment (secondary prevention)

Dental research has led to the development of a number of secondary prevention strategies that are based on the prompt treatment of disease at an early stage and include measures which arrest and/or reverse the caries formation process after initiation of clinical signs.³¹ Various treatment options are available to treat early carious lesions in permanent teeth.³²

2 Research questions

The purpose of this review is to provide evidence to assist with the development of clinical guidelines on the management of non-cavitated and cavitated caries for Ireland. Cavitated caries include caries in both crown and root. This review updates an existing evidence review³³ that was completed in 2019, but for a different purpose – that is, to inform policy deliberations on alternatives to dental amalgam to treat caries. It was decided to update the 2019 review after discussion with the Health and Safety Directorate at the Department of Health.

The research questions are:

1. What is the evidence from systematic reviews regarding strategies to manage non-cavitated* or cavitated† carious lesions in primary teeth?
2. What is the evidence from systematic reviews regarding strategies to manage non-cavitated* or cavitated† carious lesions in permanent teeth?
3. What is the evidence from systematic reviews regarding strategies to manage non-cavitated* or cavitated† carious lesions in mixed dentition?

*Non-cavitated caries include demineralisation and white spot lesions.

†Cavitated caries include caries in both crown and root, as far as a pulp cap.

The population of interest is patients with non-cavitated and/or cavitated caries in their primary, mixed, or permanent dentition. The interventions of interest are non-invasive, microinvasive, minimally invasive, and invasive treatments. The comparator is to each other, dental amalgam (for cavitated carious lesions), or a placebo. We nominated a wide set of a priori outcomes to measure in this overview of reviews at the outset, based on examples of the main outcomes from our previous review by Keane et al. Please see Table 1 for a list of specific outcomes. There are date limits from 2010 to 12 December 2020. The language limitations are a necessity, as none of the researchers speaks another language fluently. The date and language limits are dealt with in more detail in detail in Section 3.8.2.

3 Methods

3.1 Review design

This evidence review used the overview of reviews or umbrella review design to examine the evidence base for interventions to arrest or manage dental carious lesions in humans. The purpose of this review is to inform the development of clinical guidelines for dental practice in Ireland. The use of overviews of reviews in the development of clinical guidelines is currently being investigated by Lunny *et al.*³⁴ An overview of reviews synthesises findings from multiple systematic reviews, enabling reviewers to examine the evidence reported on the effectiveness of interventions and identify whether the evidence base is consistent or contradictory. Undertaking an overview of reviews requires a systematic and transparent plan that follows a set of methods consistent with the approach adopted in a systematic review. According to McKenzie and Brennan, “Overviews involve the systematic retrieval and identification, assessment of bias, and integration of results from multiple systematic reviews. They have the potential to confer many benefits and opportunities. Notably, overviews capitalise on previous research synthesis efforts bringing efficiencies that may lessen research waste.”^{35(p1)}

3.2 Definition of an overview of reviews

There have been numerous attempts to define the parameters of an overview of reviews. However, a recent consensus has emerged to agree on the key elements. The definition of ‘overview of reviews’ as cited in Gates *et al.*,³⁶ and developed by the Cochrane Collaboration,³⁷ comprises five key elements:

1. Contains a clearly formulated objective designed to answer a specific research question, typically about a healthcare intervention.
2. Intends to search for and include only systematic reviews (with or without meta-analyses).
3. Uses explicit and reproducible methods to identify multiple systematic reviews that meet the overview of reviews’ inclusion criteria and assess the quality/risk of bias of these systematic reviews.
4. Intends to collect, analyse, and present the following data from included systematic reviews: descriptive characteristics of the systematic reviews and their included primary studies; risk of bias of primary studies; quantitative outcome data; and certainty of evidence for predefined, clinically important outcomes.
5. Discusses findings as they relate to the purpose, objective(s), and specific research question(s) of the overview of reviews, including: a summary of main results, overall completeness and applicability of evidence, quality of evidence, potential biases in the overview process, and agreements and/or disagreements with other studies and/or reviews.

3.3 Why we chose an overview of reviews design

We chose an overview of reviews design as we knew from our previous review by Keane *et al.*³³ that the literature is heavily populated with systematic reviews that are relevant to our research questions. We also knew that the reviews that are available vary in design and conduct and include both Cochrane and non-Cochrane reviews. Therefore, it would be inappropriate to undertake an original systematic review while ignoring the existing evidence base in systematic reviews. Both Cochrane and non-Cochrane reviews on the management of caries include primary studies with high or unclear risk of bias and the non-Cochrane reviews cover a wider range of interventions. According to Aromataris *et al.*, “if current, multiple, good-quality, systematic reviews exist about a given topic or question, any reviewer should

reconsider the need to conduct yet another review addressing the same issue. Rather, these [existing reviews] may be the basis to conduct an umbrella review [overview of reviews] and summarize or synthesize the findings of systematic reviews already available.”^{38(p365)}

3.4 Overview of reviews as an evidence-based product for policy-makers

Overviews of reviews have become feasible mainly due to the increasing volume of systematic reviews that are published on a regular basis in many subject areas. It is estimated that between 11 and 22 systematic reviews are produced daily; according to Aromataris *et al.*, “The number of systematic reviews published to accommodate the demands of evidence-informed decision-making has increased markedly over the past two decades. One estimate [in 2015] suggests that 11 systematic reviews are published every day”.^{39(p133)} And according to Hunt *et al.*, it was estimated that around 22 new systematic reviews were published every day in 2018.⁴⁰ We chose an overview of reviews design as we knew from our previous review by Keane *et al.*³³ that the literature is heavily populated with systematic reviews that are relevant to our research questions.

According to Gates *et al.*, “It is estimated that 8,000 systematic reviews were published in 2014, more than three times the annual publication rate recorded in 2004. Around the turn of the century overviews of reviews, which compile data from multiple systematic reviews, emerged to deal with the growing volume of published systematic reviews. By taking advantage of existing syntheses, overviews of reviews can create efficiencies and answer broader research questions”.^{36(p2)}

Systematic reviews are a recognised evidence-based product that are often used by policy-makers in their deliberations and decision-making. As systematic reviews are the exclusive unit of analysis in overviews of reviews, this means that overviews of reviews can contribute to evidence-based policy-making. According to Aromataris *et al.*, “With the ever-increasing number of systematic reviews published daily, umbrella reviews [overviews of reviews] have a clear role in evidence-based healthcare and evidence-informed decision-making”.^{39(p139)}

3.5 What type of outputs can we derive from an overview of reviews?

According to Aromataris *et al.*, “The principal reason for the conduct of an umbrella review [overview of reviews] is to summarize the evidence from multiple research syntheses...Umbrella reviews are conducted to provide an overall examination of the body of information that is available for a given topic, and to compare and contrast the results of published systematic reviews. The wide picture obtainable from the conduct of an umbrella review is ideal to highlight whether the evidence base around a topic is consistent or contradictory, and to explore the reasons for the findings. Furthermore, an umbrella review allows ready assessment of whether review authors addressing similar review questions independently observe similar results and arrive at generally similar conclusions”.^{39(p133)}

3.5.1 Purpose of overviews of reviews

According to McKenzie and Brennan, “The purposes of overviews include (but are not limited to) mapping the available evidence, examining the effects of different interventions for the same condition or population, examining the effects of the same intervention for different conditions or populations (also referred to as multiple-indication reviews) or examining reasons for discordance of findings and conclusions across reviews. Overviews are more suited to some purposes than others, and careful consideration of whether they are the appropriate type of review (overview of systematic reviews or systematic review of primary studies) is required.”^{35(p1)}

3.6 Our overall methodological approach to undertaking this work

Our approach to undertaking this overview of reviews was based on the recent guidance published by Gates *et al.*, which includes important pointers on anticipating and addressing the main challenges posed for reviewers when embarking on an overview of reviews.³⁶ The recent guidance by Gates *et al.* builds on and updates previous guidance.⁴¹ The updated guidance is based on an analysis of 77 guidance documents, which were developed and used by 34 research groups with extensive experience in designing and implementing overviews of reviews.³⁶ The analysis of the 77 guidance documents is supplemented by an examination of additional literature to provide a comprehensive overview of relevant issues pertaining to the conduct of overviews of reviews.³⁶

Each step taken in designing and implementing an overview of reviews requires careful consideration by reviewers and decisions taken should be, to a large extent, based on evidence, as such decisions will ultimately affect the credibility of the findings. According to McKenzie and Brennan, “The choice of methods used in overviews may affect the trustworthiness of the findings, coverage of the evidence, and usability and usefulness of the overview, amongst other outcomes. Decisions as to which methods to use are best informed by methods research, along with theoretical considerations.”^{35(p2–3)}

3.6.1 Should an overview include non-Cochrane systematic reviews?

According to Gates *et al.*, “The decision about whether to only include Cochrane systematic reviews or to also include non-Cochrane systematic reviews can be a balance between ensuring quality and coverage of all-important interventions. Although some non-Cochrane reviews can be of poorer methodological quality and have less detailed reporting, Cochrane reviews alone may not cover all relevant interventions or be adequately up to date. If authors choose to include both Cochrane and non-Cochrane systematic reviews, it is likely that they will need to deal with primary study overlap. However, this may occur even if only Cochrane systematic reviews are included.”^{36(p15)}

We have used the decision tool developed by Pollock *et al.* to inform our decisions on including reviews in our overview of reviews.⁴² This decision tool contains four questions to assist in our decision-making:

1. Do Cochrane systematic reviews likely examine all relevant intervention comparisons and available data?
2. Do the Cochrane systematic reviews overlap?
3. Do the non-Cochrane systematic reviews overlap?
4. Are researchers prepared and able to avoid double-counting outcome data from overlapping systematic reviews, by ensuring that each primary study’s outcome data are extracted from overlapping systematic reviews only once?

Guidance is provided to help researchers answer each question, and empirical evidence is provided regarding the advantages, disadvantages, and potential trade-offs of the different inclusion decisions.

We have included both Cochrane and non-Cochrane reviews, as we know from our previous review³³ that both types of review evaluate relevant interventions. In addition, a review undertaken by the Scottish Dental Clinical Effectiveness Programme, which has been used to develop dental guidelines in the UK, also included both Cochrane and non-Cochrane reviews.⁴³

According to Pollock *et al.*, it is important to decide prior to undertaking an overview of reviews “what action will be taken if there are overlapping reviews (reviews containing the same trials)”.^{44(p16)}

To address the issue of overlapping reviews in this overview of reviews, we calculated the corrected covered area as a measure of overlap. This approach is recommended by Pieper *et al.*, who contend that “all producers of overviews should analyse the overlaps and report their analysis. Reporting should be done even if the amount of overlap is small and unlikely to have an impact on the conclusion. Otherwise, consumers will not know whether there is no meaningful overlap or if the authors simply did not [take] account of it. Consequently, overlaps should be reported by default.”^{45(p374–375)}

3.7 Eligibility criteria

Our eligibility criteria are presented in Table 1. The population of interest is patients with non-cavitated and/or cavitated caries in their primary, mixed, or permanent dentition. The interventions of interest are non-invasive, microinvasive, minimally invasive, and invasive treatments. The comparator is to each other, dental amalgam (for cavitated carious lesions), or a placebo. We nominated a wide set of a priori outcomes to measure in this overview of reviews at the outset, based on examples of the main outcomes from our previous review by Keane *et al.* There are date limits from 2010 to 12 December 2020 based on JBI guidance for umbrella reviews [overview of reviews].⁴⁶ The language limitations are a necessity, as none of the researchers speaks another language fluently. The date and language limits are dealt with in more detail in detail in Section 3.8.2.

Table 1 Eligibility criteria for systematic reviews to be included in synthesis of caries management

Criterion	Inclusion	Exclusion
Population	Primary, mixed, and permanent teeth in humans with cavitated and non-cavitated primary carious lesions. Non-carious Class V lesions were included in this review.	Non-carious lesions in primary dentition Secondary lesions In vitro, in situ, and ex vivo studies
Intervention	Non-invasive interventions or agents, such as sodium fluoride (NaF), stannous fluoride, silver diamine fluoride, acidulated phosphate fluoride, difluorsilane, ammonium fluoride, silver nitrate, polyols, chlorhexidine, calcium phosphate, amorphous calcium phosphate (ACP), casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), nano-hydroxyapatite, tricalcium phosphate, prebiotics and/or 1.5% arginine, probiotics, lasers, and xylitol. Microinvasive or minimally invasive interventions, such as resin infiltration and sealants for non-cavitated caries. Direct restorations using a material that is not amalgam, such as compomer, composite, conventional glass ionomer resin, resin-modified glass ionomer, etc., as well as associated techniques (atraumatic restorative technique, laser, or drill and fill) and adhesive strategies (such as liners and adhesives). Indirect restorations, such as inlays, onlays, overlays, or crowns. Subsequent full and partial restoration to replace amalgam. Chip and fractures of previously amalgam-restored teeth.	No orthodontics No endodontics No pulp-based interventions No root canal treatments or retrograde fillings
Comparator	Amalgam, or other (one of the above), or a placebo	
Outcomes	Lesion arrested or remineralised, restoration quality: adaptation, discolouration, anatomical form, secondary caries, fracture, retention, pain, durability, longevity or survival over time, failure, and success. Costs, both immediate and over time.	
Study design	Systematic review of RCTs and/or cohort studies (longitudinal comparative studies). All included reviews must have assessed and reported either the risk of bias or quality of the included primary studies.	Studies that are not systematic reviews. Systematic reviews of descriptive epidemiological studies and case-control studies. Systematic reviews based on searches of one bibliographic database only. Systematic reviews that have not completed and presented a quality assessment of, or risk of bias assessment of, their primary studies.
Dates	2010 to 12 December 2020	Pre-2010
Language	English	Non-English
Methods	At least two bibliographic electronic databases searched.	Fewer than two bibliographic electronic databases searched.

3.8 Information searches

3.8.1 Identifying research evidence

The planned structure of the literature search for this review included a comprehensive search of databases and other resources to identify as many of the relevant published syntheses on the review topic as possible, and following the selection of a set of papers that met the inclusion criteria, reference, citation, and protocol 'chasing' were done to attempt to identify any further relevant research. The references from the previous review by Keane *et al.* on a related topic were also screened.³³ A final database search at the end of the process was planned in the protocol,⁴⁷ but was not carried out due to time concerns. The literature search strategies were constructed, and the searches were carried out by an information specialist (CL) and were informally peer reviewed by a second information specialist (AF).

The type of evidence required to carry out an umbrella review or overview of reviews is limited to evidence syntheses only.⁴⁶ Therefore, the type of evidence sources used for the information search focused on likely sources for systematic reviews and meta-analyses, as well as standard clinical evidence resources. The range of sources used was as wide as possible given the time frame of the project, and included systematic review databases/registries, clinical databases, systematic review summary resources, preprint and open access resources.

Aromataris *et al.* suggest that a broad search is appropriate for an umbrella review or overview of reviews. This was the approach used for this search.⁴⁶ The aim of the search strategy used was to maximise sensitivity (capturing as much relevant material as possible, at the cost of including irrelevant material) over specificity (all material captured is relevant, at the cost of excluding some relevant material). The use of a multiple-stage screening process filtered out the irrelevant material (title/abstract and full-text screening) in preference to using a more tightly focused search process that might inadvertently exclude relevant papers.

While the work of Cooper *et al.*⁴⁸ has shown that the current guidance lacks a specific definition of a comprehensive search, it was intended that using searches of databases, grey literature sources, and reference/citation/protocol chasing would satisfy the general requirements of a comprehensive literature search.

3.8.2 Literature search concepts

The two basic concepts around which the search was constructed were dental restoration and caries. The population of interest in this case was patients of any age or demographic with caries. The intervention was any intervention for dental restoration of caries and the comparator was any alternative intervention. Outcomes were not included as a search concept, as the outcomes were not strictly defined in the population, intervention, comparator, and outcomes (PICO) parameters, and more importantly for the search process, outcomes may not necessarily be included in the database-indexed fields of an article and may not be 'findable'. The *Cochrane Handbook for Systematic Reviews of Interventions* guidance notes that it may not be helpful to include all aspects of a research question in a search strategy and recommends basing the search on population (or condition), intervention, and study design.⁴⁹

These two main concepts were combined to capture papers referring to any interventions, materials, or strategies used to manage non-cavitated or cavitated carious lesions in primary, mixed, and permanent dentition (Figure 1). A further broad concept was included in the search – the concept of evidence syntheses, including systematic reviews, syntheses of empirical research, and meta-analyses.

While comparisons of dental amalgam with alternative restoration materials were of interest in this review, the researchers were aware from previous work³³ that few direct comparisons of dental amalgam

and an alternative material had been published. A search constructed to find papers directly comparing amalgam with another material for restorations (for example, Boolean search structure: ((Caries) AND ((Amalgam) AND (Alternative materials)))) would not capture works investigating alternatives to amalgam which did not mention amalgam specifically.

Search limits in the form of date and publication type limits were included. As noted in the guidance by Aromataris,⁴⁶ the term 'review' encompasses many types of review.⁵⁰ Not all of these types of review will be able to contribute meaningful data to the analysis for this review, and only reviews that satisfied the adapted AMSTAR 2 (A MeaSurement Tool to Assess systematic Reviews, version 2) (see Appendix E) could be included in the final analysis. However, the search strategy aimed to capture any type of review or synthesis, which would then be screened in close detail in the review screening process, rather than only to search for 'systematic reviews' – a term that is occasionally omitted in actual systematic reviews and that is also used in reviews that are, based on their methods and results, clearly not systematic.

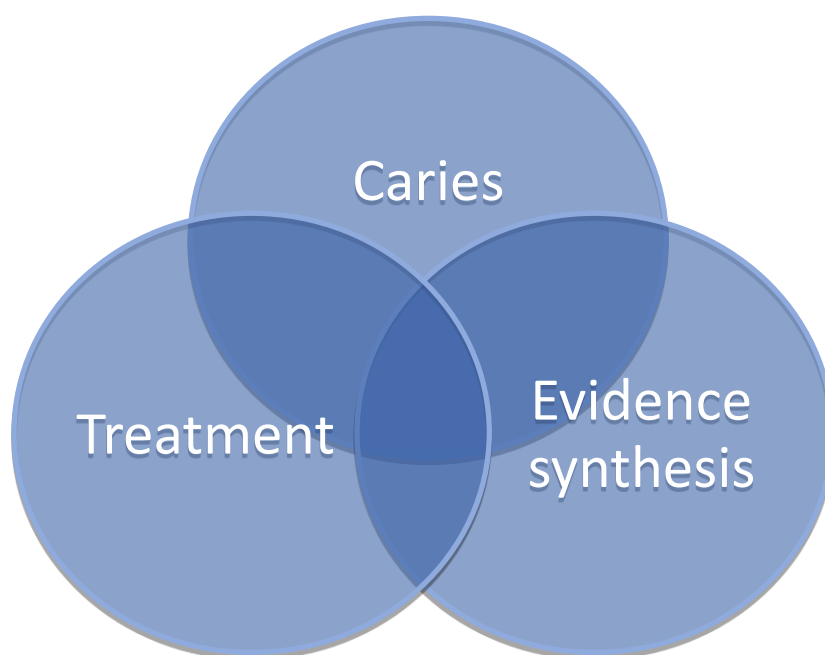


Figure 1 Graphic representation of search concepts

3.8.3 Information sources

A range of information resources was used, including clinical databases, systematic review/health technology assessment resources, search engines, open access and preprint repositories, and relevant website searches.

The literature searches for this review included searches of three clinical databases (Ovid MEDLINE, EBSCO CINAHL, and Scielo), 11 systematic review resources (the Cochrane Library, Epistemonikos, the Campbell Collaboration, Agency for Healthcare Research and Quality (AHRQ) Systematic Review Data Repository, Database of Abstracts of Reviews of Effects, Database of Promoting Health Effectiveness Reviews (DoPHER), JBI Evidence Synthesis, International Health Technology Assessment database, Health Evidence, Social Systems Evidence, and Health Systems Evidence), three search engines (Google, Google Scholar, and DuckDuckGo), and six resources for open access/grey/preprint material (Core.ac.uk, OSF.io, Research Square, medRxiv, bioRxiv, and website searches). PROSPERO, the International Prospective Register of Systematic Reviews, was searched as a part of the supplemental searches to retrieve and follow up relevant protocols for reviews.

Search engines were used as a supplemental resource to capture papers that were not indexed in databases, or where the information relevant to this review was not included in the indexed/searchable fields. The use of search engines in literature searching is not without problems, but the searches were documented as well as possible.⁵¹⁻⁵³ However, the transparency and reproducibility of searches in search engines is limited by the structure of the search engines themselves, with changing web content and unknown or changing algorithms.⁴⁹

Relevant websites were searched, including national and international dentistry sites. While reviews were not typically hosted on these sites, new publications in relevant fields were frequently noted or referenced and any mention of a relevant review was followed up.

A complete list of the resources used, with dates of searches and numbers of results, is set out in Appendix A.

3.8.4 Search terminology

The initial search strategy was constructed in Ovid MEDLINE. For both dental restoration and for caries, synonyms, related relevant terms, and thesaurus/controlled vocabulary terms were sourced using PubMed PubReMiner,⁵⁴ websites of dental organisations, known relevant articles, and the National Library of Medicine Medical Subject Headings (MeSH) Browser.⁵⁵ Search terms included controlled vocabulary (MeSH terms) and 'free' terms or keywords. Boolean operators, adjacencies, and wildcards were used to focus the search terms. After testing the search terms using MEDLINE searches, the two sets of search terms (dental restoration and caries) were combined. The Canadian Health Libraries Association systematic review filter was added to the search⁵⁶ and a date limit of 2010–2020 was also added, as per the Joanna Briggs Institute guidance on date limits for overview of reviews. This search strategy is described in Appendix A.

Regarding publication date cut-offs, the Joanna Briggs Institute guidance for overviews of reviews suggests that a cut-off date of research published in the past 10 years would be likely to capture primary research published within approximately the previous 30 years.⁴⁶ In line with this guidance, a date range of 2010–2020 for published research was selected and implemented in the literature search. For some searches, such as the Ovid MEDLINE search, the earlier date was set as 2009 to include e-publications and 'online first' or 'early cite' papers and to allow for some variation in indexing of papers as preprints.

The search strategy was translated for use in the other databases (such as EBSCO CINAHL) and resources, and these strategies are also described in Appendix A. For some evidence sources used, complex Boolean searching was not possible and abbreviated searches were used instead.

The search concepts were combined using Boolean operators in those databases where this facility was available (for example, MEDLINE and CINAHL). The broad structure of the search was as follows: (((All terms for caries) AND (All terms for dental restorations)) AND (Systematic review filter)) AND (date limit)).

For information resources not providing Boolean search options, the terms were combined in the search facility provided, where available. In some cases, abbreviated searches were carried out where more structured searches were not possible.

Some terminology that has been included in the search would appear to be redundant – it may duplicate other terms used or may return no results. The inclusion was deliberate and is designed to show that terms were included and returned no results, rather than that they were omitted, and no knowledge is gained as to whether they would have been useful or not.⁵⁷ These terms may also play a role in future iterations of this or related work.

The strategy was informally peer reviewed by a second information specialist (AF) using the headings of the PRESS checklist (outlined in the PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Explanation and Elaboration document).⁵⁸

3.8.5 Search limiters

The eligibility criteria for the review include a specification that papers in languages other than English will not be examined. However, a language limit was not used within the search strategy. The databases used primarily index English-language research, and the addition of a language filter was not considered necessary as the expected low number of non-English papers would be more accurately filtered out in the screening process. Appendix B lists the non-English language papers that may contain relevant research. While it is beyond the scope of this review to include this material, it must be acknowledged that a considerable body of work exists on this topic outside the English-language research.

No limits were included for subject ages – the review includes research on adults, children, and non-specified ages. Further examination of dentition type (primary, permanent, and mixed) would be established more precisely in the data extraction and synthesis process rather than by the search process.

3.8.6 Supplemental searching

3.8.6.1 Protocol/reference/citation searching

There is evidence that reference searching is likely to be useful: a previous Cochrane review examined the use of reference searching for systematic reviews and found positive results, but these were derived from weak study designs.⁵⁹ Reference and citation searching of studies retrieved from initial searches has been incorporated into the search plans of previous Health Research Board (HRB) reviews, with variable but generally positive results. The process is not without drawbacks (time-consuming, may result in a bubble effect where the same authors reference and cite each other, differences in ‘retrievability’ of citations between journal articles with digital object identifier numbers used in cross reference and reports where citations are not so easily identified) but can be useful, especially to retrieve newly published articles, including those not indexed in databases (e.g. reports, grey literature) or articles indexed in databases other than the ones used in the search strategy.

The process of reference/citation/protocol searching was carried out between 9 and 24 February 2021 by the information specialist (CL). The references and known citations for each paper included from the full text were recorded in an EndNote library. Between 9 and 12 February 2021, the database/research data platform Dimensions.ai was used to extract article citations and references.⁶⁰ Relevant protocols which had been identified in the screening process were tracked to find the related systematic reviews where these had been published. A brief search in PROSPERO was used to identify other protocols that may be relevant. The results of these searches were deduplicated. Preliminary screening was carried out by the information specialist (CL) using the inclusion/exclusion criteria from the earlier screening process, and the pre-screened results were then examined by the researchers (MK and JL). From this stage of searching, 12 results were included in the synthesis.

3.8.6.2 Screening of a previous review

A previous review by Keane *et al.* was published in 2020.³³ The references from this review were screened by an experienced researcher (JL) for potential reviews that would match the inclusion criteria of the present overview of reviews. From those references, one review was found that was relevant to this overview of reviews and that had not previously been included from database searches or other supplemental methods. In total, 107 papers (describing 106 systematic reviews) from the database searches and supplemental searching were included in the review synthesis.

3.8.7 Search dates

Initial database searches were carried out between 5 and 12 December 2020. Supplemental searches, comprising protocol follow-up and reference and citation searching of reviews selected from the screening process, were carried out between 9 and 24 February 2021. Search results up to 12 December 2020 were included in the review, and any reviews citing the 104 reviews selected from the full-text screening process were included.

3.8.8 Search data management

Search results for initial (n=3,712) and supplemental searches (n=13) were recorded in EndNote X9.3 and deduplicated in this software. Results were exported to EPPI-Reviewer 4 for screening.⁶¹ This software package was used to manage the screening process. Screening was carried out in several steps.⁶¹ Data extraction was carried out in Microsoft Word as described in Section 3.11.

3.9 Screening

3.9.1 Screening stage 1: title and abstract screening

The initial results (n=3,712) were double screened on title and abstract by two teams of two screeners (team 1 JL and AF, Team 2 MK and CL) using the eligibility criteria outlined in Table 1, based on the review PICO. The reasons for exclusion included study type, intervention, topic, language, and duplication. Citations and abstracts were also retained if not enough information was available to decide on inclusion. All four reviewers read the title and abstracts that two reviewers had disagreed on during screening and came to a consensus conclusion on inclusion and exclusion. After the initial title/abstract screening, 539 papers remained, and each of these were screened again by title and abstract by all four screeners using the insights gained from the initial screening round. After the second round of title/abstract screening, 195 papers were carried forward to the full-text screening stage.

3.9.2 Screening stage 2: full-text screening

The full texts of the 195 citations retained from the title and abstract stage of screening were sourced. These full-text articles were then independently screened by two researchers (MK, JL). The results of this full-text screening were then re-analysed to ensure that they fully matched the pre-agreed inclusion criteria. In addition, a decision was taken at this stage to expand the exclusion criteria to exclude papers that did not match three domains of the adapted AMSTAR 2 criteria: inadequate or absent PICO, inadequate or absent literature search, and inadequate or absent risk of bias assessment/quality assessment. Any disagreements on inclusion or exclusion were discussed with CL and resolved.

Papers which did not include a PICO description were excluded. The PICO did not have to be formally presented as a table, but the population/patient group, interventions and comparators, and the outcomes relating to these aspects did have to be described.

Papers which did not include an adequate literature search were excluded at this stage also. The concept of an 'adequate' literature search is not set and given the variety of resources appropriate for different topics, deciding what comprises an adequate or comprehensive search is not an exact science.⁴⁸ In this case, an adequate search was taken to include, at a minimum, at least two databases used, an attempt to describe the search (varying from including a few keywords to a complete listing of all search strategies used), and at least one supplemental search method used. The supplemental search methods could include use of trial registries, hand-searching of journals, reference and citation chasing, contact with subject experts, contact with authors, etc. As searches of the Cochrane Library include searches of both Cochrane systematic reviews and the Cochrane Central Register of Controlled Trials (CENTRAL) (which

derives records from, among other resources, ClinicalTrials.gov and the World Health Organization's (WHO's) International Clinical Trials Registry Platform), the use of the Cochrane Library in searches was technically allowed as a supplemental search as well as a database search. It must be stressed that these three literature factors were used as parameters to establish minimum standards for searches to include systematic reviews in this overview of systematic reviews. These factors should not be taken to indicate a comprehensive search, which should have included and reported the elements described in the extended version of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-S) reporting guide for reporting literature searches.⁶²

The quality assessment exclusion criteria were that a quality assessment must be completed using a standard tool and that the result of the quality assessment for each primary study must be reported by each domain on the selected tool. Reviews that used study design checklists were excluded. Reviews that did not provide a quality assessment for each included primary study were also excluded.

At all stages of the review, records which were published in a language other than English, but which appeared relevant (e.g. from English-language abstracts or keywords), were retained in order to recognise that the English-language literature is not the total extent of the research on this topic, even though the time frame of the project did not allow for a full examination of the non-English language body of evidence (see Appendix B). Details of the papers excluded at full-text screening and data extraction are included in Appendix C.

3.9.3 Screening stage 3: screening during data extraction

Papers meeting the eligibility criteria were forwarded to the data extraction stage of the review process (n=104). During extraction, 10 papers were removed, as they were found not to fit the criteria of the review, leaving 94 systematic review papers. The papers and reasons for exclusion are given in Appendix C; reasons for exclusion included incorrect study design (including reviews that were not fully realised systematic reviews), excluded topic or intervention (for example, papers that initially appeared to investigate caries but were in fact about post-orthodontic white spot lesions), or exclusion on inadequate risk of bias/quality assessment, as per the adjusted AMSTAR 2 criteria.

3.9.4 Screening stage 4: supplemental search results

As noted in Section 3.8.6 (supplemental searching), the results of supplemental searches (reference and citation chasing and protocol follow-up) were screened by the information specialist (CL). Initial screening was done by title and abstract. The results of this screening were then compared with the database search results. Any of these results arising from supplemental screening which had also occurred in the database search results, and had been screened previously, were excluded. A final set of potential results was examined by the two researchers and 12 systematic review papers were included.

The references of a previous review by Keane *et al.*³³ were screened by an experienced researcher (JL) using the same inclusion and exclusion criteria as for the other screening stages. From these references, one review was found that had not been discovered by the other search methods of the present review.

The flow of information for the review is illustrated in the PRISMA flow chart in Figure 2.

3.10 Assessing the quality of included systematic reviews

According to Gates *et al.*, "There is no agreement on which tool might be best to use (e.g. AMSTAR, AMSTAR 2, or ROBIS) to assess methodological quality, or how to use them in the context of an overview of reviews. It can be difficult to distinguish between methodological quality and the quality of reporting, and poor reporting in the systematic reviews can make assessment challenging. Authors often have

difficulty interpreting and coming to agreement with assessments on the available tools. It is unclear whether authors should assess systematic reviews in their entirety or only the components that are relevant to the overview question, and what to do with systematic reviews that include other embedded reviews. When overview quality is being used to choose between overlapping systematic reviews, authors need to be careful to not exclude potentially relevant information. When overlapping systematic reviews use different methodologies and come to discordant conclusions, it can be hard to tell whether their methods are appropriate.”^{36(p15)}

We have used the AMSTAR 2 instrument to assess the quality and risk of bias of all reviews that meet our inclusion criteria. The AMSTAR 2 instrument is relatively new, having been developed by Shea *et al.*⁶³ to build on the original AMSTAR instrument, which was designed to appraise systematic reviews that exclusively included RCTs. The development of AMSTAR 2 was undertaken to enable appraisal of systematic reviews of randomised and non-randomised studies of healthcare interventions. We chose to use AMSTAR 2³³ rather than AMSTAR, as based on our previous review experience, we know that relevant reviews contain both randomised and non-randomised studies; therefore, the AMSTAR 2 instrument is an appropriate assessment tool to use in our overview.

The AMSTAR 2 instrument contains 16 items to appraise the quality and the risk of bias in systematic reviews (Appendix E).⁶³ Two reviewers (JL and MK) used AMSTAR 2 to assess each full-text review. There were few differences between reviewers, and these were resolved through discussion and consensus.

We piloted AMSTAR 2 on four systematic reviews. Following this, we made several adjustments to the tool (see Appendix E). We have retained the text of the questions as per AMSTAR 2. We adjusted the scoring of Question 1, Question 4, and Question 8 to provide consistent and more stringent judgement of the parameter being scrutinised. We added text to further explain what is required when assessing Questions 1–4, Questions 8 and 9, and Questions 11–16, so as to ensure that all reviewers were making decisions using the same parameters.

According to Shea *et al.*, “responses to AMSTAR 2 items *should not* be used to derive an overall score. We accept that an overall score may disguise critical weaknesses that should diminish confidence in the results of a systematic review, and we recommend that users adopt the rating process based on identification of critical domains, or some variation based on these principles.”^{63(p6)} Shea *et al.* suggest seven critical domains in the AMSTAR 2 instrument that reviewers may use to assess critical flaws in systematic reviews (Table 2).⁶³ However, reviewers can change some of these domains depending on the focus of their overview. We excluded reviews that did not meet the criteria in domain 2 and that did not include a full assessment of bias so that we could assess domain 4. We selected four rather than seven critical domains. We highlight the critical items that were selected by us and the original AMSTAR 2 authors, and we justify domain exclusions and inclusions in Appendix E, Table 1. We did not consider domain 1 and domain 3 as critical domains. Shea *et al.* recommended assigning a confidence rating to each review using the schema shown in Table 3.⁶³ The HRB authors assigned a rating of overall confidence to each review.

Table 2 Candidate critical domains in AMSTAR 2

	Critical domain	HRB selection
1	Protocol registered before commencement of the review	Not selected as a critical domain
2	Adequacy of the literature search	Considered in full-text exclusion criteria
3	Justification for excluding individual studies	Not selected as a critical domain
4	Risk of bias from individual studies included in the review	Considered in full-text exclusion criteria
5	Appropriateness of meta-analytical methods	As per Shea <i>et al.</i> , 2017
6	Consideration of the risk of bias when interpreting the results of the review	As per Shea <i>et al.</i> , 2017
7	Assessment of presence and likely impact of publication bias	As per Shea <i>et al.</i> , 2017
	Controlled for unclear or high risk of bias in the analysis	Added by HRB authors

Table 3 Rating overall confidence in the results of the review

Score	Criteria
High	No or one non-critical weakness: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest.
Moderate	More than one non-critical weakness*: the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review.
Low	One critical flaw with or without non-critical weaknesses: the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest.
Critically low	More than one critical flaw with or without non-critical weaknesses: the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.
*Downgrade	*Multiple non-critical weaknesses may diminish confidence in the review, and it may be appropriate to move the overall appraisal down from moderate to low confidence.

Source: Shea *et al.*, 2017⁶³

3.11 Collecting and presenting data on descriptive characteristics of included systematic reviews (and primary studies)

According to Gates *et al.*, 2020, “Overview authors are challenged with data extraction at two levels, first the level of the systematic review, and then potentially the level of the primary study. When relying on the reporting of the included systematic reviews, authors may struggle when these are poorly reported and missing important details. Overview authors need to carefully check systematic reviews for errors in data extraction, as these errors will lead to errors in the overview of reviews. They also need to decide how to deal with systematic reviews with missing information of relevance to the overview of reviews. Going back to the primary studies can be time consuming, but not doing so can lead to a loss of information.”^{36(p15)}

Furthermore, Gates *et al.* stated that “Descriptive characteristics of the systematic reviews should be presented narratively and/or in a table in adequate detail to support each systematic review’s inclusion in the overview of reviews and inform the applicability of their findings”.^{36(p12)}

We have used the Joanna Briggs Institute data extraction form for systematic reviews and research syntheses to extract data on the descriptive characteristics and findings of each included systematic

review; one review author undertook the data extraction for each paper and a second author validated it (Appendix F). We extracted and documented in tabular format the following data from each included review: citation details; objectives of the review; participants; setting; interventions and comparators; search information; primary study date range; number of primary studies; study design; risk of bias tool used; risk of bias assessment, including publication bias; analysis methods; outcomes assessed; results by outcome(s); and commentary on bias, heterogeneity, and use of GRADE (Grading of Recommendations, Assessment, Development and Evaluations) (Appendices G–J). We then summarised the main findings (Appendix K) and applied GRADE to each of these outcomes (see Section 3.13). We have extracted the PICO characteristics and other study characteristics to demonstrate to the reader why each study was included (Appendix N).

3.12 Collecting, analysing, and presenting outcome data

According to Gates *et al.*, “Many difficulties may arise when collecting, analysing, and presenting findings at the overview level, because of inconsistency in methodology and reporting of findings across systematic reviews. For example, the included systematic reviews and their primary studies may use heterogeneous outcome measures. Additionally, the included systematic reviews may be incompletely reported, or may not report data on subgroups of interest. Overlapping systematic reviews might present discordant results or present similar data in different ways (e.g. different summary measures), and it can be complex and time-consuming to ensure that data from single studies are not over-represented. Interpretation of measures of overlap (e.g. matrices and corrected covered area) can be a challenge when the number of primary studies is large. To perform analyses of interest, overview authors might need to go back to individual studies or concede that the available information is incomplete. It may not always be appropriate or feasible to conduct meta-analyses in overviews, and network meta-analyses and informal indirect comparisons are usually not appropriate. However, narrative synthesis can become complex and open to bias if not adequately described. There is a concern that synthesis errors at the systematic review level could result in errors at the overview level.”^{36(p16)}

We nominated a wide set of a priori outcomes to measure in this overview of reviews. Our reasoning for this decision was based on our previous work on reviewing the dental literature, where we found that systematic reviews tend to focus on different outcomes in the management of carious lesions in human teeth.³³ In addition, the ultimate objective of our work is to identify the different interventions that tackle the same condition (i.e. carious lesions) but that are assessed using different outcomes. As characterised by Lunny *et al.*, “Overviews of systematic reviews synthesise the results of multiple systematic reviews. Overviews are typically broader in scope than systematic reviews and may examine different interventions for the same condition, the same intervention for different conditions, or the same intervention for the same condition but focusing on different outcomes.”^{64(p2)}

We were interested in interventions that arrest carious lesions, remineralise carious lesions, and restore carious lesions. These were usually measured as survival or failure and assessed using generally accepted clinical performance guidelines (Table 4).⁶⁵⁻⁶⁷ Patient experience of an intervention or technique was also an important outcome. We are also concerned about techniques or support materials that are used with such interventions. Additionally, we were interested in adverse events resulting from the use of a particular intervention, support material, or technique. We have used a narrative summary and synthesis to analyse the data, taking account of any discordant findings, highlighting overlaps, and assigning a quality of evidence. With respect to costs, we noted that systematic reviews did not include costings.

Table 4 Outcomes for treatment of caries

Type of caries treatments	Outcome	Means of measurement
Non-cavitated carious lesion treatment	Remineralisation	Radiological observation
	Arrest/progression	Clinical observation (visual-tactile assessment, e.g. using a scoring system such as the International Caries Detection and Assessment System (ICDAS). The ICDAS codes for coronal caries range from 0 to 6 depending on the severity of the lesion, with 0 denoting sound and 6 denoting extensive distinct cavitation with visible dentine. The Nyvad criteria are also used.) Radiological observation
	Need for retreatment	Yes or No
	Costs	Direct and indirect (opportunity) costs
	Adverse events	For example, nausea, fluorosis, vomiting, allergic reactions, staining, tooth sensitivity, soft tissue trauma, or raised levels of chemicals
	Subjective outcomes	Patient-reported outcomes
Cavitated carious lesion treatment	Marginal adaptation, marginal discolouration, anatomical form, surface roughness, and secondary caries. Retention and tooth integrity. Restoration success and survival at pre-specified time points (longevity). Restoration failure rate per year (annual failure rate).	The original Ryge criteria categories were colour match, cavo-surface marginal discolouration, anatomic form, marginal adaptation, and caries. The criteria were modified and were known as the Modified Ryge criteria or modified United States Public Health Service (USPHS) criteria (see subtable below). ⁶⁷
		Subtable: Modified USPHS criteria
		1. Retention
		6. Contact surfaces
		2. Marginal adaptation (marginal integrity)
		7. Recurrent caries
		8. Tooth integrity
		3. Marginal discolouration
		9. Post-operative sensitivity
		4. Loss of anatomical form
		10. Patient complaints
		5. Surface texture
		11. Patient satisfaction
		Source: FDI World Dental Federation criteria 2010. ⁶⁷
	Need to re-treat	Repair or replace
	Cost	Direct and indirect (opportunity) costs
	Adverse events	For example, nausea, fluorosis, vomiting, allergic reactions, staining, tooth sensitivity, or soft tissue trauma
	Subjective outcomes	Patient-reported outcomes

3.13 Assessing the quality of evidence of outcome data

The GRADE approach is the framework recommended by the Cochrane Collaboration to facilitate the transparent rating of quality of evidence for systematic reviews.^{68,69} The GRADE approach has been traditionally applied to rating the quality of evidence in single systematic reviews, primarily reviews that include a meta-analysis. However, the application of GRADE in systematic reviews can vary due to the

subjective reasoning of reviewers and this can have implications for the overviews of reviews that rely on the GRADE assessments reported in single systematic reviews. In addition, there appears to be a lack of consensus on how best to apply a GRADE assessment when undertaking an overview of reviews. The following extract from Gates *et al.* elaborates these difficulties quite succinctly.³⁶

According to Gates *et al.*, “It may not be possible or appropriate to simply extract existing GRADE appraisals from the included systematic reviews. The reviews might not include GRADE appraisals for the outcomes or populations of interest, or be missing details on each of the GRADE considerations. Different systematic reviews with the same studies that have made different decisions about handling data (analysis) and appraising study quality may come to different GRADE conclusions, especially related to the study limitations, consistency, and precision domains. Different researchers rating systematic reviews could come to different conclusions, due to the subjectivity of the GRADE approach. If re-doing the GRADE for each systematic review, authors are likely to encounter difficulty due to an absence of guidance on how to apply GRADE in the context of an overview, incomplete reporting at the level of the systematic review, and a lack of familiarity with the contributing primary studies.”^{36(p16)}

Nonetheless, despite these difficulties elaborated in the literature, we believe it is important to assess the quality of evidence in an overview of reviews that may be used to inform the development of clinical guidelines. And to some extent, we find some agreement with our views. For example, according to Pollock *et al.*, “An essential part of an overview is the assessment of the quality of evidence arising from the included reviews, and the [GRADE] approach is the framework recommended by the *Cochrane Handbook [for Systematic Reviews of Interventions]* to facilitate transparent rating of quality of evidence.”^{70(p1)}

However, to reiterate an earlier point, there is a lack of clear guidance on how to best apply GRADE within the conduct of an overview of reviews. For example, Pollock *et al.*, who sought to apply GRADE in an overview of Cochrane reviews, reported that “Within our overview, reviewers found that current GRADE guidance was insufficient to make reliable and consistent judgements”.^{70(p1)}

In an effort to overcome some of these challenges to applying GRADE in an overview of reviews, Pollock *et al.*⁷⁰ developed an algorithm to grade the quality of evidence in their overview based on four key criteria:

1. The number of participants within the analysis, considering imprecision based on sample size and confidence intervals around outcomes of interest.
2. The risk of bias within the trials contributing participants to the analysis with respect to randomisation and blinding of outcome ascertainment.
3. The statistical inconsistency or heterogeneity within the analysis, as determined by I².
4. The methodological quality of the review as determined by the selection of critical factors from the quality assessment tool. These can be adapted depending on the subject matter of the review.

In addition, the HRB added the study design, as we included randomised trials, non-randomised trials, and cohort studies.

Gionfriddo⁷¹ and Murad *et al.*⁷² have criticised the work of Pollock *et al.*⁷⁰ for modifying the GRADE assessment into an algorithm comprising a concrete set of rules for assessing overviews of reviews. To paraphrase the critique elaborated by Gionfriddo⁷¹ and Murad *et al.*,⁷² the algorithm developed by Pollock and colleagues undermines the subjective strength of the existing GRADE assessment for

systematic reviews as the rating of the quality of evidence is, by necessity, a matter of judgement. In response, Pollock *et al.* offered the following reply:

“We postulate that what has prompted much of the debate from both Gionfriddo (2016) and Murad *et al.* (2016) is the extent to which the purpose of rating evidence differs in an overview, as compared to guidelines or recommendations [for single systematic reviews]. Although Cochrane recommends use of GRADE to rate quality of evidence within overviews and while our algorithm built on our understanding of the GRADE approach, perhaps our algorithmic approach has moved so far from GRADE that it can no longer be labelled as such. However, regardless of name, our methodological approach has potentially got implications for assessment of quality of evidence within future overviews, with advantages relating to efficiency, reproducibility, and transparency.”^{73(p240)}

We concur with the views expressed by Pollock *et al.* regarding the advantages of using their algorithm to rate the quality of evidence in an overview of reviews relating to efficiency, reproducibility, and transparency. We believe that these properties are important in the context of assessing evidence to inform clinical guidelines, as the application of this algorithm can help to reduce subjectivity. In addition, other teams of reviewers undertaking overviews of reviews have applied the modified GRADE algorithm to assess the quality of evidence with little difficulty reported in the application of the algorithm.^{74,75}

Following on from these considerations elaborated above, we decided to use the algorithm developed by Pollock *et al.*⁷⁰ to rate the quality of evidence in our overview of reviews on strategies to manage dental caries in humans. We will apply the modified GRADE algorithm to all reviews that meet our inclusion criteria.

According to the guidance provided in Pollock *et al.*⁷⁰ on this algorithm, each review starts with a ranking of high certainty and is downgraded one level for serious methodological concerns (sample size between 100 and 199 participants; high risk of bias in randomisation and blinding for >75% of included studies; high heterogeneity ($I^2 > 75\%$); and ‘No’ on one of these AMSTAR 2 items: a priori research design, comprehensive literature search, duplicate study selection, or duplicate study abstraction) or two levels for very serious concerns (sample size <100 participants and ‘No’ on two or more of these AMSTAR 2 items: a priori research design, comprehensive literature search, duplicate study selection, or duplicate study abstraction). We have also added study design to the mix, as some of our included reviews were not based on RCTs.

We are examining a variety of different interventions to manage non-cavitated and cavitated caries, some of which will permit blinding for the operator and others which will not permit blinding. For example, when operators are comparing dental amalgam restorations with composite restorations, the operator or assessor cannot be blinded, while when comparing the caries prevention or arrest capabilities of different non-invasive strategies with each other, the operator and assessor can be blinded. This means that where blinding cannot be instituted, the highest level of evidence is most likely moderate. Cochrane Oral Health Group systematic reviews appear to retain blinding in their assessment of bias and grading, so for consistency we should also do so, as otherwise the clinical guidelines for dental operators in Ireland will not be compatible with international guidelines.

We have modified the criteria to rate the overall quality of each systematic review. We have made this change because the critical factors nominated by Pollock *et al.* were based on their use of the original AMSTAR. As we are using AMSTAR 2 to assess the methodological quality of each review, the four criteria we have nominated are more appropriate to our assessment than the four nominated by Pollock *et al.*⁷⁰ Our nominated critical factors are:

1. Appropriateness of meta-analytical methods (item 11)
2. If meta-analysis was performed, did the review authors assess the potential impact of risk of bias in individual studies on the results of the meta-analysis (through sensitivity analysis) or other evidence synthesis? (item 12)
3. Consideration of risk of bias when interpreting the results of the review (item 13, covered as a separate item in Pollock *et al.* 2016 criteria), and
4. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? (item 14, covered as a separate item in the Pollock *et al.* (2016b) criteria).⁷⁰

In addition, we included study design and applied a downgrade for the inclusion of non-randomised or cohort studies. These modifications are modest and do not materially change the principles of the formula nominated by Pollock *et al.*⁷⁰ A full elaboration of how we intend to apply the GRADE algorithm is outlined in the formula shown in Table 5.

Table 5 Formula for applying a GRADE level of evidence to overviews of reviews and number of downgrades determined using the algorithm

Area assessed	Imprecision (based on sample size)	Risk of bias (trial quality)	Inconsistency	Risk of bias (review quality)	Study design
Method of assessment	Adequate number of participants included in the pooled analysis.	Example used and reported in Pollock <i>et al.</i> (2016). ⁷⁰ Proportion of study participants included in the pooled analysis from primary trials or studies judged to have low risk of bias for randomisation and observer blinding.	Statistical heterogeneity or inconsistency, assessed by, for example, I ² or Q statistic.	Example used and reported in Pollock <i>et al.</i> (2016). ⁷⁰ Responses to AMSTAR 2 questions 1–4 (covering a priori research design, search characteristics, independence of study selection, and data extraction). We are using four items or questions from the quality assessment that we assess as critical criteria, and these are 11, 12, 13 and 14 (see bulleted list in paragraph above and Appendix E).	Randomised study design chosen.

Area assessed	Imprecision (based on sample size)	Risk of bias (trial quality)	Inconsistency	Risk of bias (review quality)	Study design
No downgrade (no serious limitations)	≥200 and included design effect for clustering (that there is more than one restoration per participant).	≥75% of study participants included in the pooled analysis from primary trials or studies judged to have low risk of bias for randomisation and observer blinding.	$I^2 \leq 75\%$	4/4 are all “yes” (i.e. low risk of bias)	Randomised study design chosen.
Downgrade 1 level (serious limitations)	100–199	<75% of study participants included in the pooled analysis from primary trials or studies judged to have low risk of bias for randomisation and observer blinding.	$I^2 > 75\%$	3/4 are “yes” and 1 is “partial” or “no” on AMSTAR 2	Non-randomised or cohort study design chosen.
Downgrade 2 levels (very serious limitations)	1–99			2 or lower/4 are “yes” and remainder are “partial” or “no” on AMSTAR 2	
Notes		If risk of bias for individual trials is not reported within the review, we can assume that less than 75% of participants had low risk of bias.	If only one trial contributed to analysis, no downgrade; if I^2 not reported, assumed to be greater than 75%.		

Source: Adapted from Pollock *et al.*, 2016⁷⁰

The number of downgrades that can be applied using the modified GRADE algorithm range from zero to seven, and these ratings can be applied within the standard GRADE level of evidence.⁷⁰ Table 6 presents an illustration of the frame for the final output we will present to report the rating of levels of evidence in our overview of reviews.

Table 6 Application of GRADE level of evidence to overview of reviews from number of downgrades determined using the algorithm

GRADE level of evidence	Number of downgrades (derived from objective assessment)
High	Score awarded when 0 downgrades are applied
Moderate	Score awarded when 1 or 2 downgrades are applied
Low	Score awarded when 3 or 4 downgrades are applied
Very low	Score awarded when 5 or lower downgrades are applied

Source: Pollock *et al.*, 2016⁷⁰

Some worked examples are: one downgrade due to inconsistency or because heterogeneity is not or cannot be dealt with appropriately; two downgrades due to imprecision based on inadequate sample size within pooled analysis; or two downgrades because the review quality or risk of bias is one of the critical domains. We have selected review quality as a critical domain.

3.14 Interpreting outcome data and drawing conclusions

According to Gates *et al.*, “Interpreting data and drawing conclusions can be difficult. The included systematic reviews (and their included primary studies) may use heterogeneous outcome measures which can limit the ability to draw useful conclusions. Procedural variation at the systematic review and overview levels (e.g. study selection, data extraction) can lead to different conclusions from the same set of data. It can be difficult to provide interpretation of analyses of multiple interventions; multiple comparisons from different systematic reviews that are included in the same overview; discordant results and conclusions across the included systematic reviews. Authors need to consider the methods used in the systematic reviews and overview and decide how best to highlight uncertainties and gaps that remain”.^{36(p16)}

To address these challenges highlighted by Gates *et al.*, we have used the Six-Item Framework proposed by Lunny *et al.* (2018) to synthesise our interpretations and conclusions.⁷⁶ Therefore, we :

1. Elaborate our interpretation and conclusions
2. Summarise the results from included systematic reviews
3. Assess and report on heterogeneity
4. Assess and report on risk of bias in the reviews
5. Assess and report on overlap of primary studies included in more than one systematic review, and
6. Assess and report on discordant results, interpretations, and conclusions among the included reviews.

Pieper *et al.* developed a methodology to assess overlap of primary studies between systematic reviews of the same interventions.⁴⁵ They title this measure the ‘corrected covered area’. We used this measure for each effectiveness outcome. in order to assess the overlap of the same primary studies across more than one systematic review. Pieper et al. grade the percentage overlap as low (0–5%), moderate (6–10%), high (11–15%), and very high (16% or over) so that reviewers can categorise the overlap.⁴⁵

4 Findings

4.1 Results of searching and screening

The completion of this review is based on a protocol registered with PROSPERO under the reference number CRD42021235201.⁴⁷

Our searches identified 5,099 records, of which 1,387 were duplicates, leaving 3,712 records for title and abstract screening. We excluded 3,517 records on title and abstract screening, leaving 195 records for full-text screening. Following full-text screening, we excluded 91 records, leaving 104 records for extraction. Extraction involved a more detailed reading of the papers and we excluded a further 10 papers at this stage, leaving 94 papers. We included an additional 13 articles from supplemental searches, resulting in 107 papers (describing 106 systematic reviews) being included in our overview of reviews. Two included papers described one review. The PRISMA flow chart⁷⁷ in Figure 2 outlines the flow of information throughout the searching and screening process. Details on results from each individual part of the search process can be found in the search table in Appendix A, and studies excluded at full text, with their reason(s) for exclusion, are presented in Appendix C. The presence or absence of community water fluoridation was not considered as part of the intervention effect in this review.



PRISMA 2009 Flow Diagram (from Moher *et al.* (2009)⁷⁷)

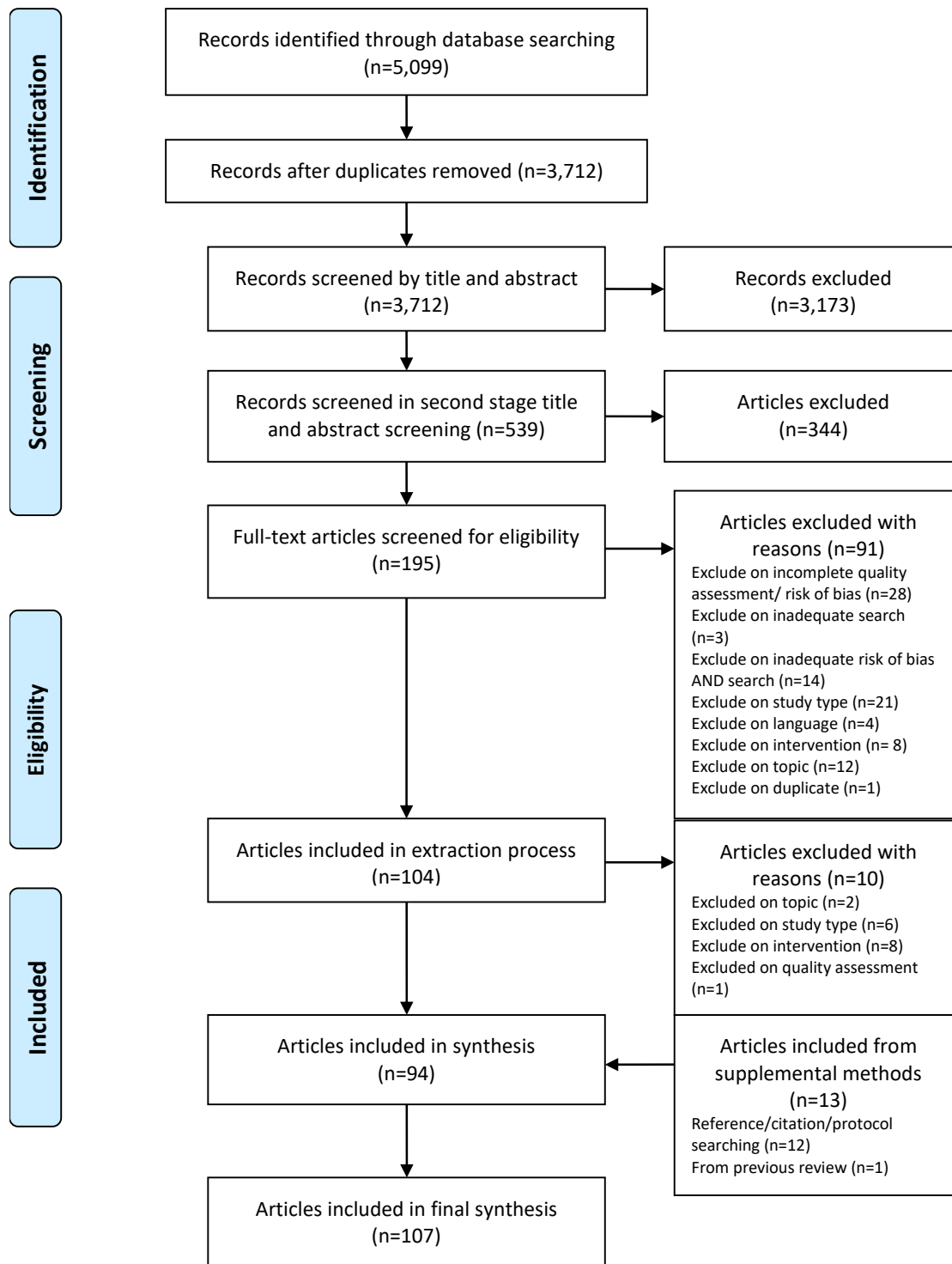


Figure 2 PRISMA flow chart

4.2 Classification of systematic review papers by dentition

The studies presented in this chapter are organised by type of dentition (primary, permanent, or mixed), then by type of lesion or cavity (cavitated caries, non-cavitated caries, and non-carious cervical lesions), and finally, by type of intervention. The interventions differed for cavitated caries compared to non-cavitated caries (Figure 3). For example, non-invasive treatments, restoration materials, restoration support materials, and restoration processes or techniques were used to manage cavitated caries, whereas non-invasive treatments, and microinvasive treatments were employed to manage non-cavitated caries. Some studies examined the treatment of both early non-cavitated and early cavitated caries in primary teeth and the interventions used for cavitated caries were like those employed for non-cavitated caries (see section 4.3.5.2.1.) One final category of lesions was included in this review, and these were non-carious cervical lesions, which were categorised by intervention type: dental factors influencing restoration, restoration material, restoration support material, and restoration processes or techniques.

Our 106 systematic reviews (107 systematic review papers) comprised 18 reviews covering aspects of primary dentition, 46 reviews covering aspects of permanent dentition, and 42 reviews covering aspects of mixed dentition. The 18 reviews on primary dentition comprised 16 reviews on the treatment of cavitated caries and 2 on the treatment of non-cavitated caries. The 46 reviews on permanent dentition comprised 26 reviews on the treatment of cavitated caries, four reviews on the treatment of non-cavitated caries, one review on the treatment of non-cavitated caries and cavitated combined, and 15 reviews on the treatment of non-carious cervical lesions. The 42 reviews on mixed dentition comprised 19 reviews on the treatment of cavitated caries, 15 reviews on the treatment of non-cavitated caries, and 8 reviews on the treatment of non-cavitated caries and cavitated combined. Adverse events were only reported for dental amalgam (no cases of mercury poisoning) and resin composite (release of bisphenol A).

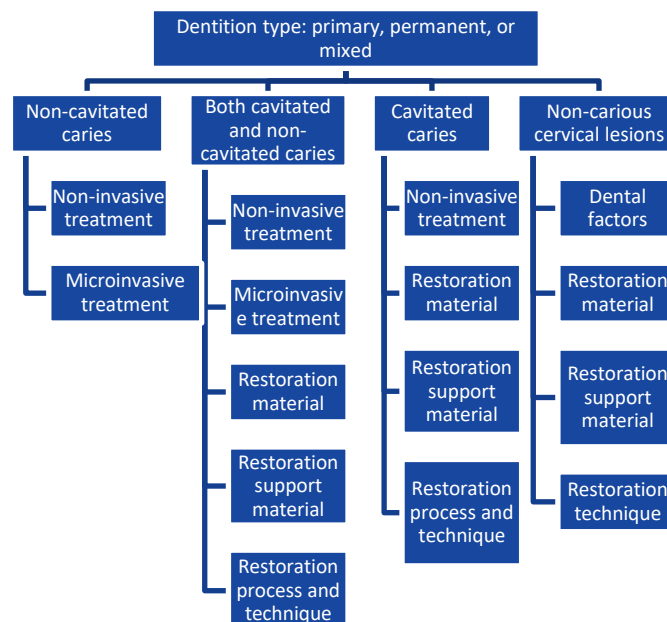


Figure 3 Overview of the treatment of caries and non-carious lesions

Figure 4 presents a more detailed outline of examples of treatment interventions for non-cavitated caries. Adverse events were only reported for silver diamine fluoride (black staining of teeth) and resin sealants (release of bisphenol A).

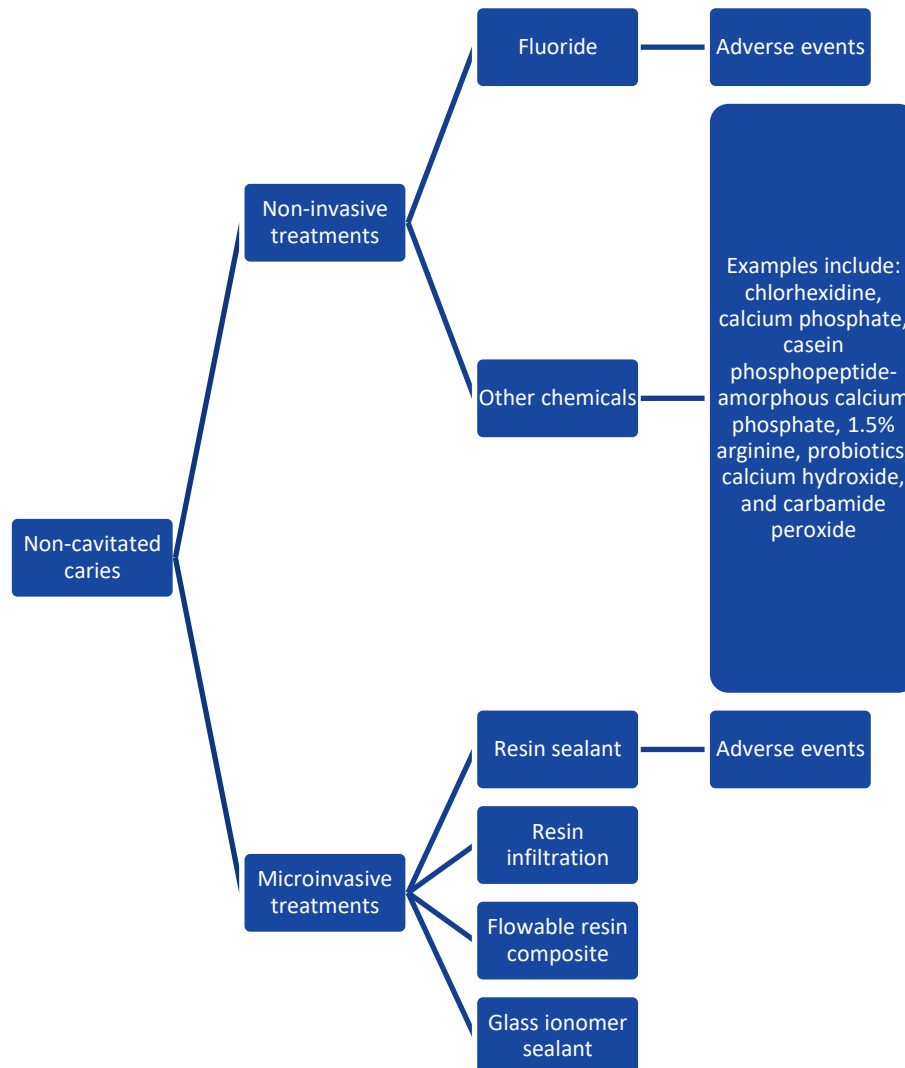


Figure 4 Overview of non-cavitated carious lesion management

Figure 5 presents a more detailed outline of examples of the main treatment interventions for cavitated caries identified in this overview of reviews. Adverse events were only reported for dental amalgam, resin composite and fluoride containing interventions.

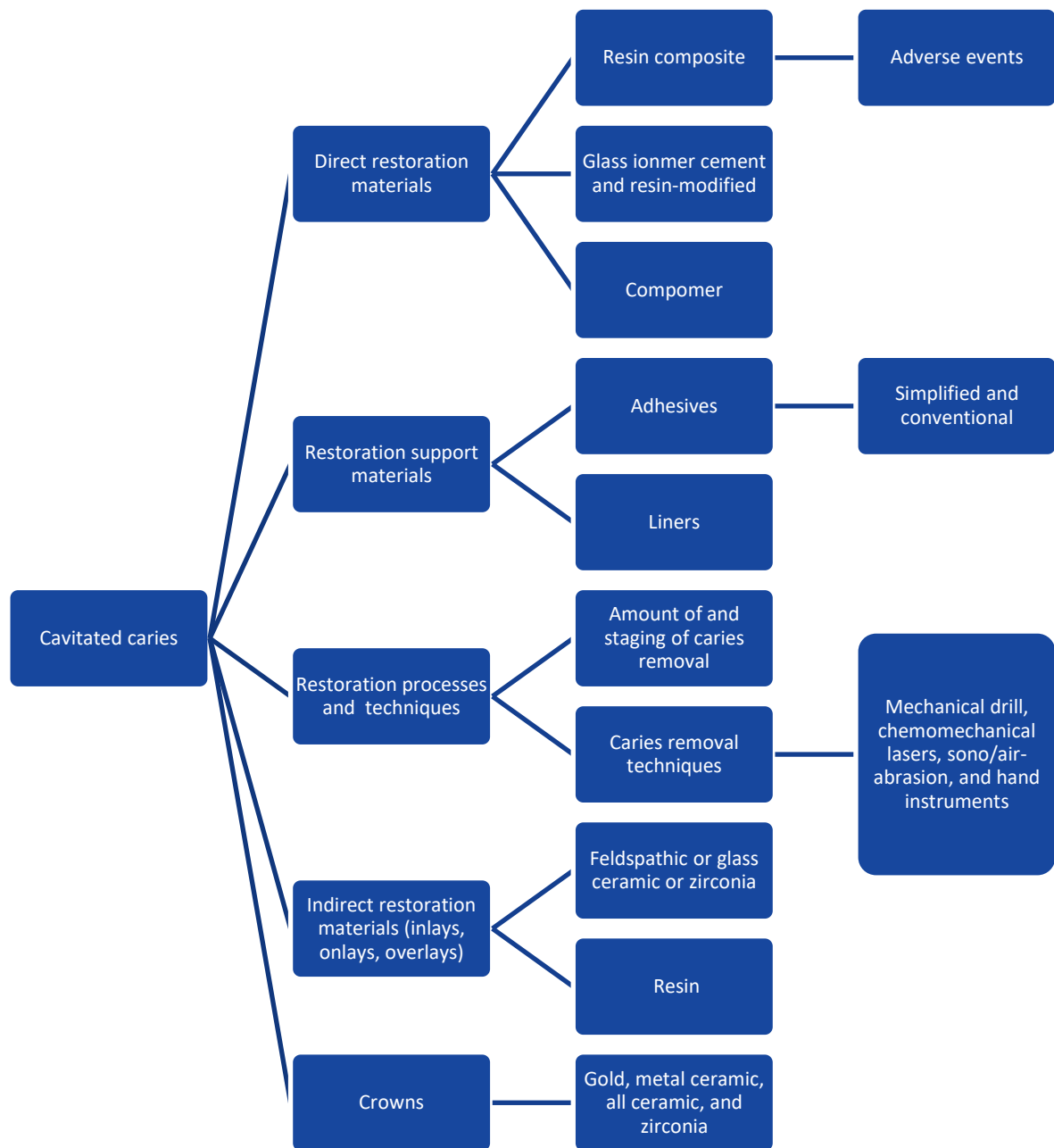


Figure 5 Overview of treatment of cavitated caries

4.3 Summarisation and synthesis of extracted data

The extracted data will be used to inform clinical guidelines, and these guidelines require a high level of accuracy and detail. With this purpose in mind, we have presented the extracted data in two formats: a structured summary for each systematic review in extraction sheets, and high-level summaries taking account of the quality of the evidence, which are presented in this chapter. We provide a detailed structured summary of each systematic review in four appendices: primary dentition (Appendix G), permanent dentition (Appendix H), mixed dentition (Appendix I), and permanent dentition with non-carious lesions (Appendix J). Each of these appendices is then organised by type of carious lesion, and finally by type of treatment. We use the same structure in this chapter, where we present a very high-level summary of the outcomes of each systematic review and compare findings testing the same interventions. We integrated the GRADE of evidence for primary outcomes within each of the high-level summaries of evidence. Appendix K presents a tabular representation of high-level summaries. Table 7 presents a summary of the overlap of primary papers evaluating the same intervention for the same outcomes across one or more systematic reviews using the Pieper *et al.* corrected covered area method.⁴⁵

Table 7 Overlap of primary papers evaluating the same intervention for the same outcomes across one or more systematic reviews

Corrected covered area	Overlap	Number of outcomes
0–5%	Slight	11
6–10%	Moderate	5
11–15%	High	7
15% or over	Very high	16

4.3.1 Introduction

The 18 systematic reviews on primary dentition covered 16 reviews on the treatment of cavitated caries and two reviews on the treatment of non-cavitated caries. The 16 reviews on the treatment of cavitated caries comprised two reviews on the topic of non-invasive treatment, four reviews on direct restoration materials, two reviews on indirect restoration materials, two reviews comparing direct and indirect restoration materials, one paper on restoration support materials, four reviews on restoration processes or techniques, and one paper on combining restoration material and technique. The two reviews on the treatment of non-cavitated caries comprised one paper on the topic of non-invasive treatment and one paper on microinvasive treatment.

4.3.2 Methodological quality of reviews and their primary studies

We reported in the methods chapter (Chapter 3) that we assigned four critical domains in the AMSTAR 2 quality assessment tool. These domains were: using meta-analysis methods appropriately; discussing the effect of heterogeneity on the findings; controlling for unclear or high risk of bias in meta-analyses; and discussing the effect of unclear or high risk of bias on the findings. The quality with respect to methodology of the 18 systematic reviews on primary dentition was varied (Appendix L). We found one review on primary dentition that did not use an appropriate approach to meta-analysis. We identified two reviews that did not take account of heterogeneity when discussing their results. We identified nine reviews that could not or did not control for unclear or high risk of bias in their meta-analysis. We observed that five reviews did not discuss the implications of unclear or high risk of bias on their results.

Six systematic reviews were judged to be of moderate quality using AMSTAR 2, indicating that they had no critical flaws. However, each of these six reviews had one or more non-critical weaknesses. Eight

systematic reviews were considered low quality, each with one critical flaw. The critical flaw was due to either failure to adequately address heterogeneity (one review), failure to control for bias in analysis (five reviews), or failure to address bias in the discussion (two reviews). Four reviews were classified as critically low quality, each with at least two critical flaws. Three reviews failed to control for and discuss the effects of bias, and one of these three reviews did not discuss heterogeneity in its results. The fourth review did not use an appropriate method of meta-analysis and did not control for risk of bias in its analysis.

4.3.3 Grading of Recommendations, Assessment, Development and Evaluations (GRADE)

The GRADE of evidence for the main outcomes for each of the systematic reviews is presented alongside each of the outcomes in the Results section 4.4.5, and the number of downgrades applied and reasons for downgrading are presented in Appendix M. For primary dentition, 6 reviews had outcomes based on moderate-quality evidence, indicating that the true effect is likely to be close to the estimate of the effect; 11 reviews had outcomes based on low-quality evidence, indicating that confidence in the effect estimate is limited; and 3 reviews had outcomes based on very low-quality evidence, indicating very little confidence in the effect estimate. The count exceeds 18, as 3 reviews had more than one GRADE of evidence. The calculated GRADE score included downgrades for inadequate conduct of the systematic review, specifically where primary study design was not randomised, a substantial proportion of studies had an unclear or high risk of bias in the primary studies, a large proportion heterogeneity across the primary studies, and/or inadequate sample sizes. It can be understood that low-quality studies had two to three of these inadequacies, whereas very low-quality studies had four or more of these shortcomings. Therefore, the GRADE score is used as a summary indicator of the quality of the evidence that is presented. It is important to note that the GRADE score takes account of the methodological quality score of the systematic review and its primary studies.

4.3.4 Characteristics of reviews and primary studies

The number of participants was reported for 16 of the 18 systematic reviews and varied from 62 to 5,115 children (Appendix N). The children's ages ranged from 2 to 15 years. Gender was not reported for 15 of the 18 systematic reviews. For the three systematic reviews that reported gender, 44–56% of the children were male. Fourteen of the 18 reviews reported the study countries where the research was completed, and there was a good global spread of countries examining aspects of primary dentition: **Africa (Egypt, South Africa); the Americas (Brazil, the USA); Asia (China, India, Indonesia, Israel, Japan, Kuwait, Pakistan, Saudi Arabia, Syria, Thailand, Turkey, the United Arab Emirates); Europe (Germany, Greece, Greenland, Ireland, the Netherlands, Norway, Sweden, the UK), and Oceania (Australia, New Zealand).** There were two worldwide surveys and two cross-European studies. In addition, there were a number of cross-country studies. The primary studies included in the systematic reviews were published between 1977 and 2018, and the primary study designs were: 103 randomised controlled trials, 22 non-randomised controlled trials, and 11 prospective or retrospective cohort studies. None of the primary studies reported the sources of funding for their research.

4.3.5 Results

4.3.5.1 Non-cavitated caries

Table 8 presents a high-level summary of treatment outcomes for non-cavitated caries in primary teeth.

4.3.5.1.1 Non-invasive treatment

We identified one systematic review on the topic of non-invasive treatment for non-cavitated caries in primary teeth.⁷⁸ Ancira-González *et al.*⁷⁸ compared the effectiveness of **fluoride varnishes, fluoride gels, casein phosphopeptide-amorphous calcium phosphate**, and other *remineralisation agents* with each other in the management of white spot lesions in children's primary teeth. There was low-quality evidence that fluoride varnishes were superior to placebo or no intervention as a remineralisation agent. In addition, there was low-quality evidence that **casein phosphopeptide-amorphous calcium phosphate combined with fluoride toothpaste** had the same remineralising effect as fluoride toothpaste alone. Furthermore, there was low-quality evidence that **fluoride varnish** had the same effect as pit-and-fissure resin sealants, Nd:YAG laser, and chlorhexidine. Finally, there was low-quality evidence that fluoride varnish alone was inferior to fluoride varnish plus chlorhexidine or Nd:YAG laser.

4.3.5.1.2 Microinvasive treatment

We identified one systematic review on the topic of microinvasive treatment for non-cavitated caries in primary teeth.⁷⁹ Lam *et al.*⁷⁹ evaluated the effectiveness of different types of **pit-and-fissure sealants**, compared with no active treatment, to arrest pit-and-fissure occlusal caries in children and adolescents. There was low-quality evidence that **resin-based sealants plus application of 5% sodium fluoride varnish** had the same arresting effect as fluoride varnish alone.

Table 8 Main intervention outcomes for non-cavitated caries in primary dentition

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Arrest caries progression	Remineralisation	Adverse events
Non-cavitated caries in primary teeth							
Fluoride varnishes, fluoride gels	1	Low	Not applicable	Low	Not measured	May be better than other non-invasive agents and as good as microinvasive or laser	Not measured
Casein phosphopeptide-amorphous calcium phosphate	1	Low	Not applicable	Low	Not measured	May be less effective when compared with other non-invasive agents	Not measured
Pit-and-fissure sealants	1	Low	Not applicable	Low	May be better than no treatment and similar to 5% fluoride varnish	Not measured	Not measured

*AMSTAR 2 overall methodological quality rating: High, moderate, low, or critically low

†Overlap: None, slight, moderate, high, or very high

‡Quality of evidence: High, moderate, low, or very low

4.3.5.2 Cavitated caries

Table 9 presents a high-level summary of treatment outcomes for cavitated caries in primary teeth.

4.3.5.2.1 Non-invasive treatment

We identified two systematic reviews on the topic of non-invasive treatment for cavitated caries in primary teeth.^{80,81} Both reviews were published in 2019, examined the intervention **38% silver diamine fluoride**, assessed caries arrest, and had similar overlapping time frames. However, the reviews had different comparators. There was no overlap of primary studies included in the two systematic reviews; that is, different primary studies were included in each systematic review. There is moderate-quality evidence that 38% silver diamine fluoride was effective in arresting cavitated caries in primary teeth.

Trieu *et al.*⁸⁰ evaluated the dentine caries arrest capabilities of 38% silver diamine fluoride compared with those of sodium fluoride in the carious teeth of children aged 12 years and under. The findings indicated moderate-quality evidence from five trials that 38% silver diamine fluoride, when compared with sodium fluoride, was a more effective fluoride-containing reagent for dentine caries arrest in children at 18-month and 30-month follow-up periods.

Tolba *et al.*⁸¹ evaluated the effectiveness (in arresting caries) of the application of 12% silver diamine fluoride, compared with 38% silver diamine fluoride, in cavitated dentine caries in children's primary teeth. The findings indicated moderate-quality evidence from two trials that the number or proportion of caries arrested was lower in the 12% silver diamine fluoride group compared with the 38% silver diamine fluoride group at 24-month and 30-month follow-up periods, and these differences were statistically significant. The black discolouration of the carious dentine after silver diamine fluoride treatment was the most notable side effect.

4.3.5.2.2 Direct restoration material

We identified four systematic reviews on the topic of direct restoration material for treating cavitated caries in primary teeth.^{23,82-84} Each of the reviews examined aspects of clinical performance for **glass ionomer cement and composite resin** compared with each other and with other restoration materials. Three systematic reviews measured the outcome survival and/or failure, and there was high overlap, with 15% of the 24 primary studies included in two or more of the three reviews that measured this outcome. Two systematic reviews measured the outcome secondary caries, and there was moderate overlap, with 10% of the 10 primary studies included in the two systematic reviews measuring this outcome. There was no overlap of primary studies in the four reviews for the other outcomes measured. Overall, clinical performances in restored primary teeth were similar for conventional glass ionomer cement and composite resin in one review (based on low-quality evidence) and lower for glass ionomer cement in two reviews (one based on moderate-quality evidence and one based on low-quality evidence). However, the clinical performance of resin-modified glass ionomer cement was similar to that of composite resin in three reviews (one based on moderate-quality evidence and two based on low-quality evidence). Of note, glass ionomer cement was more effective in preventing secondary caries on some primary teeth surfaces in two reviews, based on moderate-quality evidence.

Dias *et al.*²³ compared failure and clinical performance of **glass ionomer cement** with composite resin in Class II restorations in primary teeth, and the findings indicated moderate-quality evidence that glass ionomer cement and composite resin were similar on failure and on three aspects of clinical performance (marginal discolouration, marginal adaptation, and anatomical form) in Class II restorations in primary teeth. In addition, there was moderate-quality evidence that glass ionomer cements were significantly better than composite resins at preventing the occurrence of secondary carious lesions in primary teeth.

Weber Pires *et al.*⁸² evaluated the clinical performance of different conventional restorative materials placed in posterior primary teeth and found low-quality evidence that the relative risk of failure was significantly higher for **glass ionomer cement when compared with compomer, resin-modified glass ionomer cement, amalgam, and composite resin**. The material with the highest probability of failure was glass ionomer cement (0.99), followed by amalgam, with a much lower probability (0.008); compomer (0.004); resin-modified glass ionomer cement (0.0009); and composite resin (0.0008).

Raggio *et al.*⁸³ compared **glass ionomer cements with other restorative materials (amalgam, resin composite, or polyacid-modified resin composite [compomers])** to prevent adjacent (secondary) carious lesions in the margins of occlusal and occlusoproximal restorations in primary teeth. There was moderate-quality evidence that secondary caries prevention in the margins of occlusal restorations was equal among the groups. In addition, there was moderate-quality evidence that caries prevention in the margins of occlusoproximal restorations, when examined on their own, was better in the glass ionomer cements group.

Santos *et al.*⁸⁴ compared different **glass ionomer cements, composite resins, and compomers** to determine which was superior in terms of restoration survival in the primary (molar) teeth of children. The review authors identified low-quality evidence that the median survival time of silver-reinforced glass ionomer cement was less than that of glass ionomer cement and resin-modified glass ionomer cement, and two studies found that glass ionomer cement had a lower median survival time than both resin-modified glass ionomer cement and compomer. There was low-quality evidence that composite resin, compomer, and resin-modified glass ionomer cement did not differ significantly regarding the number of restorations that survived up to 24 months. The authors' overall conclusion was that low-quality evidence demonstrated that the assessed materials were equal in performance to each other for restoring primary teeth in children, excluding silver-reinforced glass ionomer cement, which was inferior and not recommended for use in primary teeth.

4.3.5.2.3 Crowns and restorative techniques

We identified two systematic reviews on the topic of crowns for treating cavitated caries in primary teeth. Both reviews examined the use of the **Hall Technique to apply crowns** on children's carious teeth.^{85,86} There was no overlap of primary studies included in the two reviews. The placement of crowns in primary teeth using the Hall Technique provided signals of successful outcomes, but the quality of the evidence in the reviews was low or very low.

Badar *et al.*⁸⁵ assessed the outcomes (retention and absence of pulpal symptoms) of placement of a crown using the Hall Technique on primary carious molars in children and compared it with conventional dental restorations or stainless steel crowns. The meta-analysis using three trials comparing the Hall Technique to restore primary carious molars with conventional methods found that the Hall Technique was more successful than the comparative treatment modalities, but this evidence was very low quality.

Innes *et al.*⁸⁶ compared the effectiveness and safety of all types of preformed crowns (using the Hall Technique) with conventional filling materials for restoring primary molar teeth in children. The main findings suggested low-quality evidence that crowns were more likely to reduce the risk of major failure, pain, and infection in the long term, compared with using conventional filling materials. In addition, there was low-quality evidence that crowns fitted using the Hall Technique were more likely to reduce discomfort at the time of treatment, compared with using other restorations. Finally, there was low-quality evidence that the incidence of gingival bleeding was not different across interventions.

4.3.5.2.4 Comparison of direct restoration material and crowns

We identified two systematic reviews on comparing **direct restoration material and crowns** for restoring cavitated caries in primary teeth.^{87,88} Surprisingly, there was no overlap of primary studies in the two reviews. The findings of both reviews were uncertain as to which restoration materials were superior, and these findings were based on low-quality evidence.

Chisini *et al.*⁸⁷ investigated the longevity of **direct and crown** restorations in posterior primary teeth and the reasons for failure. The restoration success rates for each type of material, based on low-quality evidence, were: amalgam: 82% at 3 years; composite resin: 79% at 4 years; glass ionomer cement: 89% at 4 years; compomers: 91% at 3 years; resin-modified glass ionomer cement: 94% at 4 years; modified resin glass ionomer cement: 57% at 3 years; and steel crowns: 96% at 3 years. Based on low-quality evidence, the overall annual failure rate ranges were as follows: composite resin: 2–13% over 4 years; amalgam: 1–28% over 3 years; glass ionomer cement: 0.8–17% over 4 years; compomers: 2–15% over 3 years; resin-modified glass ionomer cement: 1–17% over 4 years; steel crowns: 1–19% over 3 years; and modified resin glass ionomer cement: 10–29% over 3 years. The main finding in this review suggested that there was little consensus regarding the best material for posterior restorations in primary teeth, due to a wide range of time points for data collection and different year end points for individual studies.

Aiem *et al.*⁸⁸ evaluated the clinical effectiveness (success or failure of restorations based on five criteria) of all types of **aesthetic preformed crowns** for restoring primary teeth, compared with conventional filling materials or other types of crowns. The authors could not conclude the direction of the findings on the clinical effectiveness of interventions (aesthetic preformed crowns) and comparators (conventional filling materials or other types of crowns) for restoring primary teeth due to clinical and methodological heterogeneity between the primary studies. Overall, the evidence was low quality.

4.3.5.2.5 Restoration support material

We identified one systematic review on the topic of a restoration support material that assists resin composite restoration of cavitated caries in primary teeth.⁸⁹ Schwendicke *et al.*⁸⁹ evaluated the risk of restoration failure (proportion of teeth requiring retreatment) following restoration due to dentine caries in primary molar teeth, comparing restorations with **cavity lining** to restorations without cavity lining. The follow-up was one year or more. There was low-quality evidence that there was no difference in failure of adhesive restorations based on the presence or absence of a liner in primary teeth.

4.3.5.2.6 Restoration processes or techniques

We identified four systematic reviews on the topic of restoration processes or techniques that assist restoration of cavitated caries in primary teeth: three on the stages and amount of caries removed⁹⁰⁻⁹² and one on the method of caries removal.⁹³ For the outcomes of survival or failure when examining the stages and amount of caries removed, there was very high overlap of primary studies, with 50% of the seven studies across at least two of the three systematic reviews reporting on this topic. Selective caries removal, compared with complete caries removal, was associated with higher restoration failure rates and reduced pulp exposure in two reviews – one based on low-quality evidence and the second based on moderate-quality evidence. The third review on the stages and amount of caries removal did not complete a direct comparison. The review comparing chemomechanical caries removal (Papacarie) with conventional mechanical caries removal provided evidence of reduced pain and anxiety among children, but the dentist required a longer time period to complete the chemomechanical caries removal procedure. These findings were based on low- or very low-quality evidence.

4.3.5.2.6.1 Stages and amount of caries removed

Aïem *et al.*⁹⁰ compared the efficacy (measured by pulp exposure and absence of pulpal or periodontal complications or restorative failures) of three caries removal techniques – **complete caries removal**, **selective caries removal**, and **stepwise caries removal** – for deep carious lesions in vital (absence of irreversible pulpitis or pulpal necrosis) primary teeth. During clinical protocol, the pulp exposure risk was lower for selective caries removal, compared with complete caries removal, based on moderate-quality evidence. At the end of the treatment follow-up, pulpo-periodontal complications (clinical and/or radiographic failures) were similar in the selective caries removal and complete caries removal groups, based on moderate-quality evidence. The intention-to-treat meta-analysis based on United States Public Health Service (USPHS) criteria for testing composite restorations demonstrated significantly higher restorative success for complete caries removal when compared with selective caries removal (low-quality evidence). The intention-to-treat meta-analysis based on the Frencken criteria found no difference between selective caries removal and complete caries removal (low-quality evidence). Two trials compared pulp exposure at the time of intervention for stepwise caries removal with that of complete caries removal. The odds of pulp exposure in the stepwise caries removal group were significantly lower when compared with the complete caries removal group (low-quality evidence). The pulpo-periodontal complications at follow-up (clinical and/or radiographic failures) did not differ significantly between the stepwise caries removal and complete caries removal groups (low-quality evidence). Two trials compared pulp exposure for selective caries removal with stepwise caries removal. There was no difference in the risk of pulp exposure in the selective caries removal and stepwise caries removal groups (low-quality evidence). In addition, the risk of pulpal or periodontal complications (clinical and radiographic failures) in the selective caries removal and stepwise caries removal groups was not different.

Pedrotti *et al.*⁹¹ evaluated whether **selective carious tissue** removal of soft dentine from deep cavitated lesions in primary teeth increased the risk of experiencing restoration failure, compared with **complete carious tissue** removal. There was moderate-quality evidence that restorations placed following selective carious tissue removal of soft dentine from deep cavitated lesions in primary teeth increased the risk of experiencing restoration failure, compared with complete carious tissue removal.

Aparecida Silva Martins *et al.*⁹² evaluated the clinical evidence of **selective caries removal** in the primary dentition, regardless of liner and restorer materials, measuring the longevity of the restorative treatment and clinical and radiographic success. There was low-quality evidence that selective caries removal had high clinical and radiographic success rates and that the longevity of the associated restorations was satisfactory. The longevity of restorations in primary molars preceded by selective caries removal compared with restorations preceded by **complete caries removal** was not statistically significantly different.

4.3.5.2.6.2 Method of caries removal

Deng *et al.*⁹³ compared the efficiency (operation time, bacterial count, and restoration survival) and acceptability of **chemomechanical caries removal (Papacarie)** in primary molar caries in children and adolescents with the conventional drilling method (controls). There was low-quality evidence that microbiota in carious dentine was significantly reduced using the Papacarie treatment compared with the conventional drilling method. There was very low-quality evidence that pain scores evaluated before and after caries removal were reduced in both the Papacarie and conventional drilling method. There was low-quality evidence of longer time required for the Papacarie treatment compared with the conventional drilling method. The children reported that less pain and anxiety were experienced with the Papacarie method compared with the conventional drilling method, and this was graded as very low-quality evidence. There were no significant differences in retention of restoration and incidence of

secondary caries at follow-up with the Papacarie method compared with the conventional drilling method, based on very low-quality evidence.

4.3.5.2.7 Restoration material and technique

We identified one systematic review on the topic of combining restoration material and technique for restoring cavitated caries in primary teeth.⁹⁴ Tedesco *et al.*⁹⁴ determined the best treatment for **dentine carious lesion arrestment** and the success rate of different treatments of the dentine carious lesions of primary teeth. The purpose of the review was to bridge a gap in the evidence by considering whether lesions of different depths, and the number of surfaces involved, affect treatment outcomes. There was very low-quality evidence that resin composite restoration had a higher success rate than resin sealant. However, when caries arrest was considered as the primary outcome, no difference was observed between the restorative treatments.

For the studies that considered only the occlusal surface without information about the depth of progression, the success rates were similar in all mixed-treatment comparisons, based on very low-quality evidence. The treatment with the highest probability of success was using conventional restorative treatment with composite resin or conventional restorative treatment with compomer. After that, the ranking was: (2) atraumatic restorative treatment; (3) conventional restorative treatment high-viscosity ionomer cement; (4) conventional restorative treatment with amalgam; and (5) conventional restorative treatment with resin composite.

The primary outcome of the comparison of **dentine carious lesions on occlusoproximal surfaces**, without information about the depth of progression, was a comparison of success rates. The Hall Technique, compared with non-restorative caries treatment, had a statistically significantly higher success rate based on very low-quality evidence. No other mixed-treatment comparisons were statistically significantly better than their comparators in this analysis. The rank probability showed that the best result for occlusoproximal cavities was the Hall Technique based on very low-quality evidence. After that, the final ranking was: (2) non-restorative caries treatment; (3) conventional restorative treatment using compomer; (4) conventional restorative treatment using high-viscosity glass ionomer cement; (5) conventional restorative treatment using resin composite; (6) atraumatic restorative treatment; (7) conventional restorative treatment using amalgam; and (8) ultraconservative treatment.

Three studies evaluated caries arrest on **occlusal and smooth surfaces of primary teeth**, and three treatment comparisons were statistically significantly better than their comparators, based on very low-quality evidence: 38% silver diamine fluoride (two or three applications per year) compared with silver diamine fluoride (one application per year); low-viscosity glass ionomer cement compared with silver diamine fluoride (two applications per year); and interim restorative treatment compared with silver diamine fluoride (one application of either 30% or 38%). The rank probability showed that the best performance for this type of dentine carious lesion was two applications of 38% silver diamine fluoride per year, and this was significantly better than other silver diamine fluoride treatment doses and frequencies. After that, the final ranking was: (2) low-viscosity glass ionomer cement; (3) one annual application of silver diamine fluoride; (4) three applications per year of silver diamine fluoride; (5) three applications per year of sodium fluoride; and (6) interim restorative treatment.

Table 9 Main intervention outcomes for cavitated caries in primary dentition

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Arrest caries progression	Higher restoration success or survival	Lower restoration failure	Better clinical performance	Adverse events
Cavitated caries in primary teeth									
38% silver diamine fluoride	2	1 low and 1 moderate	None	Moderate	Probably positive when compared with lower doses or other fluoride products	Not applicable	Not applicable	Not applicable	Probable increase in black staining
Composite resin	4 (3 survival and 2 secondary caries)	1 critically low, 2 low, and 1 moderate	Moderate and high	2 low and 2 moderate	Not applicable	Probable higher success in 2 reviews and similar in 1 review when compared with conventional glass ionomer	Not measured	May not be as good for secondary caries prevention when compared with conventional glass ionomer	Not measured
Resin-modified glass ionomer cement	4 (3 survival and 2 secondary caries)	1 critically low, 2 low, and 1 moderate	Moderate and high	2 low and 2 moderate	Not applicable	Probable similar restoration success to composite for all 3 reviews	Not measured	Not measured	Not measured
Glass ionomer cement	4 (3 survival and 2 secondary caries)	1 critically low, 2 low, and 1 moderate	Moderate and high	2 low and 2 moderate	Not applicable	May have lower success for 2 reviews and similar for 1 review	Not measured	May be better for secondary caries prevention when compared with resin composite.	Not measured
Hall Technique for applying crowns	2	1 critically low and 1 low	None	1 low and 1 very low	Not applicable	May have higher success for 1 review	May have lower failure for 1 review	May be positive for lower pain and infection	Not measured

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Arrest caries progression	Higher restoration success or survival	Lower restoration failure	Better clinical performance	Adverse events
Direct compared with crown restorations	2	2 moderate	None	Low	Not applicable	May have similar success for 1 review	May have similar failure for 1 review	Not measured	Not measured
Liner for adhesive restoration compared with no liner	1	Low	Not applicable	Low	Not applicable	Not measured	May be no difference	Not measured	Not measured
Selective caries removal compared with complete caries removal	3	1 low and 2 moderate	Very high	1 low, 1 moderate or low, and 1 moderate	Not applicable	Not measured	May be higher failure for 2 reviews; no comparison for 1 review	Not measured	Not measured
Chemomechanical method of caries removal (Papacarie) compared with conventional mechanical removal	1	Critically low	Not applicable	Low or very low	Not applicable	Not measured	Not measured	May have: Reduced pain and anxiety Longer operating time.	Not measured
Treatments of the dentine carious lesions	1	Critically low	Not applicable	Very low	No difference	Best outcome with composite resin or compomer though quality of evidence is uncertain	Not measured	Not measured	Not measured

*AMSTAR 2 overall methodological quality rating: High, moderate, low, or critically low

†Overlap: None, slight, moderate, high, or very high

‡Quality of evidence: High, moderate, low, or very low

4.4 Permanent dentition

4.4.1 Introduction

The 46 systematic reviews on permanent dentition included 26 reviews on the treatment of cavitated caries, 4 reviews on the treatment of non-cavitated caries, 1 paper on the treatment of non-cavitated caries and cavitated combined, and 15 reviews on the treatment of non-carious cervical lesions. The 26 reviews on the treatment of cavitated caries comprised 10 reviews about direct restoration material, 7 reviews on indirect restoration material and one of these also compared direct and indirect restoration material, 3 reviews comparing direct and indirect restoration material, 2 reviews on restoration support material, and 4 reviews on restoration processes or techniques. The four reviews on the treatment of non-cavitated caries all covered the topic of non-invasive treatment. The single paper on the treatment of non-cavitated caries and cavitated combined was a comparison of non-invasive, microinvasive, and minimally invasive treatments with each other. The 15 reviews on the treatment of non-carious cervical lesions included 1 paper on the topic of dental factors influencing restoration, 3 reviews on direct restoration material, 7 reviews on restoration support material, and 4 reviews on restoration processes or techniques.

The characteristics of the studies on caries in permanent dentition and of the studies on non-carious cervical lesions are each described separately in the following sections due to differing aetiology.

4.4.1.1 Caries in permanent dentition

4.4.1.1.1 Methodological quality of reviews and their primary studies

We reported in the Methods chapter (Chapter 3) that we assigned four domains in the AMSTAR 2 quality assessment tool as critical domains, and these domains were: using meta-analysis methods appropriately, discussing the effect of heterogeneity on the findings, controlling for unclear or high risk of bias in meta-analyses, and discussing the effect of unclear or high risk of bias on the findings. The quality, with respect to methodology, of the 31 systematic reviews on permanent dentition with caries was mixed (see Appendix L). We found seven reviews on permanent dentition that did not use an appropriate approach to meta-analysis. We identified six reviews that did not take account of heterogeneity when discussing their results. We identified 16 reviews that could not or did not control for unclear or high risk of bias in their meta-analysis. And we observed that nine reviews did not discuss the implications of unclear or high risk of bias on their results.

Ten reviews were rated moderate quality, indicating that they had no critical flaws, but they had one or more non-critical weaknesses. Eight reviews were judged low quality with one critical flaw, and this was due to either failure to adequately address heterogeneity (three reviews) or failure to control for bias in analysis (five reviews). Eleven reviews were considered critically low quality, with at least two critical flaws. One review had all four critical flaws. Six reviews had three critical flaws. Four of the reviews with three critical flaws failed to control for and discuss the effects of bias and to use appropriate meta-analysis methods. Two of the reviews with three critical flaws failed to control for the effects of bias, discuss heterogeneity, and use of appropriate meta-analysis methods. Four reviews had two critical flaws, and these were failure to control for and discuss the effects of bias. Two of the systematic reviews on permanent teeth did not find any studies on their topic of interest, and therefore could not have a quality assessment completed.

4.4.1.1.2 Grading of Recommendations, Assessment, Development and Evaluations (GRADE)

The GRADE of evidence for the main outcomes for each of the systematic reviews is presented alongside each of the outcomes in the Results section 4.5.1.1.4, and the number of downgrades applied and reasons for downgrading are presented in Appendix M. For permanent dentition, 1 review had outcomes based on high-quality evidence, indicating a high level of confidence that the true effect lies close to that of the estimate of the effect; 7 reviews had outcomes based on moderate-quality evidence, indicating that the true effect is likely to be close to the estimate of the effect; 17 reviews had outcomes based on low-quality evidence, indicating that confidence in the effect estimate is limited; and 6 reviews had outcomes based on very low-quality evidence, indicating very little confidence in the effect estimate. Two reviews found no evidence to answer their research question, while another two reviews found no evidence for one of their primary outcomes. The count exceeds 31, as 2 reviews had more than one GRADE of evidence. The calculated GRADE score included downgrades for inadequate conduct of the systematic review, specifically where primary study design was not randomised, a substantial proportion of studies had an unclear or high risk of bias in the primary studies, a large proportion heterogeneity across the primary studies, and/or inadequate sample sizes. It can be understood that low-quality studies had two to three of these inadequacies, while very low-quality studies had four or more of these inadequacies. Therefore, the GRADE score is used as a summary indicator of the quality of the evidence that is presented. It is important to note that the GRADE score takes account of the methodological quality score of the systematic review and its primary studies.

4.4.1.1.3 Characteristics of reviews and primary studies

The number of participants in the studies on caries in permanent teeth was reported for 25 of 31 systematic reviews and varied from 65 to 10,136 participants (see Appendix N). For the 22 studies that reported age, the participants' ages ranged from 7 to 101 years. Gender was not reported for 20 of the 31 systematic reviews. Among the 11 systematic reviews that reported gender, more females than males were included. Seventeen of the 31 reviews reported the study countries where the research was sited, and there was an extensive spread of countries across the globe: **Africa (Egypt, Zimbabwe), the Americas (Brazil, Canada, Colombia, Uruguay, the USA), Asia (China, Indonesia, Iran, Israel, Japan, Republic of Korea, Saudi Arabia, Thailand, Turkey), and Europe (Albania, Austria, Belgium, Denmark, Germany, Hungary, Ireland, Italy, Liechtenstein, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, the UK)**. In addition, there was one multiregional study and one European-based cross-country trial. The primary study designs included in the systematic reviews were: 221 randomised controlled trials, 42 non-randomised controlled trials, and 82 prospective or retrospective cohort studies; these primary studies were published between 1976 and 2019. Five of the systematic reviews had primary studies that reported industry funding for their research and 24 systematic reviews did not report primary funding sources, or were unable to identify such funding sources.

4.4.1.1.4 Results: non-cavitated caries

Table 10 presents a high-level summary of treatment outcomes for non-cavitated caries in permanent teeth.

4.4.1.1.4.3 Non-invasive treatment

We identified four systematic reviews on the topic of non-invasive treatment for non-cavitated caries in permanent teeth.⁹⁵⁻⁹⁸ One covered non-invasive treatment of coronal caries⁹⁶ and the other three covered non-invasive treatment of root caries.^{95,97,98} There was very high overlap of the three primary studies across the three systematic reviews evaluating non-invasive treatment for root caries, with 83% of the three primary studies being included in more than one of the three reviews. The single systematic

review that covered non-invasive treatment of coronal caries evaluated **fluoride monotherapy** and fluoride combined with casein phosphopeptide-amorphous calcium phosphate (CPP-ACP).

All three reviews (one with moderate-quality evidence, one with moderate- and low-quality evidence, and one with low-quality evidence) of non-invasive treatment of root caries found that **silver diamine fluoride** provided a higher caries arrest effect than comparators in root carious lesions in adults' permanent teeth; this was not surprising, as the systematic reviews' analyses were based on the same primary studies.^{95,97,98} In addition, one of the three reviews reported low-quality evidence that **dentifrice containing 5,000 parts per million (ppm) fluoride** and professionally applied chlorhexidine varnish inactivated existing root carious lesions and/or reduced the initiation of root carious lesions.

Coronal carious lesions

Tao *et al.*⁹⁶ evaluated the efficacy of combining **CPP-ACP and fluorides**, compared with fluorides monotherapy, on patients with early carious lesions in permanent teeth. Based on low-quality evidence and analysis of laser fluorescence results, the random-effects pairwise meta-analysis showed that the combination of CPP-ACP and fluoride treatment was better at decreasing the size of early occlusal carious lesions than fluorides monotherapy. However, there was low-quality evidence that fluoride combined with CPP-ACP achieved the same results as fluorides monotherapy for early carious lesions on smooth surfaces.

Root carious lesions

Oliveira *et al.*⁹⁵ assessed the effect of professionally applied **silver diamine fluoride**, compared with no intervention, placebo, or other active intervention, in preventing and arresting caries in exposed root surfaces of adults. There was moderate-quality evidence that silver diamine fluoride applications had a better preventive effect in comparison to placebo and were as effective as either chlorhexidine or sodium fluoride varnish in preventing new root carious lesions in adults' permanent teeth. There was low-quality evidence that silver diamine fluoride applications provided a higher caries arrest effect than placebo treatments in root carious lesions in adult permanent teeth.

Hendre *et al.*⁹⁷ evaluated the effectiveness (preventing, arresting, or remineralising) of **silver diamine fluoride** in the management of *root carious lesions* in older adults. The comparators were other preventive agents (fluoride, chlorhexidine) or placebo. There was moderate-quality evidence that silver diamine fluoride effectively arrested root caries in older adults.

Wierichs and Meyer-Lueckel⁹⁸ evaluated results of clinical studies investigating **chemical agents** to reduce initiation of root carious lesions, or to inactivate or arrest existing lesions. There was low-quality evidence that dentifrice containing 5000 ppm fluoride and professionally applied chlorhexidine or silver diamine fluoride varnish inactivated existing root carious lesions and/or reduced the initiation of root carious lesions.

Table 10 Main intervention outcomes for non-cavitated caries in permanent dentition

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Arrest caries progression	Remineralisation	Adverse events
Non-cavitated caries							
Silver diamine fluoride (root caries) compared with other non-invasive interventions and placebo	3	2 critically low and 1 low	Very high	1 low, 1 moderate and low, and 1 moderate	May be positive for intervention	Not measured	Not measured
Dentifrice containing 5000 ppm fluoride compared with other non-invasive interventions and placebo	1	Critically low	Not applicable	Low	May be positive for intervention	Not measured	Not measured
Professionally applied chlorhexidine compared with other non-invasive interventions and placebo	1	Critically low	Not applicable	Low	May be positive for intervention	Not measured	Not measured
Combining CPP-ACP and fluorides, compared with fluorides monotherapy	1	Low	Not applicable	Low	Not measured	May be better for early occlusal carious lesions. May be no difference for early carious lesions on smooth surfaces.	Not measured

*AMSTAR 2 overall methodological quality rating: High, moderate, low, or critically low

†Overlap: None, slight, moderate, high, or very high

‡Quality of evidence: High, moderate, low, or very low

4.4.1.1.5 Results: Non-cavitated and cavitated caries

Table 11 presents a high-level summary of treatment outcomes for non-cavitated caries and cavitated caries in permanent teeth.

4.4.1.1.5.1 Comparison of non-invasive, microinvasive, and minimally invasive treatment

One systematic review by Schwendicke *et al.*³² compared **non-invasive, microinvasive, and minimally invasive treatments** with each other, with no active treatment or a placebo treatment, or with standard oral home care for treating pit-and-fissure lesions in permanent posterior teeth in adults. The authors found very low-quality evidence that microinvasive and minimally invasive treatments were potentially effective in avoiding retreatments of pit-and-fissure lesions in permanent posterior teeth. In addition, there was some very low-quality evidence that non-invasive treatments might also be effective in avoiding retreatments of pit-and-fissure lesions in permanent posterior teeth. Based on very low-quality evidence, microinvasively sealed lesions required re-sealing regularly, increasing the overall need for re-interventions compared especially with minimally invasive treatments.³²

4.4.1.1.6 Results: cavitated caries

Table 11 presents a high-level summary of treatment outcomes for cavitated caries in permanent teeth.

4.4.1.1.6.1 Direct restoration material

We identified 10 systematic reviews on the topic of **direct restoration materials** for cavitated caries in permanent teeth. Four systematic reviews examined different forms of composite resin compared with each other and in one review glass ionomer cement.⁹⁹⁻¹⁰² For the outcome of clinical performance, there was moderate overlap of primary studies across the four systematic reviews, with 6% of the 59 primary studies being cited in two or more of the four reviews. Three reviews compared amalgam with composite resin.^{11,13,103} There was complete overlap of the six primary RCTs included in two of the three systematic reviews for almost all primary outcomes^{11,103} and no overlap of the eight primary studies in the third systematic review, as it included mainly cohort and other non-randomised studies.¹³ Two reviews attempted to evaluate amalgam and composite resin repairs with replacements.^{14,104} One review evaluated restoration materials for root caries.¹⁰⁵

The four systematic reviews (two with moderate-quality evidence and two with low-quality evidence) that compared newer forms of composite resin with conventional composite resin in patients with direct restorations in posterior permanent teeth found that their clinical performance was similar. The three systematic reviews that compared the restoration failure of direct composite resin fillings with amalgam fillings for permanent posterior teeth found low- or very low-quality evidence that resin composite had higher failure rates and higher secondary caries rates than amalgam. In addition, there was low- or very low-quality evidence that restoration fracture was the same for both amalgam and resin composite. The two reviews that attempted to evaluate amalgam and composite resin repairs with replacements found no studies that met their inclusion criteria. The review that evaluated restoration materials for root caries found insufficient and low-quality evidence to recommend any specific material for routine use in the restoration of root carious lesions; all had high failure rates.

Different forms of composite resin compared with each other and/or glass ionomer cement

Medeiros Maran *et al.*⁹⁹ evaluated survival or clinical performance (two primary outcomes: colour match and surface texture; and six secondary outcomes) of **nanofilled/nanohybrid restorations compared with hybrid composite restorations** in patients with direct posterior restorations. The meta-analyses revealed no significant differences between nanofilled and hybrid composite for colour match (moderate-quality evidence) or surface texture (moderate-quality evidence). The meta-analyses revealed no significant differences between nanohybrid and hybrid restorations for colour match (moderate- or low-quality

evidence) or surface texture (moderate- or low-quality evidence). The low-quality evidence was at the 72-month follow-up period and the moderate-quality evidence was at earlier follow-ups.

Raiane Mamede Veloso *et al.*¹⁰⁰ evaluated whether the clinical performance (measured by eight criteria) of **bulk-fill resin composites** was comparable to that of conventional composites in restored permanent posterior (molar and premolar) teeth. There was moderate-quality evidence that the clinical performance of bulk-fill and conventional resin composites in direct restorations of posterior teeth was similar, within a follow-up period of 12–72 months.

de Castro Kruly *et al.*¹⁰¹ compared the clinical behaviour (marginal integrity/adaptation, marginal discolouration, recurrent caries, retention of composite restorations, and post-operative sensitivity) of restorations performed with low polymerisation shrinkage resin composite (**bulk fill**) resin with methacrylate-based (conventional) **composite resin** (in humans with Class I or II restorations in permanent dentition). There was low-quality evidence that restorations performed with low polymerisation shrinkage resin composites, such as silorane, ormocer, and bulk-fill type, demonstrated a clinical performance similar to direct conventional resin composite restorations.

Monsarrat *et al.*¹⁰² evaluated the clinical performance (such as survival rates or quality of restorations) of the first generation of **ormocer**-based fillings against those of conventional **composite resin** restorations and **glass ionomer restorations**, and explored the influence of different clinical factors and the impact of the quality of studies on published results. There was low-quality evidence that the clinical performance of the first generation of ormocer-based fillings was similar to conventional composite restorations. No factor emerged to explain global failures, although an increase in age, an increase in the proportion of females, and a decrease in the number of restorations per patient were associated with fewer marginal adaptation failures for ormocers in Class I and II cavities.

Amalgam compared with composite resin

The Canadian Agency for Drugs and Technologies in Health (CADTH) evaluated the comparative efficacy and safety of direct dental restorations made of **composite resin** compared with **amalgam** for the treatment of dental caries in posterior permanent teeth.¹⁰³ CADTH reported that it found one additional study, and this study (Kemaloglu *et al.*, 2016) reported zero events of restoration failure and secondary caries in either treatment arm at three years, or 100% survival in both arms. CADTH reported that, due to methodological and clinical heterogeneity, incorporation of the data from this 2016 split-mouth RCT with the 2014 Cochrane systematic reviews data¹¹ was not possible. Therefore, there is no additional evidence for findings on efficacy, and the Rasines Alcaraz *et al.* review remains valid.¹¹

With respect to safety, there was low-quality evidence that statistically significant differences in urinary mercury excretion between patients receiving amalgam and those receiving composite resin at follow-up time points of up to 5–6 years were reported in two large trials.¹⁰³ One of these two trials reported that the prevalence of microalbuminuria was found to be statistically significantly higher in the amalgam-treated group at 3- and 5-year follow-ups, but this finding was based on low-quality evidence. There were some statistically significant findings on physical development, neuropsychological function, and psychosocial outcomes in one of the two large trials, but not consistently across both, and these findings were based on low-quality evidence. There was low-quality evidence that there were no observed statistically significant differences between treatment groups in evaluations of neurological symptoms, immune function, and urinary porphyrin excretion.

There was low-quality evidence that post-operative sensitivity did not differ between amalgam and composite resin restorations at follow-ups between 2 and 52 weeks, although a statistically significant difference was reported at 36 months follow-up in two studies, favouring the composite resin group.¹⁰³

Moraschini *et al.*¹³ compared the failure rates of **amalgam and composite resin** in occlusal and occlusoproximal restorations in posterior permanent teeth. There was very low-quality evidence that resin composite had higher failure rates and higher secondary caries rates than amalgam. In addition, there was very low-quality evidence that restoration fracture was the same for both amalgam and resin composite.

Rasines Alcaraz *et al.*¹¹ compared the restoration failure of **direct composite resin** fillings with that of **amalgam** fillings for permanent posterior teeth and there was low-quality evidence that resin composite had higher failure rates and higher secondary caries rates than amalgam. In addition, there was low-quality evidence that restoration fracture was the same for both amalgam and resin composite.

Repairs or replacements of restoration materials

Sharif *et al.* (2014a)¹⁴ attempted to compare the effects (retention, survival) of **replacing resin composite** with repairing it (resin composite) in the management of defective resin composite dental restorations in permanent molar and premolar teeth. However, no trials met the inclusion criteria and there was no evidence on the effectiveness of such interventions.

Sharif *et al.* (2014b)¹⁰⁴ attempted to compare the effects (retention, survival) of **replacing amalgam** compared with repairing it (amalgam) in the management of defective amalgam dental restorations in permanent molar and premolar teeth. However, no trials met the inclusion criteria and there was no evidence on the effectiveness of such interventions.

Restoration materials for root caries

Hayes *et al.*¹⁰⁵ compared the clinical performance of **restorative materials** for the treatment of root caries in the permanent teeth of adult patients. There was insufficient and low-quality evidence to recommend any specific material for routine use in the restoration of root carious lesions; all had high failure rates. There is a need to evaluate restorative materials in a more generalised population, as many of the studies included in Hayes *et al.*'s systematic review were confined to post-radiation, xerostomic patients.

4.4.1.1.6.2 Indirect restoration materials (inlay, onlay, and/or overlay) and crowns

We identified seven systematic reviews on the topic of indirect restoration materials for cavitated caries in permanent teeth.^{29,106-111} Six of the seven reviews examined indirect restorations.^{29,106,108-111} One study calculated the survival and complications of onlays only in adults' permanent posterior teeth.¹⁰⁶ One study evaluated the survival rate of indirect composite and ceramic inlays, onlays, and overlays in permanent posterior teeth.¹⁰⁸ One study investigated the survival rates and complications of different types of indirect restorations (inlay, onlay, both inlay and onlay), and crowns used for single permanent anterior, premolar, or molar teeth.¹⁰⁹ One study evaluated the survival rate of resin and ceramic inlays, onlays, and overlays at 5 years and 10 years in permanent teeth, and identified the types of complications.²⁹ Two reviews evaluated the clinical performance of indirect composite inlays, compared with ceramic inlays and/or onlays, in adults with permanent vital teeth restorations.^{110,111} One of these two reviews also examined gold inlays.¹¹⁰

All six reviews that examined indirect restorations had overlaps between interventions and comparators, yet no reviews had the exact same interventions or comparators. All six of these reviews assessed survival as the outcome, and three identified complications. However, the time points at which survival was assessed were different. There was moderate overlap across the six reviews assessing survival, with 7% of the 51 primary papers being included in more than one of those six reviews.^{29,106,108-111} One review on a different topic (crowns) had no overlap of its primary studies with the other six reviews.¹⁰⁷

Five of the six reviews of indirect restorations revealed that the survival rate at 3 years was over 94%, at 5 years was over 90%, and at 10–11 years was over 87%.

One study compared ceramic prostheses made by a computer-aided design/computer-aided manufacturing system with those made by a conventional manufacturing (milling) system.¹⁰⁷ There was low-quality evidence that the longevity of tooth-supported ceramic prostheses made by the computer-aided design/computer-aided manufacturing system was lower than that of crowns made by a conventional manufacturing (milling) system.

Bustamante-Hernández *et al.*¹⁰⁶ evaluated the clinical behaviour (survival) and the possible complications of posterior region **onlays** in adults' permanent posterior teeth by the type of material used for the onlay restoration 1 year or more after restoration intervention. Based on very low-quality evidence, the estimated percentage survival for onlays was 94.2% (95% confidence interval (CI): 92.3–96.1). The survival, based on very low-quality evidence, varied by type of onlay material: hybrids (resin nanoceramic and hybrid ceramic) (99%), feldspathic ceramic reinforced with lithium disilicate (98%), conventional feldspathic ceramic reinforced with leucite (93%), and resin composites (90%). The longest follow-ups were 2–15 years.

Becker Rodrigues *et al.*¹⁰⁷ evaluated the difference in longevity of tooth-supported **ceramic prostheses (crowns)** made by a computer-aided design/computer-aided manufacturing system compared with those made by a conventional manufacturing (milling) system. The meta-analysis results suggested that the longevity of tooth-supported ceramic prostheses made by the computer-aided design/computer-aided manufacturing system was lower than that of crowns made by a conventional manufacturing (milling) system, but the findings were based on low-quality evidence.

Sampaio *et al.*¹⁰⁸ evaluated the survival rate of indirect **composite and ceramic inlays, onlays, and overlays** following different manufacturing methods in children's and adults' permanent teeth. There was low-quality evidence that the pooled estimated survival rates at the follow-up times of 5 and 10 years were 97% and 89%, respectively.

After 5 years, survival rate for pressable glass ceramics was 95% (low-quality evidence). For the stratified group, survival rates at the follow-up times of 5 and 10 years were 88% and 93%, respectively (low-quality evidence).

Vagropoulou *et al.*¹⁰⁹ investigated whether different types of indirect restorations (**inlay, onlay, both inlay and onlay, and crown**) used for single permanent anterior, premolar, or molar teeth had different biological or technical complications, or different survival rates. Based on the narrative and descriptive analysis of the included studies, there was low-quality evidence that the mean survival rate of inlays was 90.9% at 5 years, while for onlays and crowns it was 93.5% and 95.4%, respectively. For the fourth study group, consisting of both inlays and onlays, the survival rate was found to be 99.4%. This means that there was low-quality evidence that indirect restorations demonstrated survival rates over 90%, which was judged to be very high by the review authors. There was no evidence for comparisons between direct and indirect restoration materials.

Morimoto *et al.*²⁹ evaluated the survival rate of **resin and ceramic inlays, onlays, and overlays** at 5 years and 10 years in permanent teeth and identified the types of complications associated with the main negative clinical outcomes. The main findings from this review suggested that there was very low-quality evidence that ceramic inlays, onlays, and overlays produced acceptable high restoration survival rates of over 90% regardless of the ceramic material, study design, or study setting. The pooled estimated survival rate was 95% at 5-year follow-up (95% for glass ceramic and 92% for feldspathic porcelain), and the survival rate decreased to 91% after 10-year follow-up (93% for glass ceramic and 91% for feldspathic

porcelain). According to 13 included studies reporting 106 failures out of 4,800 restorations, the fracture/chipping rate of teeth and/or inlay, onlay, and overlay restorations was 4%. The incidence of endodontic problems was reported as 3%.

Grivas *et al.*¹¹⁰ evaluated clinical performance (longevity, colour match, and post-operative sensitivity) at 12 months or longer of **indirect composite inlays** compared with **direct composite restorations** as well as with **ceramic and gold inlays** in adults with permanent vital teeth restorations. There was low-quality evidence that the survival rate of composite inlays ranged from 100% after 3 years to 51% after 10 years, and that it was not significantly different from that of ceramic or gold materials. There was conflicting evidence on colour match over time and there was no difference for post-operative sensitivity at a follow-up of 1 month. Five primary studies that compared indirect composite inlays with direct composite fillings had follow-up periods ranging from 3.5 to 11 years, and the survival rates for indirect composite inlays varied from 100% after 3.5 years to 87.3% after 11 years, based on low-quality evidence. The authors reported that the studies provide insufficient evidence to identify whether there is a difference in longevity between indirect composite inlays and direct composite fillings. Most of the studies concurred that differences between composite inlays and direct composite fillings with respect to aesthetic quality (colour match and marginal discolouration) and post-operative sensitivity were insignificant. Based on low-quality evidence, composite inlays had similar longevity, colour match, and post-operative sensitivity as ceramic inlays, gold inlays, and direct composite fillings.

Fron Chabouis *et al.*¹¹¹ compared performance of **composite inlays and onlays with ceramic inlays** or onlays for restoring posterior permanent teeth in adults. There was low-quality evidence that the overall 3-year success rate was 94.2% for composite inlays and 97.1% for ceramic inlays. The reported clinical acceptable scores showed considerable heterogeneity between trials and could not be combined. Visual examination of results of the two trials for each measure indicated no difference in outcome.

4.4.1.1.6.3 Comparison of direct and indirect restoration material

We identified four systematic reviews comparing direct and indirect restoration materials for cavitated caries in permanent teeth.^{110,112-114} One review compared all direct and indirect restoration materials with each other,¹¹² while the other three reviews compared direct and indirect resin composite restorations with each other.^{110,113,114} There was very high overlap of the 18 primary studies across the three systematic reviews comparing clinical performance of direct and indirect resin composite restorations, with 17% of the primary studies used in more than one of these three reviews.

The single review comparing all direct and indirect restoration materials in permanent teeth, using data from RCTs, found that the best annual failure rate for **direct restorations** was for amalgam (at 1.9%), and for **indirect restorations** it was metal ceramic (at 0.3%); however, these findings were based on very low-quality evidence. Based on very low-quality evidence, the highest annual failure rate for any method was for zirconia-based ceramic (at 5.1%). Indirect composite resin (3.5%) had a marginally higher failure rate than direct composite resin (2.7%). The failure rate for gold was 0.75%.¹¹²

The other three reviews (one based on moderate-quality evidence and two based on low-quality evidence) found no difference with respect to the clinical performance of direct and indirect resin composite restorations in permanent teeth for most parameters.^{110,113,114} Angeletaki *et al.* found that there was low-quality evidence that direct restorations were statistically significantly less likely to experience marginal discolouration.¹¹³

All direct and indirect restoration materials

Vetromilla *et al.*¹¹² evaluated restorative treatment types and materials for large tooth cavity restorations in permanent posterior teeth in adults with respect to tooth or restoration longevity and ranked them

from best to worst. Based on the results of RCTs (well-designed RCTs are considered the highest-quality source of primary clinical evidence), the best annual failure rate for **direct restorations** was for amalgam (at 1.9%), and for **indirect restorations** it was metal ceramic (at 0.3%); however, these findings were based on very low-quality evidence. Based on very low-quality evidence, the highest annual failure rate for any method was for zirconia-based ceramic (at 5.1%). Indirect composite resin (3.5%) had a marginally higher failure rate than direct composite resin (2.7%). The failure rate for gold was 0.75%.¹¹² From RCTs, indirect methods appear to perform better than direct methods.

Direct and indirect resin composite restorations

Angeletaki *et al.*¹¹³ evaluated the clinical parameters of longevity (secondary caries, post-operative sensitivity, marginal discolouration, and colour match) for **direct and indirect composite restorations** in posterior (molar or premolar) teeth at follow-ups of 3 years or longer. There was low-quality evidence that there were similar survival rates, failure rates, post-operative sensitivity, and colour match of composite restorations in premolars for direct and indirect techniques. In addition, there was low-quality evidence that direct restorations were statistically significantly less likely to experience marginal discolouration.¹¹³

Antonelli da Veiga *et al.*¹¹⁴ compared the differences in clinical performance and longevity of **direct and indirect resin composite restorations** in Class I and Class II cavities in permanent molar and premolar teeth, with at least 2 years of follow-up. There was moderate-quality evidence showing no difference in terms of clinical longevity between direct and indirect resin composite restorations. This conclusion remained valid even when the type of restored tooth was considered. The most common general failures reported were fracture of restoration, anatomical form, tooth fracture, and marginal adaptation for direct resin composite; marginal discolouration, marginal adaptation, fractures, and debonding of restoration for indirect resin composite; and secondary caries for direct inlay/onlay.

Grivas *et al.*¹¹⁰, also mentioned in the section above on indirect restoration material, evaluated clinical performance (longevity, colour match, and post-operative sensitivity) at 12 months or longer of **indirect composite inlays** compared with **direct composite restorations** as well as with **ceramic and gold inlays** in adults with permanent vital teeth restorations. Five primary studies that compared indirect composite inlays with direct composite fillings had follow-up periods ranging from 3.5 to 11 years, and the survival rates for indirect composite inlays varied from 100% after 3.5 years to 87.3% after 11 years, based on low-quality evidence. The authors reported that the studies provide insufficient evidence to identify whether there is a difference in longevity between indirect composite inlays and direct composite fillings. Most of the studies concurred that differences between composite inlays and direct composite fillings with respect to aesthetic quality (colour match and marginal discolouration) and post-operative sensitivity were insignificant.¹¹⁰

4.4.1.1.6.4 Restoration support material

We identified two systematic reviews evaluating restoration support material for cavitated caries in permanent teeth.^{115,116} and the other evaluated adhesives alongside posterior resin composite restorations in permanent teeth.¹¹⁶ As the two systematic reviews measured different interventions, the overlap of primary studies across the two reviews was not assessed.

Schenkel *et al.*¹¹⁵ compared the effects of using **dental cavity liners** with those of not using liners in the placement of Class I and Class II resin-based composite posterior restorations in permanent teeth in children and adults. There was low-quality evidence that the use of liners did not add any benefit to the routine resin-based restorations in permanent posterior teeth in adults in the studies examined. There was no evidence for permanent teeth in children aged under 15 years by 2019.

Reis *et al.*¹¹⁶ compared the effects of posterior resin composite restorations that were bonded using **self-etching** with posterior resin composite restorations that were bonded using **etch-and-rinse adhesives** on the risk and intensity of post-operative sensitivity in permanent dentition (posterior restorations) of adult patients. There was high-quality evidence that the type of adhesive strategy (etch-and-rinse or self-etch) did not seem to influence the risk and intensity of post-operative sensitivity in posterior resin composite restorations.

4.4.1.1.6.5 Restoration processes or techniques

We identified four systematic reviews evaluating restoration processes or techniques for cavitated caries in permanent teeth.¹¹⁷⁻¹²⁰ Each of these four reviews evaluated a different technique. As the four systematic reviews measured different interventions, there was no overlap of primary studies across the four reviews.

Arcanjo Frota Barros *et al.*¹¹⁷ evaluated the risk or benefit (pulp exposure, dentine deposition, microbiological examination, quality of the restoration, and success of maintaining pulpal health) of **selective caries removal** for the treatment of dentinal caries in permanent teeth compared with **non-selective (complete) or stepwise caries removal**. There was very low-quality evidence that selective removal resulted in greater success of maintaining pulp vitality compared with both non-selective (complete) and stepwise excavation.

Göstemeyer *et al.*¹¹⁸ evaluated the efficacy of **atraumatic restorative treatment** compared with conventional restorative treatment for restoring root carious lesions in older adults. There was moderate-quality evidence that there was no significant difference in the failure rates of restorations using atraumatic restorative treatment compared with those using conventional restorative treatment.

Solon de Mello *et al.*¹¹⁹ evaluated whether the survival rates of indirect restorations cemented with self-adhesive resin (cement) in permanent teeth were influenced by the presence or absence of **selective enamel etching**. There was moderate-quality evidence of no statistically significant difference in the clinical longevity of indirect restorations cemented with self-adhesive resin cement in permanent teeth, with or without selective enamel etching, for the time periods 36 months, 48 months, and 78 months.

Deng *et al.*¹²⁰ evaluated the effects of **direct pulp capping using laser treatment** compared with pulpectomy or pulpotomy in patients who required such treatment for their deep carious lesions, and estimated the success of restorations. There was low-quality evidence that the success rate of pulp capping using laser treatment (89.9%) -was statistically significantly higher than that of control groups (67.2%) who had pulpectomy or pulpotomy.

Table 11 Main intervention outcomes for cavitated caries in permanent dentition

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Higher restoration success or survival	Lower restoration failure	Better clinical performance	Adverse events
Non-cavitated caries and cavitated								
Non-invasive, microinvasive, and minimally invasive treatments compared with each other and with other interventions	1	Low	Not applicable	Very low	Not measured	Not measured	Better for non-invasive, microinvasive, and minimally invasive treatments in avoiding retreatments though evidence is uncertain	Not measured
Cavitated caries in permanent teeth								
Different forms of composite resin compared with each other	4	2 low and 2 moderate	Moderate	2 low, 1 moderate or low, and 1 moderate	Not measured	Not measured	May be no difference in all 4 reviews	Not measured
Amalgam compared with composite resin	3	1 critically low, 1 Low, and 1 moderate,	Complete overlap across 2 reviews and none with the other 1: overall very high overlap	Low or no additional evidence	Not measured	May be lower for amalgam	May be better for amalgam (fracture and secondary caries)	Inconsistent findings
Restorative materials for the treatment of root caries	1	Moderate	Not applicable	Low	Not measured	May have high failure for all materials tested	No difference	Not measured
Inlay, onlay, both inlay and onlay, and crown	6	3 critically low and 3 moderate	Moderate	2 very low and 4 low	May have overall high survival at 5 and 10 years	Not measured	Not measured	Not measured

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Higher restoration success or survival	Lower restoration failure	Better clinical performance	Adverse events
Ceramic prostheses (crowns) made by a computer-aided design/computer-aided manufacturing system, compared with those made by a conventional manufacturing system	1	Critically low	Not applicable	Low	May be lower for computer-aided design	Not measured	Not measured	Not measured
All direct and indirect restorations	1	Critically low	Not applicable	Very low	Not measured	Lowest annual failure rate for direct restorations was for amalgam, and for indirect restorations it was metal ceramic. However the evidence is uncertain for findings from this review.	Not measured	Not measured
Direct compared with indirect composite resin restorations	3	1 low and 2 moderate	Very high	2 low and 1 moderate	May have similar survival rates in all 3 reviews	Not measured	Direct restorations may be less likely to experience marginal discolouration in 1 review, and may be no difference in 2 reviews	Not measured
Dental cavity liners compared with no liner	1	Low	Not applicable	Low	May have no difference	Not measured	Not measured	Not measured
Self-etching compared with etch-and-rinse adhesives for bonding posterior resin composite restorations	1	Moderate	Not applicable	High	Not measured	Not measured	No difference for post-operative sensitivity	Not measured

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Higher restoration success or survival	Lower restoration failure	Better clinical performance	Adverse events
Selective caries removal for the treatment of dentinal caries, compared with complete or stepwise caries removal	1	Critically low	Not applicable	Very low	Not measured	Not measured	Better outcome for pulp vitality with selective caries removal, but the evidence is uncertain	Not measured
Atraumatic restorative treatment compared with conventional restorative treatment (root carious lesions)	1	Critically low	Not applicable	Moderate	Not measured	Probably no difference	Not measured	Not measured
Self-adhesive resin cement and presence or absence of selective enamel etching	1	High	Not applicable	Moderate	Not measured	Probably no difference	Not measured	Not measured
Laser treatment of direct pulp capping, compared with pulpectomy or pulpotomy	1	Critically low	Not applicable	Low	May be higher for laser treatment	Not measured	Not measured	Not measured

*AMSTAR 2 overall methodological quality rating: High, moderate, low, or critically low

†Overlap: None, slight, moderate, high, or very high

‡Quality of evidence: High, moderate, low, or very low

4.4.1.2 Non-carious cervical lesions in permanent dentition

4.4.1.2.1 Methodological quality of reviews and their primary studies

We reported in the Methods chapter (Chapter 3) that we assigned four domains in the AMSTAR 2 quality assessment tool as critical domains, and these domains were: using meta-analysis methods appropriately, discussing the effect of heterogeneity on the findings, controlling for unclear or high risk of bias in meta-analyses, and discussing the effect of unclear or high risk of bias on the findings. The quality, with respect to methodology, of the 15 systematic reviews on non-carious cervical lesions was varied (see Appendix L). We identified two reviews on non-carious cervical lesions that did not take account of heterogeneity when discussing their results. We identified eight reviews that could not or did not control for unclear or high risk of bias in their meta-analysis. And we identified four reviews that did not discuss the implications of unclear or high risk of bias in their results.

Seven systematic reviews were judged to be of moderate quality using AMSTAR 2, indicating that they had no critical flaws. However, these seven reviews each had one or more non-critical flaws. Three systematic reviews were considered low quality, with one critical flaw each: failure to control for bias in meta-analysis. Five reviews were classified as critically low quality, with at least two critical flaws each. Four of these reviews failed to control for and discuss the effects of bias, and one of these four reviews did not discuss heterogeneity in its results. The fifth review did not discuss heterogeneity and did not control for risk of bias in its meta-analysis.

4.4.1.2.2 Grading of Recommendations, Assessment, Development and Evaluations (GRADE)

The GRADE of evidence for the main outcomes for each of the systematic reviews of non-carious cervical lesions in permanent dentition is presented alongside each of the outcomes in the Results section 4.5.1.2.4, and the number of downgrades applied and reasons for downgrading are presented in Appendix M. For non-carious cervical lesions in humans' permanent teeth, six reviews had outcomes based on moderate-quality evidence, indicating that the true effect is likely to be close to the estimate of the effect. Ten reviews had outcomes based on low-quality evidence, indicating that confidence in the effect estimate is limited. The count exceeds 15 reviews, as 1 review had more than one GRADE of evidence. The calculated GRADE score included downgrades for inadequate conduct of the systematic review, specifically where primary study design was not randomised, a large proportion of studies had an unclear or high risk of bias in the primary studies, a substantial proportion heterogeneity across the primary studies, and/or inadequate sample sizes. It can be understood that low-quality reviews had two to three of these inadequacies, whereas very low-quality studies had four or more of these shortcomings. Therefore, the GRADE score is used as a summary indicator of the quality of the evidence that is presented. It is important to note that the GRADE score takes account of the methodological quality score of the systematic review and its primary studies.

4.4.1.2.3 Characteristics of reviews and primary studies

The number of participants in the studies on non-carious cervical lesions was reported for 14 of 15 systematic reviews and varied from 112 to 1,486 participants (Appendix N). The participants' ages ranged from 18 to 88 years in the 12 reviews that reported age. Gender was not reported for 10 of the 15 systematic reviews. For the five systematic reviews that reported gender, 21–75% of the participants were male. Only 7 of the 15 reviews reported the study countries where the research was sited, and there was limited global spread of countries: **Africa (Egypt), the Americas (Brazil, Chile, the USA), Asia (China, Japan, Republic of Korea, Turkey), Europe (Belgium, Denmark, Germany, Italy, Liechtenstein, Serbia, Sweden, Switzerland), and Oceania (Australia)**. The primary study designs included in the systematic

reviews were 239 randomised controlled trials and 5 non-randomised controlled trials, and these primary studies were published between 1988 and 2019. None of the primary studies reported the sources of funding for their research.

4.4.1.2.4 Results

Table 12 presents a high-level summary of treatment outcomes for non-carious cervical lesions in permanent dentition.

4.4.1.2.4.1 Factors influencing direct restoration

We found one systematic review that identified **factors influencing direct restorations** in non-carious cervical lesions in permanent teeth.¹²¹ de Oliveira Correia *et al.*¹²¹ evaluated how tooth- and cavity-related properties of non-carious cervical lesions in humans' permanent teeth that already had resin composite restorations affect the retention of such restorations. There was low-quality evidence that the location of the tooth in the dental arch and the presence of wear facets interfere with the retention rate of resin composite restorations in non-carious cervical lesions. In contrast, there was low-quality evidence that other aspects – such as dentine sclerosis, shape, size, depth, occlusogingival distance, and margin location of the cavity – demonstrated no influence on the retention rate.

4.4.1.2.4.2 Direct restoration material

We found three systematic reviews that evaluated direct restorations in non-carious cervical lesions in permanent teeth.^{26,122,123} Two systematic reviews evaluated the performance of composite resin restorations and glass ionomer restorations, and had very high overlap, with 30% of the 27 primary studies being included in both reviews.^{26,122} The third review compared flowable resin composite restorations with conventional resin composite restorations.¹²³ There was low- to moderate-quality evidence that glass ionomer restorations had higher retention rates than composite resin restorations at 3–5 years. There was low-quality evidence that resin composite viscosity does not influence retention rates at 3-year follow-up.

Composite resin restorations and glass ionomer cements

Bezerra *et al.*¹²² evaluated, through a systematic review and meta-analysis, the clinical performance/longevity of **composite resin restorations and glass ionomer restorations** used in adults with non-carious cervical lesions and found low-quality evidence that there was no difference in the colour, surface texture, and incidence of secondary caries between composite resin restorations and glass ionomer restorations used in adults with non-carious cervical lesions at follow-up. All meta-analyses grouped only the data available for the clinical parameters in common, with follow-up times of 12, 24, and 36 months. In addition, there was low-quality evidence that there was a difference in marginal discolouration and marginal adaptation at 36-month follow-up only, with better results obtained from restorations with glass ionomer over composite resin. Finally, there was low-quality evidence that there was a difference in retention at 36 months, with better results obtained from restorations with glass ionomer over composite resin.¹²²

Boing *et al.*²⁶ compared retention and colour match of **glass ionomer restorations with resin-based composite restorations** in non-carious cervical lesions in the permanent teeth of adults. The authors found low- to moderate-quality evidence in favour of glass ionomers, when compared with resin-based composites, for retention up to 3 years (moderate-quality evidence) and 5 years (low-quality evidence).

Flowable resin composite compared with conventional resin composite

Szesz *et al.*¹²³ compared **flowable resin composite restorations with regular (or conventional) resin composites** for improving the marginal adaptation, marginal discolouration, and retention rates of

restorations placed in non-carious cervical lesions in permanent adult teeth. There was low-quality evidence that resin composite viscosity does not influence retention rates at 3-year follow-up. There was low-quality evidence that resin composite viscosity does not influence marginal discolouration or marginal adaptation at 2- and 3-year follow-up, but does influence marginal adaptation at 1-year follow-up.

4.4.1.2.4.3 Restoration support material

We found seven systematic reviews that evaluated restoration support material in non-carious cervical lesions in permanent teeth.¹²⁴⁻¹³⁰ Four reviews evaluated the performance of adhesive systems compared with each other.^{124,127-129} However, only two of the four systematic reviews had similar interventions and comparators, and there was high overlap, with 11% of the 46 primary studies being included across the two reviews for the outcome of marginal discolouration.^{127,129} Two reviews evaluated the chemical composition of different adhesives.^{125,126} One review evaluated the sandwich technique (a lining of glass ionomer cement or resin-modified glass ionomer cement).¹³⁰

The four reviews evaluating the performance of **adhesives** had different comparators, making it difficult to bring the findings together. One review compared the clinical performance of one-step self-etching and two-step self-etching adhesive systems with each other for the treatment of non-carious cervical lesions in the permanent teeth of adults, and found no difference in all except one clinical parameter (marginal adaptation) based on moderate-quality evidence.¹²⁴ Marginal adaptation with two-step self-etching adhesive systems performed better than one-step self-etching for restoration of non-carious cervical lesions. Another review compared two-step self-etch and one-step self-etch with conventional adhesives (three-step etch-and-rinse and two-step etch-and-rinse) and found low-quality evidence that one- or two-step self-etch adhesives had similar clinical performance for treating non-carious cervical lesions as other adhesive systems.¹²⁹ A third review evaluated using either self-etch adhesives or an etch-and-rinse bonding strategy for composite restorations in non-carious cervical lesions in adults' permanent teeth and found that it did not influence retention or the risk of post-operative sensitivity (moderate-quality evidence).¹²⁷ However, there was moderate-quality evidence that using etch-and-rinse adhesives can result in a better reduction of marginal discolouration when compared with using self-etch adhesives at 18-month to 2-year follow-up and at 4–5-year follow-up. A fourth review evaluated the retention rates associated with adhesives and found that glass ionomer had a lower risk of loss (low-quality evidence).¹²⁸ Three-step etch-and-rinse, two-step etch-and-rinse, two-step self-etch, and one-step self-etch adhesive systems had similar risk of loss, indicating equal effect (low-quality evidence). Finally, a two-step self-etch adhesive system had a significantly lower risk of loss of a non-carious cervical lesion restoration compared with a two-step etch-and-rinse adhesive system based on low-quality evidence.

One review, based on moderate-quality evidence, reported that there is no significant difference at follow-ups of 6–72 months in the clinical performance of composite restorations using **alcohol-based compared with acetone-based adhesives**.¹²⁵ The second review, based on low-quality evidence, found that there was no difference in restoration effectiveness between **2-hydroxyethyl methacrylate (HEMA)-free adhesive systems and HEMA-containing** adhesive systems.¹²⁶

There was low-quality evidence that there was no significant difference in restoration retention between the **sandwich technique** and composite resin on its own at 1- and 2-year follow-ups.¹³⁰

Adhesive systems

De Assis *et al.*¹²⁴ evaluated whether there were any differences in clinical performance (including retention) between **one-step self-etching and two-step self-etching adhesive** systems in non-carious cervical lesions. There was moderate-quality evidence that there was no statistically significant difference

in retention of restoration between the use of one-step self-etching compared with two-step self-etching adhesive systems in non-carious cervical lesions. In addition, there was moderate-quality evidence that there were no statistically significant differences in post-operative sensitivity, incidence of secondary caries, colour match, marginal discolouration, and anatomical form between the use of one-step self-etching compared with two-step self-etching adhesive systems for restoration of non-carious cervical lesions. Finally, there was moderate-quality evidence that there was a statistically significant difference in marginal adaptation, with two-step self-etching adhesive systems performing better than one-step self-etching for restoration of non-carious cervical lesions.

Schroeder *et al.*¹²⁷ compared composite restorations in non-carious cervical lesions in adults' permanent teeth bonded using **self-etch adhesives** with those bonded using **etch-and-rinse adhesives** in order to determine post-operative sensitivity, retention rates, and marginal discolouration. There was moderate-quality evidence that using either self-etch adhesives or etch-and-rinse adhesives for composite restorations in non-carious cervical lesions in adults' permanent teeth did not influence the risk of post-operative sensitivity. In addition, there was moderate-quality evidence that using etch-and-rinse adhesives to bond composite restorations in non-carious cervical lesions in adults' permanent teeth can result in a better reduction of marginal discolouration when compared with using self-etch adhesives at 18-month to 2-year follow-up and at 4–5-year follow-up. Finally, there was moderate-quality evidence that there was no difference in retention between etch-and-rinse compared with self-etch adhesives.

Moraes Coelho Santos *et al.*¹²⁸ assessed the effect of different **adhesive systems**, surface treatments, and tooth preparation techniques on the retention of tooth-coloured restorative materials placed in non-carious cervical lesions. There was low-quality evidence that glass ionomer cement has a significantly lower risk of loss of a non-carious cervical lesion restoration compared with either a three-step etch-and-rinse or a two-step etch-and-rinse adhesive system. Also, a three-step etch-and-rinse adhesive system had a significantly lower risk of loss of a non-carious cervical lesion restoration compared with a two-step etch-and-rinse adhesive system. In addition, there was low-quality evidence that there was no significant difference in the risk of loss of a tooth-coloured non-carious cervical lesion restoration between a three-step etch-and-rinse adhesive system and either a two-step self-etch or a one-step self-etch adhesive system, indicating equal effect. Finally, a two-step self-etch adhesive system had a significantly lower risk of loss of a non-carious cervical lesion restoration compared with a two-step etch-and-rinse adhesive system, based on low-quality evidence.

Chee *et al.*¹²⁹ compared simplified adhesives (**two-step self-etch and one-step self-etch**) with conventional adhesives (**three-step etch-and-rinse and two-step etch-and-rinse**) for the treatment of non-carious cervical lesions in the permanent teeth of adults. There was low-quality evidence that one- or two-step self-etch adhesives had similar clinical performance for treating non-carious cervical lesions as other adhesive systems.

Chemical composition of adhesives

Lins *et al.*¹²⁵ assessed whether the type of **solvent** (acetone-based compared with alcohol-based) *in dental adhesives* for composite resin restorations influences the clinical performance (including survival and 10 other parameters) of composite restorations placed in adults with non-carious cervical lesions (Class V restorations). There was moderate-quality evidence that there is no significant difference in the clinical performance of composite restorations at follow-ups of 6–72 months using alcohol-based compared with acetone-based adhesives in terms of retention, marginal adaptation, and marginal discolouration. In addition, there was moderate-quality evidence that there was no statistical difference in survival between the two solvents, indicating that composite restorations placed using either type of adhesive had equal survival rates up to 72-month follow-up.

Sousa Pamplona da Silva *et al.*¹²⁶ compared **HEMA-free adhesive systems with HEMA-containing** systems to treat non-carious cervical lesions in permanent teeth in adults. There was low-quality evidence that there was no difference in restoration effectiveness between HEMA-free adhesive systems and HEMA-containing adhesive systems.

Sandwich technique

Mara de Paula *et al.*¹³⁰ evaluated whether the retention rates of non-carious cervical lesion restorations in adults' permanent teeth that used the **sandwich technique** (a lining of glass ionomer or resin-modified glass ionomer) were greater than those of *composite resin only* restorations. There was low-quality evidence that there was no significant difference in restoration retention between restorations that used the sandwich technique and those that used composite resin on its own at 1- and 2-year follow-ups. In addition, there was low-quality evidence that the sandwich restoration technique had higher retention rates than resin composite on its own at the 3-year follow-up. Finally, there was low-quality evidence that there was no significant difference in restoration colour match, marginal discolouration, marginal adaptation, or incidence of secondary caries between restorations that used the sandwich technique and those that used composite resin on its own at 1-, 2-, and 3-year follow-ups.

4.4.1.2.4.4 Restoration material and support material

We found one systematic review by Schwendicke *et al.*²⁵ that compared the survival of **combinations of adhesive and restorative materials** placed in one of two types of cavitated lesions (cervical cavitated lesions or load-bearing posterior cavitated lesions) with each other in permanent and primary teeth. The lesions may or may not be due to caries. This review is classified as a mixed dentition review; however, we have included these findings in this section of the review as they pertain to non-carious cervical lesions. There was low-quality evidence that resin-modified glass ionomers or, if aesthetics are an issue, conventional resin composites or compomers placed via two-step self-etch adhesives or three-step etch-and-rinse adhesives might be preferred to restore cervical lesions. Additionally, there was low-quality evidence that adhesives combining primer and bonding (two-step etch-and-rinse or one-step self-etch adhesives) were inferior to support restorations of cervical lesions with conventional resin composites or compomers.

4.4.1.2.4.5 Restoration processes or techniques

We found four systematic reviews that evaluated three restoration techniques for non-carious cervical lesions in permanent teeth.¹³¹⁻¹³⁴ None of the reviews examined the same interventions and so comparison across reviews was not feasible.

Rocha *et al.*¹³¹ evaluated the influence of different **dentine surface treatments** on the retention rate of resin composite restorations in non-carious cervical lesions. There was low-quality evidence of reduced risk of restoration loss following removal of sclerotic dentine using a bur. In addition, there was low-quality evidence of reduced risk of restoration loss following application of an adhesive system using a frictional technique. Moreover, there was low-quality evidence of similar risk of restoration loss following application of an adhesive system to dried or untreated dentine.

Szesz *et al.*¹³² compared **selective etching of enamel margins** with no etching to improve the retention rates and marginal discolouration of cervical composite restorations in non-carious cervical lesions in the permanent teeth of adults. There was moderate-quality evidence that the selective enamel etching technique was better than controls for improving the marginal adaptation, discolouration (low at 3-year follow-up only), and retention of composite restorations in non-carious cervical lesions in the adult population.

Schroeder *et al.*¹³³ compared **enamel bevelling with no enamel bevelling** to improve the retention of composite restorations in non-carious cervical lesions in the permanent teeth of adult patients. There was moderate-quality evidence that outcomes for bevelling prior to restoration were similar to no bevelling.

Qin *et al.*¹³⁴ compared the clinical effectiveness (retention, marginal defects, and marginal discolouration) of self-etching adhesives, with or without previous **enamel bevelling and selective phosphoric acid etching**, in restorations of non-carious cervical lesions in adults' permanent teeth. There was low-quality evidence that the differences in restoration retention rates between self-etching adhesives, with or without previous enamel bevelling, were not statistically significant. In addition, there was low-quality evidence that the prevalence of marginal defects and marginal discolouration in the self-etching adhesives without previous enamel bevelling group was significantly higher than that in the self-etching adhesives with enamel bevelling group.

Table 12 Main intervention outcomes for non-carious cervical lesions in permanent dentition

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Higher restoration success or survival	Lower restoration failure	Better clinical performance	Adverse events
Non-carious cervical lesions in permanent teeth								
Effect of tooth- and cavity-related properties of non-carious cervical lesions on existing resin composite restorations (retention)	1	Moderate	Not applicable	Low	Not measured	Not measured	Location of the tooth in the dental arch and the presence of wear facets may interfere with the retention rate	Not measured
Glass ionomer cement compared with resin-based composites (retention)	2	2 low	Very high	1 low and 1 moderate or low	Not measured	Not measured	May be better for retention in intervention group	Not measured
Flowable resin composite restorations compared with conventional resin composites	1	Low	Not applicable	Low	Not measured	Not measured	May have no difference	Not measured
One-step self-etching compared with two-step self-etching adhesive systems	1	Critically low	Not applicable	Moderate	Not measured	Not measured	Probably negative for marginal adaptation in the intervention group and no difference for other parameters	Not measured
Adhesive systems compared with each other	1	Critically low	Not applicable	Low	Not measured	Not measured	Glass ionomer cement may be the best performer	Not measured
Simplified adhesives (two-step self-etch and one-step self-etch) compared with conventional adhesives (three-step etch-and-rinse and two-step etch-and-rinse)	2	2 moderate	Not applicable	1 low and 1 moderate	Not measured	Not measured	Simplified adhesives may not be as good for marginal discolouration, and may have no difference for all other parameters	Not measured
HEMA-free adhesive systems compared with HEMA-containing adhesive systems	1	Critically low	Not applicable	Low	Not measured	Not measured	May have no difference	Not measured
Acetone-based solvent compared with alcohol-	1	Moderate	Not applicable	Moderate	Not measured	Not measured	Probably have no difference	Not measured

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Higher restoration success or survival	Lower restoration failure	Better clinical performance	Adverse events
based solvent in dental adhesives								
Combinations of adhesive systems with restoration support materials (conventional resin composites or compomers)	1	Low	Not applicable	Low	Not measured	Not measured	May have positive outcomes for two-step self-etch adhesives or three-step etch-and-rinse adhesives when compared with two-step etch-and-rinse or one-step self-etch adhesives.	Not measured
Retention rate of resin composite restorations using different dentine surface treatments, compared with each other	1	Critically low	Not applicable	Low	Not measured	Not measured	May have positive outcome for removing sclerotic dentine. May have positive outcome for application of an adhesive system using a frictional technique.	Not measured
Etching of enamel margins, compared with no etching, to improve retention rates and marginal discolouration	1	Moderate	Not applicable	Moderate	Not measured	Not measured	Probable positive for both measures	Not measured
Enamel bevelling, compared with no enamel bevelling, to improve the retention of composite restorations	1	Moderate	Not applicable	Moderate	Not measured	Not measured	Probably no difference	Not measured
Clinical effectiveness of self-etching adhesives, with or without previous enamel bevelling and selective phosphoric acid etching	1	Critically low	Not applicable	Low	Not measured	Not measured	May have no difference in retention. May have positive outcomes for marginal defects and marginal discolouration in no bevelling group.	Not measured

*AMSTAR 2 overall methodological quality rating: High, moderate, low, or critically low

†Overlap: None, slight, moderate, high, or very high

‡Quality of evidence: High, moderate, low, or very low

4.5 Mixed dentition

4.5.1 Introduction

Mixed dentition systematic reviews included studies that reported including young people who had, at the time of the study, both primary and permanent teeth in their oral cavity, as well as studies that covered both the primary and permanent teeth populations, and studies that reported including human teeth that could not be classified as either primary or permanent teeth.

The 42 reviews on mixed dentition included 19 reviews covering the treatment of cavitated caries, 15 reviews on the treatment of non-cavitated caries, and 8 reviews on the treatment of non-cavitated caries and cavitated combined. The 19 reviews on the treatment of cavitated caries included 2 reviews on direct restoration material, 5 reviews on restoration support material, 1 paper on combining restoration material and support material, and 11 reviews on restoration processes or techniques. The 15 reviews on the treatment of non-cavitated caries comprised 7 reviews on non-invasive treatment and 8 reviews on microinvasive treatment. The eight reviews on the treatment of non-cavitated caries and cavitated combined included three reviews on the topic of non-invasive treatment, one paper on microinvasive and invasive treatment, one paper on non-invasive and microinvasive treatments, two reviews on microinvasive and restorative treatment, and one paper on treatment technique.

4.5.2 Methodological quality of reviews and their primary studies

We reported in the Methods chapter (Chapter 3) that we assigned four domains in the AMSTAR 2 quality assessment tool as critical domains, and these were: using meta-analysis methods appropriately, discussing the effect of heterogeneity on the findings, controlling for unclear or high risk of bias in meta-analyses, and discussing the effect of unclear or high risk of bias on the findings. The quality, with respect to methodology, of the 42 systematic reviews on mixed dentition with caries was varied (see Appendix L). We found six reviews on mixed dentition that did not use an appropriate approach to meta-analysis. We identified eight reviews that did not take account of heterogeneity when discussing their results. We identified 22 reviews that could not or did not control for unclear or high risk of bias in their meta-analysis. And we observed that nine reviews did not discuss the implications of unclear or high risk of bias on their results.

Two reviews were judged high quality using AMSTAR 2, indicating that the reviews had no flaws or weaknesses. Twelve reviews were rated moderate quality, indicating that they had no critical flaws, but that they had one or more non-critical weaknesses. Sixteen reviews were judged low quality, indicating that they had one critical flaw; for 15 of these reviews, this was due to failure to control for bias in the meta-analysis, and for the remaining review this was due to failure to address bias in the discussion. Eleven reviews were considered critically low quality, with each having at least two critical flaws. Two reviews had all four critical flaws. Three reviews each had three critical flaws: the first failed to control for and discuss the effects of bias and did not discuss heterogeneity; the second failed to discuss the effects of bias and heterogeneity in the discussion, and did not use the appropriate method of meta-analysis; and the third failed to use the appropriate method of meta-analysis, did not control for the effects of bias in the meta-analysis, and did not discuss heterogeneity. Six reviews had two critical flaws each: the first failed to control for and discuss the effects of bias, the second failed to control for the effects of bias and discuss heterogeneity, the third did not use the appropriate method of meta-analysis and did not control for the effects of bias, the fourth did not use the appropriate method of meta-analysis and did not discuss the effects of bias on its findings and the remaining two did not discuss heterogeneity and did not discuss risk of bias in the results. One of the systematic reviews on mixed dentition did not find any studies on the topic of interest, and therefore, could not receive a complete quality assessment.

4.5.3 Grading of Recommendations, Assessment, Development and Evaluations (GRADE)

The GRADE of evidence for the main outcomes for each of the systematic reviews is presented alongside each of the outcomes in the Results section 4.6.5, and the number of downgrades applied and reasons for downgrading are presented in Appendix M. For mixed dentition, 14 reviews had outcomes based on moderate-quality evidence, indicating that the true effect is likely to be close to the estimate of the effect; 24 reviews had outcomes based on low-quality evidence, indicating that confidence in the effect estimate is limited; and 12 reviews had outcomes based on very low-quality evidence, indicating very little confidence in the effect estimate. One review had no evidence with which to carry out a GRADE analysis. The count exceeds 42 reviews, as 9 reviews had more than one GRADE of evidence. The calculated GRADE score included downgrades for inadequate conduct of the systematic review, specifically where primary study design was not randomised, a large proportion of studies had an unclear or high risk of bias in the primary studies, a substantial proportion heterogeneity across the primary studies, and/or inadequate sample sizes. It can be understood that low-quality reviews had two to three of these inadequacies, whereas very low-quality reviews had four or more of these shortcomings. Therefore, the GRADE score is used as a summary indicator of the quality of the evidence that is presented. It is important to note that the GRADE score takes account of the methodological quality score of the systematic review and its primary studies.

4.5.4 Characteristics of reviews and primary studies

The number of participants in the studies on mixed dentition was reported for 37 of 42 systematic reviews and varied from 48 to 13,603 participants (Appendix N). For the 31 reviews that reported age, the participants' ages ranged from 2 to 101 years. Gender was not reported for 32 of the 42 systematic reviews. For the nine systematic reviews that reported gender, 22–63% of participants were male. Twenty-two of the 42 reviews reported the study countries where the research was sited, and there was a spread of countries across the globe: **Africa (Egypt, Kenya, Nigeria, South Africa, Tanzania, Zimbabwe), the Americas (Argentina, Brazil, Canada, Chile, Colombia, Cuba, Ecuador, Mexico, Panama, Suriname, Uruguay, the USA), Asia (China [including Hong Kong], India, Indonesia, Iran, Iraq, Kuwait, Malaysia, Nepal, Pakistan, Republic of Korea, Saudi Arabia, Syria, Taiwan, Thailand, Turkey), Europe (Albania, Bulgaria, Denmark, Estonia, Germany, Greenland, Ireland, Latvia, the Netherlands, Poland, Serbia, Spain, Sweden, Switzerland, the UK), and Oceania (Australia, New Zealand).** The primary study designs included in the systematic reviews consisted of 408 randomised controlled trials, 69 non-randomised controlled trials, and 31 prospective or retrospective cohort studies; these primary studies were published between 1969 and 2020. Ten of the systematic reviews had primary studies that reported industry funding for their research, and 1 systematic review reported that its primary studies had no industry funding. Thirty systematic reviews did not report or were unable to identify funding sources for the included primary studies.

4.5.5 Results

4.5.5.1 Non-cavitated caries

Table 13 presents a high-level summary of treatment outcomes for non-cavitated caries in mixed dentition.

4.5.5.1.1 Non-invasive treatment

We identified seven systematic reviews on the topic of non-invasive treatment for non-cavitated caries in primary and permanent teeth.¹³⁵⁻¹⁴¹ One review evaluated the remineralisation potential of NovaMin.¹³⁵

Two reviews examined the remineralisation ability of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) on its own. There was no overlap of primary studies across these two systematic reviews.^{136,137} Four reviews evaluated the remineralisation and arresting potential of fluoride.¹³⁸⁻¹⁴¹ There was very high overlap (40%) of five primary papers across two of the four systematic reviews evaluating the same fluoride intervention.^{139,140} These reviews examined the effectiveness of professionally applied fluoride products. One of the other two reviews compared different remineralisation agents (fluoride products, CPP-ACP, and resin infiltration (ICON plc. resin) and techniques with each other, and there was slight overlap (one primary paper) between this systematic review by Paula *et al.*¹⁴¹ and the reviews by Gao *et al.*^{139,142} and Lenzi *et al.*,¹⁴⁰ with one primary study used across all three reviews. There was no overlap with the review by Chong *et al.*¹³⁸

One review found low-quality evidence based on one trial that there was no statistically significant difference between the NovaMin group and the control group (Crest toothpaste) in remineralising capacity.¹³⁵ Three reviews found that CPP-ACP was as effective for remineralisation as fluoride (moderate- or low-quality evidence),^{136,137,141} and it was better than no intervention in two reviews (moderate- or low-quality evidence).^{136,141} There was low-quality evidence, based on a review with one trial, that slow-release fluoride devices (glass beads) helped reduce dental decay.¹³⁸ Three reviews (two based on low-quality evidence and one based on moderate-quality evidence) reported that fluoride varnish was an effective remineralising agent for targeting early caries in primary teeth¹³⁹⁻¹⁴¹ and two of the three reviews reported a similar finding for permanent teeth.^{140,141} One review, based on very low-quality evidence, found that silver diamine fluoride was more effective than controls for remineralising and arresting the progression of active caries in both primary and permanent teeth in children and adolescents.¹³⁹

4.5.5.1.1.1 NovaMin

Khijmatgar *et al.*¹³⁵ evaluated the **remineralisation potential of NovaMin** compared with placebo or no intervention in humans with evidence of demineralisation (white spot lesions and/or cavitation) on teeth. There was low-quality evidence based on one trial that there was no statistically significant difference between the NovaMin group and the control group (Crest toothpaste) with respect to remineralising capacity.

4.5.5.1.1.2 Casein phosphopeptide-amorphous calcium phosphate

Ma *et al.*¹³⁶ evaluated the efficacy of **CPP-ACP** compared with no intervention or a placebo for the remineralisation of white spot lesions. There was moderate-quality evidence that there was no significant difference between using tooth mousse with CPP-ACP or fluoride toothpaste with active tooth mousse and the comparators (standard fluoride toothpaste or standard fluoride toothpaste with placebo tooth mousse).

Li *et al.*¹³⁷ compared the use of **CPP-ACP** in any modality **with the use of fluoride** toothpastes or mouthwashes, placebos, topical creams, and chewing gum in order to assess their long-term (>3 months) remineralising effect on early carious lesions. There was low-quality evidence that CPP-ACP was better than no intervention; however, it offered no advantage as a supplement to fluoride.

4.5.5.1.1.3 Fluoride

Chong *et al.*¹³⁸ compared the retention, effectiveness, and safety of different types of **slow-release fluoride devices** for preventing, arresting, or reversing the progression of carious lesions on all surface types of primary and permanent teeth at 12-month follow-up. There was low-quality evidence based on one trial to determine whether slow-release fluoride devices (glass beads) help reduce dental decay. The incidence of decayed, missing, and filled permanent teeth or primary teeth or their surfaces at 2-year

follow-up was statistically significantly better in treated than in non-treated populations. Caries increment was significantly lower at 24 months in the intervention group. The primary study authors stated that no irritations or other harms were reported.¹³⁸

Gao *et al.*^{139,142} compared professionally applied **fluoride therapy** with other active treatments, with placebo, or with no intervention in remineralising and arresting dental caries in primary and permanent teeth in children. There was low-quality evidence to suggest that fluoride varnish was an effective remineralising agent for targeting early caries in primary teeth and very low-quality evidence that silver diamine fluoride was more effective than controls for remineralising and arresting the progression of active caries in both primary and permanent teeth in children and adolescents.¹³⁹

Lenzi *et al.*¹⁴⁰ evaluated the effectiveness of professional topical **fluoride** application (gels or varnishes) on the reversal of incipient enamel carious lesions in primary or permanent dentition in children. There was very low-quality evidence that fluoride varnish was an effective treatment for the reversal of incipient carious lesions in primary and permanent dentition. Additionally, there was very low-quality or no evidence as to the effectiveness of fluoride gel as a treatment for the reversal of incipient carious lesions in primary and permanent dentition.¹⁴⁰

4.5.5.1.1.4 Combination of remineralisation agents

Paula *et al.*¹⁴¹ compared **different remineralisation agents** (fluoride products, CPP-ACP, and resin infiltration) and techniques with each other for the treatment of white spot lesions in both permanent and primary teeth. There was no age cut-off, and both permanent and primary teeth were included. Most of the 13 studies included in this narrative analysis reported that therapy with remineralising agents reduces white spot lesions (in terms of their size or visual appearance) and this finding is based on moderate-quality evidence. Most of the six primary studies evaluating remineralising agents reported that such agents reduced white spot lesions (in terms of their size or visual appearance), although only two demonstrated a statistically significant improvement, and this finding was based on moderate-quality evidence. Three studies of the effects of CPP-ACP on remineralising white spot lesions demonstrated improvements, and the improvements were significant in two of these studies; this finding is based on moderate-quality evidence. One study on ICON resin, based on low-quality evidence, indicated significant regression of white spot lesions, either in size or in their clinical visual appearance. There was moderate-quality evidence that when fluoride was compared with CPP-ACP, both products demonstrated improvements in white spot lesions but neither product was significantly better than the other.¹⁴¹

4.5.5.1.2 Microinvasive treatment

We identified eight systematic reviews on the topic of microinvasive treatment for non-cavitated caries in primary and permanent teeth.¹⁴³⁻¹⁵⁰ Five examined infiltration and sealing^{143,147-150} and three examined infiltration only.¹⁴⁴⁻¹⁴⁶ For the intervention of sealing, there was very high overlap (30%) of 15 primary studies across the 5 systematic reviews examining the outcome of arresting or slowing caries progression. In addition, there was very high overlap (17%) of the 31 primary studies across the 8 systematic reviews examining the outcome of arresting or slowing caries progression for the intervention of resin infiltration.

There was consistent evidence reported in eight systematic reviews that resin infiltration is effective for reducing and/or arresting the progression of non-cavitated proximal carious lesions in primary and permanent teeth (moderate- or low-quality evidence).¹⁴³⁻¹⁵⁰ Five reviews reported that sealing demonstrated effectiveness for reducing and/or arresting the progression of non-cavitated proximal carious lesions in primary and permanent teeth (moderate- or low-quality evidence).^{143,147-150}

Chen *et al.*¹⁴³ evaluated the caries-arresting effectiveness of **infiltration and sealing** for proximal non-cavitated carious lesions and beyond, including different dentition types and caries risk levels in humans.

For both primary and permanent dentition, there was moderate-quality evidence that both infiltration and sealing were more effective at reducing lesion progression than both placebo and non-invasive treatments. There was low-quality evidence that the overall positive effects of infiltration and sealing were significantly better in those classified as having high or low caries risk compared with the effects of control interventions.

Elrashid *et al.*¹⁴⁴ evaluated the efficacy (clinical performance) of **resin infiltration** (compared with placebo or control material) on non-cavitated proximal carious lesions in primary and permanent teeth in humans. The risk of carious lesion progression in primary teeth and in permanent teeth was significantly lower with resin infiltration compared with that of control or placebo based on moderate-quality evidence.

Faghihian *et al.*¹⁴⁵ evaluated the efficacy (clinical performance) of the **resin infiltration** technique in arresting initial caries progression in both primary and permanent teeth compared with control groups such as placebo, fluoride therapy, and oral health instruction. There was moderate-quality evidence that resin infiltration significantly reduced the risk of caries progression in primary and permanent teeth compared with the control groups.

Chatzimarkou *et al.*¹⁴⁶ set out to provide a comprehensive synthesis of **resin infiltration** effects, in vivo, on early proximal carious lesions in primary and permanent teeth. There was moderate-quality evidence that resin infiltration combined with non-invasive oral hygiene measures resulted in significantly (86%) lower odds for early proximal carious lesion progression when compared with non-invasive methods (control) at 18–24-month follow-up, and there were similar findings with respect to resin infiltration at 36-month follow-up.

Krois *et al.*¹⁴⁷ evaluated **microinvasive treatments** compared with each other, non-invasive treatments, placebo, or no treatment to arrest early non-cavitated proximal carious lesions in the primary and permanent teeth of children, adolescents, and young adults. There was moderate-quality evidence that **sealing and/or infiltration** was effective for arresting early (non-cavitated) proximal lesions compared with non-invasive treatment or no intervention. However, there was moderate-quality evidence that sealing was neither superior nor inferior to infiltration for arresting proximal caries.

Liang *et al.*¹⁴⁸ compared the effectiveness of **microinvasive interventions** with non-invasive measures (e.g. fluoride), a placebo, or no treatment in arresting non-cavitated proximal carious lesions and analysed their effectiveness in acting on carious lesions of different depths. There was moderate-quality evidence in favour of **resin infiltration and sealant** for arresting the progression of non-cavitated proximal caries. However, there was insufficient and low-quality evidence upon which to judge the effectiveness of glass ionomer cements or resin sealants at different caries depths.

Dorri *et al.*¹⁴⁹ compared **microinvasive treatments** with non-invasive measures, invasive measures, no intervention, or a placebo for managing proximal carious lesions in primary and permanent dentition in children and adults. There was moderate-quality evidence for microinvasive treatment (**resin infiltration or sealing**) for managing proximal carious lesions in primary and permanent dentition over non-invasive professional treatment (e.g. fluoride varnish) or advice (e.g. to floss).

Ammari *et al.*¹⁵⁰ evaluated the effectiveness (caries arrest and control) of **sealing and/or infiltration** compared with placebo or other materials or techniques to treat non-cavitated proximal lesions in primary and permanent teeth. There was moderate-quality evidence favouring infiltration over placebo to arrest caries in non-cavitated proximal lesions in primary and permanent teeth.

Table 13 Main intervention outcomes for non-cavitated caries in mixed dentition

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Arrest caries progression	Remineralisation	Adverse events
Non-cavitated caries							
NovaMin and the control group (Crest toothpaste)	1	Moderate	Not applicable	Low	Not measured	May have no difference	Not reported
CPP-ACP compared with commercial fluoride products and no intervention	3	Moderate	None	1 low, 1 moderate or low, and 1 moderate	Not measured	Mixed findings	Not reported
Fluoride compared with other active treatments, with placebo, or with no intervention	3	1 critically low, 1 moderate, and 1 high	Very high for 2 reviews on fluoride varnish and gel	2 low and 1 moderate	Not measured	May have positive effect for fluoride beads, fluoride varnish, and silver diamine fluoride. No evidence for fluoride gel.	Not reported
Sealing compared with each other, with non-invasive treatments (e.g. fluoride), with placebo, or with no treatment	5	3 low and 2 moderate	Very high	3 moderate and 2 moderate and low	May be better for sealing	Not measured	Not reported
Infiltration compared with each other, with non-invasive treatments (e.g. fluoride), with placebo, or with no treatment	8	1 critically low, 5 low, and 2 moderate	Very high	6 moderate and 2 moderate and low	May be better for infiltration	Not measured	Not reported

*AMSTAR 2 overall methodological quality rating: High, moderate, low, or critically low

†Overlap: None, slight, moderate, high, or very high

‡Quality of evidence: High, moderate, low, or very low

4.5.5.2 Non-cavitated and cavitated caries

Table 14 presents a high-level summary of treatment outcomes for non-cavitated caries and cavitated caries in mixed dentition.

4.5.5.2.1 Non-invasive treatment

We identified three systematic reviews on the topic of non-invasive treatment for non-cavitated caries and cavitated caries in primary and permanent teeth: one covering ozone therapy¹⁵¹ and two covering silver diamine fluoride.^{139,152} There was high overlap (11%) of the 18 primary studies across the two systematic reviews covering the silver diamine fluoride intervention.

One review reported low or very low-quality evidence that ozone therapy was more effective for reducing lesion progression and severity compared with no ozone (compressed air) or no treatment. The same review reported that ozone therapy was as effective as fluoride varnish, and it was less effective than chlorhexidine digluconate.¹⁵¹

Two reviews (one with moderate-quality evidence and one with very low-quality evidence) reported that 38% and/or 30% concentrations of silver diamine fluoride arrested caries in primary teeth.^{139,152} The two reviews reported differing findings for permanent teeth: one review concluded there was not enough evidence to assess the effectiveness in permanent molars¹⁵² whereas the other review reported that silver diamine fluoride was not more effective than comparators (very low-quality evidence).¹³⁹

Marcílio Santos *et al.*¹⁵¹ evaluated the effectiveness (antimicrobial effect and lesion progression or regression) and safety (adverse events) of **ozone therapy** compared with no treatment, sham, or any other antibacterial intervention (including pharmacological and non-pharmacological treatments) for treating cavitated and non-cavitated dental caries in participants of any age. There was low-quality evidence that ozone therapy was more effective for reducing lesion progression and severity compared with no ozone (compressed air) or no treatment. Additionally, there was low-quality evidence that ozone therapy was less effective than chlorhexidine digluconate in the short and medium term, but not in the long term, for reducing the total bacterial count. Analysis of this outcome based on bacteria species indicates that chlorhexidine was effective in reducing both *Streptococcus mutans* and *Lactobacillus*, but the effect was stronger for *Lactobacillus* based on low-quality evidence. Based on low-quality evidence, ozone therapy demonstrated a significantly higher reduction in total bacterial counts compared with sealant at the time of temporary restoration removal, and no difference after final excavation and permanent restoration. There was a significant decrease in lesion progression favouring the sealant group over the ozone group at long-term follow-up; however, there was no difference at short- and medium-term follow-ups. The results showed no significant difference in lesion progression between ozone added to sealant and sealant alone in the short and long term, based on low-quality evidence. One included study examined lesion progression following ozone therapy compared with fluoride varnish and showed no significant reduction in lesion progression between groups at long-term follow-up. Another primary study assessed the effects of ozone therapy compared with fluoride gel and presented improvement in favour of ozone therapy for lesion progression at long-term follow-up. The meta-analysis of two trials found no statistically significant difference between ozone and fluoride with respect to the severity of carious lesions following treatment. All these findings are based on very low-quality evidence. No adverse events were reported for any of the five comparisons.¹⁵¹

Chibinski *et al.*¹⁵² evaluated the efficacy of **silver diamine fluoride** in controlling (arresting) caries progression in children's primary or permanent teeth when compared with active treatments (different doses of silver diamine fluoride, fluoride varnish, sealant, and atraumatic restorative technique) or placebos (water or saline). There was moderate-quality evidence that the arrestment of caries in primary

teeth at 12 months promoted by silver diamine fluoride (at both 38% and 30% concentrations, and nanosilver fluoride) was significantly higher than that by other active material or placebo. There was not enough evidence to assess the effectiveness in permanent molars.

Gao *et al.*¹³⁹ evaluated the effectiveness of **silver diamine fluoride** in arresting dental caries in primary or permanent teeth in children, using prospective clinical studies. Two studies investigating the caries-arresting effect of 38% silver diamine fluoride in permanent teeth did not find that it was better than its comparators, based on very low-quality evidence. The pooled analysis of eight studies found that the caries-arresting rate of 38% silver diamine fluoride treatment in children's primary teeth was 81%. Apart from staining the arrested carious lesions black, the 19 clinical trials did not report any significant complications arising from silver diamine fluoride use among children, based on very low-quality evidence.

4.5.5.2.2 Microinvasive and invasive treatment

We identified one systematic review on the topic of microinvasive and invasive treatment for non-cavitated caries and cavitated caries in primary and permanent teeth.¹⁵³ de Amorim *et al.*¹⁵³ evaluated the survival rate of **atraumatic restorative treatment glass ionomer restorations and atraumatic restorative treatment sealants** in primary and permanent posterior teeth. There was very low-quality evidence that the survival rates of single-surface and multiple-surface atraumatic restorative treatment restorations in primary posterior teeth over the first 2 years were 94.3% and 65.4%, respectively. Additionally, there was very low-quality evidence that single-surface atraumatic restorative treatment restorations in permanent posterior teeth over the first 3 years had a survival rate of 87.1%, and multiple-surface atraumatic restorative treatment restorations in permanent posterior teeth over the first 5 years had a survival rate of 77.0%. Based on very low-quality evidence, the weighted average annual failure rates of completely lost atraumatic restorative treatment sealants in permanent posterior teeth over the first 3 and 4 years were 10.7% and 9.6%, respectively. The average annual failure percentages for dentine carious lesions in previously sealed pits and fissures using atraumatic restorative treatment sealants in permanent posterior teeth were 0.9% at 3 years and 1.9% at 5 years, again based on very low-quality evidence.

4.5.5.2.3 Non-invasive and microinvasive treatment

We identified one systematic review on the topic of non-invasive and microinvasive treatment for non-cavitated caries and cavitated caries in primary and permanent teeth. Urquhart *et al.*¹⁵⁴ compared **non-restorative treatments** with other active intervention(s), or with no treatment or a placebo, for the arrest or reversal of non-cavitated and cavitated carious lesions in primary and permanent teeth in children and adults. This systematic review was prepared to inform the development of clinical guidelines in the USA. There was a series of findings from this large-scale systematic review, as follows:

- There was low-quality evidence that the combination of either **resin infiltration or sealants with 5% sodium fluoride varnish** for arrest or reversal of non-cavitated carious lesions on occlusal surfaces in primary and permanent teeth is superior to most other treatments.
- There was very low-quality evidence that the **combination of resin infiltration and 5% sodium fluoride varnish** was better than no treatment for non-cavitated carious lesions on approximal surfaces in primary and permanent teeth.
- There was very low-quality evidence that **sealants or resin infiltration** were more effective than no treatment intervention for arrest or reversal of non-cavitated carious lesions on approximal surfaces in primary and permanent teeth.

- There was low-quality evidence that **30% silver diamine fluoride** solution, applied annually, is better than 30% silver diamine fluoride solution applied once per week for 3 weeks or 5% sodium fluoride varnish applied once per week for 3 weeks on any coronal surface for arrest or reversal of carious lesions.
- There was low-quality evidence that **38% silver diamine fluoride** solution, applied biannually, was better than 38% silver diamine fluoride solution applied annually or 12% silver diamine fluoride solution applied annually on any coronal surface for arrest or reversal of carious lesions.
- There was low-quality evidence that **5% sodium fluoride varnish** was more effective than some other non-invasive treatments or no treatment for arresting or reversing carious lesions on any coronal surface of primary and permanent teeth.
- There was low-quality evidence that the use of **1.23% acidulated phosphate fluoride gel** on facial/lingual lesions for arresting or reversing such lesions was more effective than oral health education, although only at longer follow-up times.
- There was low-quality evidence to suggest that **5000 ppm fluoride** (1.1% sodium fluoride) **toothpaste** or gel was more effective than no intervention for arresting or reversing non-cavitated and cavitated carious lesions on root surfaces in permanent teeth.

4.5.5.2.4 Microinvasive and restorative treatment

We identified two systematic reviews on the topic of microinvasive and restorative treatment for non-cavitated caries and cavitated caries in primary and permanent teeth.^{155,156} One review included studies that measured bisphenol A in urine only¹⁵⁵ while the other review included studies that measured bisphenol A in saliva and blood as well as in urine.¹⁵⁶ Both covered the release of bisphenol A into the body after the use of composite resins and/or dental sealants. There was very high overlap (50%) of the 10 primary studies measuring urinary bisphenol A across the two systematic reviews.

There was low-quality evidence in both reviews that there is bisphenol A exposure in humans from resin-based dental sealants and restorations, but its consequences were not yet known (no evidence).^{155,156} On the other hand, one primary study, in an evaluation of resin use followed immediately by mouthwash, demonstrated an abrupt decrease in bisphenol A levels.¹⁵⁶

Marzouk *et al.*¹⁵⁵ evaluated **bisphenol A exposure** in humans from resin-based dental sealants and restorations which contain bisphenol A glycidyl methacrylate by retrieving all clinical studies that measured urinary bisphenol A concentrations in patients before and after resin-based dental treatments. Additionally, the authors explored the degree to which baseline bisphenol A concentrations were associated with prior resin-based dental treatments. There was low-quality evidence that urinary bisphenol A concentrations increased 24 hours after treatment. There was also some suggestion of an increase at 7 days post-treatment. Beyond 1 week of treatment, the evidence was uncertain.

Paula *et al.*¹⁵⁶ estimated the **release of bisphenol A** after the use of composite resins and/or dental sealants in order to determine if the increase is higher than the acceptable daily exposure and whether it may cause harmful effects to the health of children, adolescents, and pregnant adults. However, harmful effects were not examined. All 15 primary studies of salivary content showed an increase in the levels of bisphenol A within 1 hour of the treatments, either with composite resins or with sealants, and these findings were based on low-quality evidence. This increase in bisphenol A in most studies ranged from 2 to 42 ng/mL (nanograms per millilitre), although there are some reports of extreme values ranging from 120 to 931 ng/mL. In follow-ups, the levels decrease over time – for example, from immediately after treatment to 1 week after treatment. Some studies have evaluated the levels of bisphenol A by the

number of surfaces restored or sealed, with an exponential increase in levels from six surfaces upwards. On the other hand, one study performed the evaluation after the treatment followed by mouthwash, demonstrating an abrupt decrease in bisphenol A levels. The authors do not mention the age cut-off for rinsing with mouthwash.

Two of the four primary studies that evaluated levels of bisphenol A in the blood reported that it was not detected in serum at any of the follow-up time points; however, these findings were based on low-quality evidence. Five primary studies evaluating urinary levels of bisphenol A immediately after treatment reported that levels increase slightly after resin-based treatments, but not as markedly as levels detected in saliva.

One study measured the estrogenic assay, and an increase immediately after treatment from 0.1 to 1.43 ppm was observed, with only one type of fissure sealant (Delton®); however, levels decreased to below 0.1 ppm after 24 hours. This finding was based on low-quality evidence.

4.5.5.2.5 Treatment technique

We identified one systematic review on the topic of treatment technique for non-cavitated caries and cavitated caries in primary and permanent teeth.¹⁵⁷ Wang *et al.*¹⁵⁷ compared the effects (survival and failure) of **rubber dam isolation** compared with other types of isolation (cotton roll) used for direct and indirect restorative treatments in children's molars. There was low-quality evidence that dental restorations had a significantly higher survival rate in the rubber dam isolation group compared with the cotton roll isolation group at 6-month follow-up in participants receiving composite restorative treatment of non-carious cervical lesions. In addition, there was low-quality evidence that the rubber dam group had a lower risk of failure at 2-year follow-up in children undergoing proximal atraumatic restorative treatment in primary molars. Finally, there was low-quality evidence from one trial that reported limited data showing that rubber dam usage during fissure sealing might shorten the treatment time.

Table 14 Main intervention outcomes for non-cavitated caries and cavitated caries in mixed dentition

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Arrest caries progression	Remineralisation	Higher restoration success or survival	Lower restoration failure	Better clinical performance	Adverse events
Non-cavitated caries and cavitated										
Ozone therapy compared with no treatment, sham, or any other antibacterial intervention	1	Low	Not applicable	Low or very low	May be more effective compared with no ozone or no treatment. No difference compared with fluoride varnish (uncertain evidence). Less effective than chlorhexidine digluconate (uncertain evidence).	Not measured	Not applicable	Not applicable	Not applicable	None identified
Silver diamine fluoride compared with other active treatments	2	1 critically low and 1 low	High	1 very low and 1 moderate	May be more effective for primary teeth. Inadequate evidence for permanent teeth.	Not measured	Not applicable	Not applicable	Not applicable	Probable black discolouration
5% sodium fluoride varnish on occlusal surfaces, compared with other active treatments	1	Low	Not applicable	Low	May be positive	May be positive for 5% sodium fluoride varnish	Not applicable	Not applicable	Not applicable	Not reported
Sealants on occlusal surfaces, compared with other treatments	1	Low	Not applicable	Low	May be positive for sealants	May be positive for sealants	Not applicable	Not applicable	Not applicable	Not reported

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Arrest caries progression	Remineralisation	Higher restoration success or survival	Lower restoration failure	Better clinical performance	Adverse events
Combination of resin infiltration and 5% sodium fluoride varnish on approximal surfaces compared with no treatment	1	Low	Not applicable	Very low	Positive compared with no treatment (uncertain evidence).	Positive compared with no treatment (uncertain evidence).	Not applicable	Not applicable	Not applicable	Not reported
Sealants or resin infiltration alone on approximal surfaces, compared with no treatment	1	Low	Not applicable	Very low	Positive (uncertain evidence).	Positive for sealants and infiltration (uncertain evidence).	Not applicable	Not applicable	Not applicable	Not reported
30% silver diamine fluoride solution applied annually on any coronal surface, compared with other doses and frequencies, and fluorides	1	Low	Not applicable	Low	May be positive 30% silver diamine fluoride	May be positive for 30% silver diamine fluoride	Not applicable	Not applicable	Not applicable	Not reported
38% silver diamine fluoride solution applied biannually on any coronal surface, compared with other doses and frequencies	1	Low	Not applicable	Low	May be positive for 38% silver diamine fluoride	May be positive for 38% silver diamine fluoride	Not applicable	Not applicable	Not applicable	Not reported

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Arrest caries progression	Remineralisation	Higher restoration success or survival	Lower restoration failure	Better clinical performance	Adverse events
5% sodium fluoride varnish on any coronal surface, compared with some other non-invasive treatments or no treatment	1	Low	Not applicable	Low	May be positive for 5% sodium fluoride varnish	May be positive for 5% sodium fluoride varnish	Not applicable	Not applicable	Not applicable	Not reported
Bisphenol A levels in the body following the use of composite resins and/or dental sealants	2	1 moderate and 1 critically low	Very high for studies measuring bisphenol A in urine	Low	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Levels are high following dental treatment with resin products. No data on health effects.
Rubber dam isolation compared with other types of isolation	1	High	Not applicable	Low	Not applicable	Not applicable	May have higher success for non-carious cervical lesions	May have lower success for atraumatic restorative treatments	Treatment time may be reduced for sealants	None reported

*AMSTAR 2 overall methodological quality rating: High, moderate, low, or critically low

†Overlap: None, slight, moderate, high, or very high

‡Quality of evidence: High, moderate, low, or very low

4.5.5.3 Cavitated caries

Table 15 presents a high-level summary of treatment outcomes for cavitated caries in mixed dentition.

4.5.5.3.1 Direct restoration material

We identified two systematic reviews on the topic of direct restoration materials for cavitated caries in primary and permanent teeth.¹⁵⁸⁻¹⁶⁰ Each of the reviews evaluated the clinical performance of different restoration materials, so overlap of primary studies in the two systematic reviews was not an issue. One review examined the performance of bulk-fill direct resin composites,¹⁵⁸ and the other examined high-viscosity glass ionomers combined with a resinous coating (glass hybrids).^{159,160}

One review, based on low-quality evidence, reported that there were no significant differences in the clinical performance of bulk-fill resin composites compared with that of conventional resin composites, regardless of the type of restoration, type of tooth restored, or technique used.¹⁵⁸ The second review, based on low-quality evidence, reported no differences in survival between high-viscosity glass ionomer and resin composite or other glass ionomers.^{159,160}

Arbildo-Vega *et al.*¹⁵⁸ evaluated the clinical performance (based on 11 parameters) of **bulk-fill direct resin composites** used in direct restorations in human teeth compared with that of conventional direct resin composites. There was low-quality evidence that there were no significant differences in the clinical performance of bulk-fill resin composites compared with conventional resin composites, regardless of the type of restoration, type of tooth restored, or technique used. This meant that there was low-quality evidence that there were no significant differences between bulk-fill resin composites and conventional resin composites in terms of the absence of fractures, absence of discolouration or marginal staining, adequate marginal adaptation, absence of secondary caries, adequate colour stability and translucency, proper surface texture, proper anatomical form of the restoration, adequate integrity of the tooth without the presence of wear, adequate restoration integrity, and proper occlusion.

Kielbassa *et al.*^{159,160} compared the clinical performance of **high-viscosity glass ionomer covered with a resinous coating (glass hybrids)** with the use of amalgam (no studies), **resin composite, or other glass ionomer** in Class I and Class II restorations of posterior primary or permanent teeth. In a narrative analysis based on low-quality evidence, the authors reported that two of the three included studies reported high survival of Class I restorations and good colour matching using either glass ionomer or resin-modified glass ionomer. On the other hand, the third study reported a high proportion of unsatisfactory multi-surface Class II restorations. The three trials reported no differences in survival between high-viscosity glass ionomer cement and resin composite or other glass ionomer cements.

4.5.5.3.2 Restoration support material

We identified five systematic reviews on the topic of restoration support materials for cavitated caries in primary and permanent teeth.^{89,161-164} Two reviews examined the usefulness of cavity pretreatment, and there was no overlap of primary studies across these two systematic reviews.^{161,163} Two reviews evaluated the effectiveness of cavity liners, and both examined different outcomes.^{89,162} The remaining review attempted to examine the effects of antibacterial agents incorporated into composite restorations, but the review authors did not identify any eligible primary studies.¹⁶⁴

Overall, the two reviews of cavity pretreatments reported that cavity pretreatment with chlorhexidine (two reviews), ethanol wet-bonding (one review), or quaternary ammonium compounds (one review), compared with no treatment, placebo, or alternative pretreatments, did not increase restoration survival; these findings were based on low- or moderate-quality evidence.^{161,163} There was very low-quality evidence, from one review that evaluated liners, indicating that calcium hydroxide liners had better clinical success for deep carious lesion treatments than glass ionomer cement in restored primary teeth,

and there was low-quality evidence of no difference in success when compared with inert materials or adhesive systems.¹⁶² For permanent teeth, there was low-quality evidence, from the other review that evaluated liners, that calcium hydroxide liners did not increase the clinical success (based on bacterial counts) of carious lesion treatments.⁸⁹

4.5.5.3.2.1 Cavity pretreatment

Elkady *et al.*¹⁶¹ evaluated the effect of **chlorhexidine** as a **cavity pretreatment** or mix-in on the survival of atraumatic restorative treatment restorations in primary or permanent teeth with occlusal or occlusoproximal cavities. There was moderate-quality evidence that there were no significant differences in the survival of atraumatic restorative treatment restorations between chlorhexidine as a cavity pretreatment or mix-in compared with no treatment.

Göstemeyer and Schwendicke¹⁶³ evaluated the risk of retention loss and failure of adhesively placed resin-based restorations after degradation inhibitory cavity pretreatment with **chlorhexidine, ethanol wet-bonding, or quaternary ammonium compounds** compared with no treatment, placebo, or alternative pretreatments. There was low-quality evidence that risk of retention loss or failure was not significantly decreased after pretreatment with chlorhexidine, ethanol wet-bonding, or quaternary ammonium compounds compared with no treatment, placebo, or alternative pretreatments using intention-to-treat analysis. Scenario analyses found that great uncertainty was introduced by participant attrition at follow-up. According to trial sequential analysis, no firm conclusion was reached.

4.5.5.3.2.2 Cavity liners

Da Rosa *et al.*¹⁶² evaluated the role of **calcium hydroxide liners** in the treatment of deep carious lesions in primary or permanent teeth with respect to restoration failure. There was low-quality evidence that calcium hydroxide liners did not reduce restoration failure or increase clinical success of selective or stepwise removal of carious tissue. For primary teeth, the quality of evidence was very low that calcium hydroxide liners had better clinical success for deep carious lesion treatments than glass ionomer cement, and there was low-quality evidence of no difference in success compared with inert materials or adhesive systems. For permanent teeth, there was very low-quality evidence that calcium hydroxide liners did not increase the clinical success of deep carious lesion treatments.

Schwendicke *et al.* (2015b)¹⁶⁵ compared the antibacterial effects of different **cavity liners** with each other, a placebo, or no liner. There was low-quality evidence and conflicting evidence upon which to judge the performance of different liners for their antibacterial effects.

4.5.5.3.2.3 Antibacterial agents incorporated into composite restorations

Pereira-Cenci *et al.*¹⁶⁴ compared **antibacterial agents incorporated into composite restorations** with composite restorations containing no antibacterial agents for the prevention of negative clinical outcomes. There was no evidence, as no trials met the inclusion criteria.

4.5.5.3 Restoration material and support material

One systematic review by Schwendicke *et al.*²⁵ compared the survival of **combinations of adhesive and restorative materials** placed in one of two types of cavitated lesions (cervical cavitated lesions or load-bearing posterior cavitated lesions) with each other in permanent and primary teeth. The lesions may or may not be due to caries. There was low-quality evidence that conventional and bulk-fill resin composites seem suitable for load-bearing lesions. Of note, bulk fills had not all been placed in bulk but in increments in included studies, which possibly improved this material class's performance. There was low-quality evidence that etch-and-rinse adhesives might be preferable in permanent teeth, whereas self-etch systems might be suitable for primary teeth.

4.5.5.3.4 Restoration processes or techniques

We identified 11 systematic reviews on the topic of restoration processes or techniques for cavitated caries in primary and permanent teeth.^{30,166-175} Nine reviews evaluated methods of caries removal using chemomechanical methods, laser, or air- and/or sono-abrasion, and compared them with the traditional mechanical method (drill).^{30,166-173} The other two reviews compared the effects of different stages and amount of caries removal.^{174,175}

There was high (12%) overlap of 17 primary studies across two systematic reviews for two outcomes (pain and patient experience) and very high (25%) overlap of 8 primary studies across two systematic reviews for one outcome (need for anaesthesia) evaluating the effectiveness of the chemomechanical methods compared with the conventional drilling method for removing carious tissue.

There was moderate overlap (9%) of 22 primary studies across three systematic reviews for the outcome of procedure time, one of several metrics evaluating the effectiveness of lasers for removing carious tissue. Additionally, there was moderate overlap (8%) of 24 primary studies across four systematic reviews for the outcome of restoration survival. There was high overlap (11%) of 27 primary studies across four reviews for one outcome (pain). There was very high overlap (18%) of 22 primary studies across two systematic reviews evaluating the efficacy of lasers for removing carious tissue for the outcome of patient experience.

There was very high overlap (50%) of two primary studies across two systematic reviews evaluating the effectiveness of the intervention of air- and/or sono-abrasion for removing carious tissue for three outcomes (procedure time, need for anaesthesia, and patient experience).

Six of the nine reviews evaluating chemomechanical methods of caries removal measured procedure time, and all six reported that the alternative treatment methods had longer treatment times compared with the conventional method.^{166,168-170,172,173} The quality of evidence for the six reviews was mixed: two reviews were based on moderate-quality evidence, one was based on low-quality evidence, and three were based on very low-quality evidence. Only three reviews (one based on moderate-quality evidence, one based on low-quality evidence, and one based on very low-quality evidence) examined the adequacy of caries removal using alternative methods compared with the conventional method, and all three reported no difference.^{166,171,173} One review estimated bacterial counts in the excavated cavity and reported reductions with all methods.¹⁶⁶ Seven reviews (two based on moderate-quality evidence, three based on low-quality evidence, and two based on very low-quality evidence) evaluated pain, and six of the seven reviews reported that the pain experienced was lower for the alternative methods compared with the conventional method.^{166,168-171,173} However, the pain experience associated with atraumatic restorative treatment and conventional drilling was reported to be similar.³⁰ Four reviews (one based on moderate-quality evidence, one based on low-quality evidence, and two based on very low-quality evidence) documented the need for anaesthesia and reported a reduced need among patients receiving the alternative method of caries removal.^{166,169,171,173} Four reviews explored patient experience.^{166,169,170,173} One review (based on moderate-quality evidence) reported better experiences for patients receiving the alternative caries removal method.¹⁷³ Two reviews (one based on low-quality evidence and one based on very low-quality evidence) reported that laser treatment was associated with an unpleasant smell and taste, which therefore reduced acceptance.^{166,170} The remaining review (based on very low-quality evidence) reported no difference between intervention and comparator with respect to fear and anxiety.¹⁶⁹ Five reviews (one based on moderate-quality evidence, two based on low-quality evidence, and two based on very low-quality evidence) reported similar restoration survival rates across the methods of caries removal.^{30,168-171} However, one of these reviews reported lower survival for high-viscosity glass ionomer cement placed using atraumatic restorative treatment compared with being

placed using the conventional method.³⁰ One review, based on very low-quality evidence, measured microleakage, and reported that the incidence of microleakage was not statistically significantly higher after employing a traditional bur compared with the Er,Cr:YSGG laser on either the dentine or the whole marginal line.¹⁶⁷

Two reviews compared the effects of different stages and amounts of caries removal. The outcomes measured in the two studies were different. Schwendicke *et al.* (2015c)¹⁷⁴ evaluated the effects of using different criteria for caries removal in primary and permanent teeth (removal of non-stainable dentine versus removal of softened dentine) and found non-statistically significant differences with respect to risk of complications (highest when excavating to non-stainable dentine), pain (lowest when excavating using chemomechanical or laser methods), time required for excavation (shorter if less dentine was removed), and/or number of bacteria remaining (greatest number of bacteria remained when only softened dentine was removed). These findings were based on low-quality evidence.

Schwendicke *et al.* (2013a)¹⁷⁵ compared selective and stepwise removal with complete (non-selective) caries removal of carious lesions requiring restoration in primary or permanent teeth and found significant differences with respect to risk of pulpal exposure and no significant differences with respect to, post-operative pulpal symptoms, overall failure, and caries progression; however, the authors reported that the evidence was inconclusive and low quality.

4.5.5.3.4.1 Method of caries removal

Cardoso *et al.*¹⁶⁶ evaluated the efficiency (time for treatment, caries removal, anaesthesia, and colony-forming units count) of alternative methods (**chemomechanical methods, laser, and air- and/or sono-abrasion**) for caries removal, compared with the conventional mechanical method (rotary or hand instruments), for removing dental caries from primary and permanent decayed teeth. The alternative methods had longer treatment times compared with the conventional methods, based on very low-quality evidence. Both conventional and alternative approaches reduced cariogenic flora within the cavities based on very low-quality evidence. Alternative methods for caries removal showed a tendency to produce more comfortable treatment experiences and had reduced requests for anaesthesia, based on very low-quality evidence. Although every method decreased self-reported pain in patients when compared with conventional mechanical treatment, the chemomechanical treatments were statistically significantly better than the other alternative methods (Er:YAG and Er,Cr:YSGG laser systems), based on very low-quality evidence. The vector system (air- and/or sono-abrasion) also resulted in significantly less induced pain, based on very low-quality evidence. However, smell and taste were found to be factors for increased anxiety. The longevity and survival of restorations performed by each method did not significantly differ from each other, based on very low-quality evidence. Papacarie was the most studied chemomechanical treatment and presented efficiency for caries removal and high acceptance by patients, based on very low-quality evidence.¹⁶⁶

Zhang *et al.*¹⁶⁷ evaluated the extent of microleakage from tooth cavities in humans prepared using **Er,Cr:YSGG lasers** compared with microleakage from cavities prepared using traditional burs, and the effectiveness of acid etching on the adhesive potential of self-etch and etch-and-rinse adhesives after laser preparation compared with no etching. The incidence of microleakage was not statistically significantly higher after employing a traditional bur compared with the Er,Cr:YSGG laser on either the dentine or the whole marginal line, based on very low-quality evidence. In addition, the results of the enamel margin subgroup revealed a non-significant increase in microleakage in the Er,Cr:YSGG laser group. It was reported that prior acid etching improved the adhesive potential of self-etching adhesives and significantly decreased microleakage after laser preparations, based on very low-quality evidence. The significant difference was detected in both the enamel and dentine margin subgroups. Prior acid

etching did not improve the adhesive potential of the etch-and-rinse adhesives, and the incidence of microleakage when compared with no etching was not different, based on very low-quality evidence. The result revealed substantial statistical heterogeneity among the studies.¹⁶⁷

Li *et al.* (2019)¹⁶⁸ evaluated the clinical efficacy (operation time, pain, and long-term outcomes) of the **Er:YAG laser** for caries removal and cavity preparation in children compared with that of the conventional mechanical method. There was low-quality evidence that the operation time required for the Er:YAG laser treatment was longer than the conventional mechanical method. However, there was low-quality evidence that the pain caused by the Er:YAG laser was reduced compared with the conventional mechanical method. Additionally, there was low-quality evidence that there were no statistically significant differences for retention rates, complete restoration, marginal discolouration, and marginal adaptation between the Er:YAG laser and conventional mechanical method.¹⁶⁸

Cianetti *et al.*¹⁶⁹ evaluated the effectiveness (treatment time, need for anaesthesia, clinical performance, and pulpal complications) and degree of acceptance (pain, discomfort, and fear) for children and adolescents of the use of **sonic and ultrasonic devices** with oscillating tips compared with conventional rotating drills to remove carious tissue from primary or permanent teeth. The effectiveness of sonic and ultrasonic tips for managing pain and dental fear in children and adolescents who required caries removal remains unproven due to the very low-quality evidence available, although there were signals that time required for treatment was longer for the sonic and ultrasonic tips than for the mechanical drill, and the other measures (need for anaesthesia, clinical performance, pulpal complications, pain, discomfort, and fear) favoured the sonic and ultrasonic tips over the mechanical drill.¹⁶⁹

Dorri *et al.*³⁰ compared **atraumatic restorative treatment** with conventional treatment (the drill and fill approach) for managing dental carious lesions in the primary and permanent teeth of children and adults. Compared with conventional treatment using high-viscosity glass ionomer cement, atraumatic restorative treatment may increase the risk of restoration failure in the primary dentition over a follow-up period ranging from 12 to 24 months based on low-quality evidence. Pain experienced by children during the procedure using atraumatic restorative treatment was similar to conventional treatment, based on low-quality evidence. Comparisons of atraumatic restorative treatment with conventional treatment using composite or resin-modified glass ionomer cement for restoration failure over a 24-month follow-up period showed that the two groups were not different, based on low-quality evidence. Comparisons of atraumatic restorative treatment with conventional treatment placing resin-modified glass ionomer cement restorations in the permanent teeth of older adults with root carious lesions for restoration failure over a 6-month follow-up period was not different, based on low-quality evidence.³⁰

Tao *et al.*¹⁷⁰ evaluated the comparative clinical success (restoration loss, pulpal vitality, and post-operative sensitivity) and efficacy (procedure time, requirement for anaesthesia, and acceptability) of **erbium laser**, compared with traditional drilling, in individuals with carious lesions. There was moderate-quality evidence that there was a significantly shorter time required for cavity preparation using conventional rotary instruments compared with erbium laser equipment. However, there was moderate-quality evidence that fewer persons in the laser group experienced pain during cavity preparation and asked for the use of local anaesthesia compared with those in the conventional rotary instruments group. There was low-quality evidence, as well as conflicting results, for patient acceptance of the erbium laser equipment over conventional rotary instruments. There was moderate-quality evidence that there was no significant difference between the erbium laser equipment compared with conventional rotary instruments for subsequent restoration loss, pulpal vitality, and experiencing post-operative sensitivity.¹⁷⁰

Montedori *et al.*¹⁷¹ compared **laser-based** methods with conventional mechanical methods for removing dental caries in deciduous and permanent teeth, measuring the outcomes of pain, anaesthesia, durability

of restoration, and pulp damage. There was low-quality evidence to suggest that lasers or drills had similar effectiveness for caries removal. The incidence of moderate or high pain, based on low-quality evidence, was greater in the drill group compared with the laser group using the Wong-Baker FACES Pain Rating Scale. The need for anaesthesia, based on low-quality evidence, was significantly higher in the drill group than in the laser group among both children and adults. There was very low-quality evidence that there was no difference in marginal integrity and durability of restoration between the laser and drill comparisons that were evaluated. Only two trials investigated the recurrence of caries, but no events occurred during the 6-month follow-up period (very low-quality evidence). There was very low-quality evidence and insufficient evidence of a difference between laser and drill in terms of pulpal inflammation or necrosis.¹⁷¹

Hamama *et al.*¹⁷² compared the time required for **chemomechanical** (a sodium hypochlorite-based agent, known as CariSolv, and an enzyme-based agent, known as Papacarie) caries removal with the other conventional caries removal methods in primary and permanent teeth. There was very low-quality evidence that the shortest estimated mean excavation time was recorded during rotary caries excavation (2.99 minutes, standard deviation: ± 0.001 minutes), followed by the enzyme-based (Papacarie) chemomechanical caries removal method (6.36 minutes, standard deviation: ± 0.08 minutes), the hand excavation method (6.98 minutes, standard deviation: ± 0.17 minutes), and CariSolv chemomechanical caries removal (8.12 minutes, standard deviation: ± 0.02 minutes). Li *et al.* (2014b)¹⁷³ evaluated CariSolv for *chemomechanical* caries removal from primary or permanent teeth, compared with the conventional rotary instrument method, with respect to complete caries removal rate, the treatment time (in minutes), and the use of local anaesthesia. There was moderate-quality evidence that there was not a statistically significant difference in complete caries removal between the CariSolv group and rotary instruments group in teeth with caries. Additionally, there was moderate-quality evidence that the treatment time required for caries removal using CariSolv was significantly longer than the time required for removal using the rotary instrument. Finally, there was moderate-quality evidence that fewer patients in the CariSolv group experienced discomfort and used local anaesthesia than in the rotary instrument group.¹⁷³

4.5.5.3.4.2 Stages and amount of caries removed

Schwendicke *et al.* (2015c)⁸⁹ evaluated and compared the effects (with respect to risk of complications, pain, time required for excavation, and/or number of bacteria remaining) of using **different criteria for caries removal** in primary and permanent teeth. There was low-quality evidence that the risk of complications was highest when excavating until only non-stainable dentine remained, and lowest when not attempting to remove all softened dentine. There was low-quality evidence that the risk of pain significantly decreased if self-limiting chemomechanical excavation or fluorescence-assisted lasers were used instead of excavating until only hard dentine remained. There was low-quality evidence that, when not attempting to remove all softened dentine, the time required for excavation was shortest, while the greatest number of bacteria remained. There was low-quality evidence that not attempting to remove all softened dentine resulted in the highest number of bacteria remaining and the highest chance of leaving any cultivable bacteria. However, none of these detected differences was statistically significant.⁸⁹

Schwendicke *et al.* (2013a)¹⁷⁵ compared **selective and stepwise incomplete removal with complete (non-selective) caries removal** of primary or permanent teeth with primary carious lesions requiring a restoration with respect to risk of pulpal exposure, post-operative pulpal symptoms, overall failure, and caries progression. Pairwise random-effects meta-analysis, based on low-quality evidence, showed significant risk reduction for pulpal exposure and a non-significant reduction for pulpal symptoms for teeth treated with *selective and stepwise* incomplete excavation. There was low-quality evidence based on inconclusive, limited data that risk of failure seemed to be similar for both complete and incomplete excavation.

Table 15 Main intervention outcomes for cavitated caries in mixed dentition

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Higher restoration success or survival	Lower restoration failure	Better clinical performance	Adverse events
Cavitated caries intervention								
Bulk-fill direct resin composites used in direct restorations, compared with conventional direct resin composites	1	Critically low	Not applicable	Low	Not measured	Not measured	May have no difference	Not reported
High-viscosity glass ionomer cement covered with a resinous coating, compared with resin composite or other glass ionomer cements, in Class I and Class II restorations	1	Critically low	Not applicable	Low	May have no difference	Not measured	Good colour matching for Class I in 2 primary studies, and poor clinical performance for Class II in 1 primary study	Not reported
Chlorhexidine as a cavity pretreatment compared with alternative treatments or no treatment	2	1 low and 1 moderate	None	1 low and 1 moderate	May have no difference	Not measured	Not measured	Not reported
Ethanol wet-bonding, or quaternary ammonium compounds as a cavity pretreatment, compared with alternative treatments	1	Low	Not applicable	Low	May have no difference	Not measured	Not measured	Not reported
Calcium hydroxide liner in the treatment of deep carious lesions with respect to restoration failure, compared with each other or no liner	2	Critically low	None	Low or very low	Not measured	May have no difference in 2 reviews	1 review found there may be no difference and 1 review found conflicting evidence relating to bacterial outcomes	Not reported
Combinations of adhesive and restorative materials	1	Low	Not applicable	Low	Not measured	Not measured	Etch-and-rinse adhesives may be preferable in permanent teeth,	Not reported

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Higher restoration success or survival	Lower restoration failure	Better clinical performance	Adverse events
							whereas self-etch systems may be suitable for primary teeth.	
Chemomechanical caries removal compared with mechanical removal	3	1 critically low, 1 low, and 1 moderate	High and very high	2 very low and 1 moderate	Similar restoration survival (evidence uncertain)	Not measured	Chemomechanical caries removal had uncertain evidence of: Longer procedure time No difference caries removal Reduced pain Reduced need for anaesthesia Better patient experience	Not reported
Laser caries removal compared with mechanical removal	5	1 critically low, 2 low, and 2 moderate	Moderate, high, and very high	Very low, low, or moderate	May have similar restoration survival	Not measured	Laser caries removal may have: Longer procedure time No difference caries removal Reduced pain Reduced need for anaesthesia Mixed patient experience	Taste in mouth and unpleasant smell
Air- and/or sono-abrasion caries removal compared with mechanical removal	2	1 low and 1 moderate	Very high	Very low	Similar restoration survival (evidence uncertain)	Not measured	Air- and/or sono-abrasion had uncertain evidence of: Longer procedure time No difference caries removal Reduced pain Reduced need for anaesthesia No difference in patient experience	Not reported

Intervention	Number of systematic reviews	AMSTAR 2 quality of reviews*	Overlap of primary studies†	Quality of evidence‡	Higher restoration success or survival	Lower restoration failure	Better clinical performance	Adverse events
Different criteria for caries removal	1	Low	Not applicable	Low	Not measured	Not measured	May have no difference	Not reported
One- or two-step incomplete caries removal compared with complete caries removal	1	Low	Not applicable	Low	Not measured	Not measured	May have significantly reduced pulpal exposure and no significant differences with respect to risk of post-operative pulpal symptoms, overall failure, and caries progression	Not reported

*AMSTAR 2 overall methodological quality rating: High, moderate, low, or critically low

†Overlap: None, slight, moderate, high, or very high

‡Quality of evidence: High, moderate, low, or very low

5 Discussion

5.1 Summary findings

5.1.1 Primary dentition

5.1.1.1 Non-cavitated caries

We identified one systematic review on the topic of non-invasive treatment for non-cavitated caries in primary teeth.⁷⁸ The authors compared the effectiveness of fluoride varnishes, fluoride gels, casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), and other remineralisation agents with each other in the management of white spot lesions in children's primary teeth. There was low-quality evidence that fluoride varnishes were superior to placebo or no intervention as a remineralisation agent. In addition, there was low-quality evidence that CPP-ACP combined with fluoride toothpaste had the same remineralising effect as fluoride toothpaste alone. Furthermore, there was low-quality evidence that fluoride varnish had the same effect as pit-and-fissure resin sealants, Nd:YAG laser, and chlorhexidine. Finally, there was low-quality evidence that fluoride varnish alone was inferior to fluoride varnish plus chlorhexidine or Nd:YAG laser.

We identified one systematic review on the topic of microinvasive treatment for non-cavitated caries in primary teeth.⁷⁹ There was low-quality evidence that resin-based sealants plus application of 5% sodium fluoride varnish had the same arresting effect as fluoride varnish alone.

The presence or absence of community water fluoridation was not considered as part of the intervention effect in this review.

5.1.1.2 Cavitated caries

We identified two systematic reviews on the topic of non-invasive treatment for cavitated caries in primary teeth.^{80,81} There was no overlap of primary studies included in the two systematic reviews. There is moderate-quality evidence that 38% silver diamine fluoride was effective in arresting cavitated caries in primary teeth.

We identified four systematic reviews on the topic of direct restoration material for treating cavitated caries in primary teeth.^{23,82-84} Each of the reviews examined aspects of clinical performance for glass ionomer and composite resin compared with each other and with other restoration materials. For the investigation outcomes of survival or failure and secondary caries, there was overlap of some primary studies included in the four systematic reviews. Overall, clinical performances in restored primary teeth were similar for conventional glass ionomer and composite resin in one review (based on low-quality evidence) and lower for glass ionomer in two reviews (one based on moderate-quality evidence and one based on low-quality evidence). However, the clinical performance of resin-modified glass ionomer was similar to that of composite resin in three reviews (one based on moderate-quality evidence and two based on low-quality evidence). Of note, glass ionomer was more effective in preventing secondary caries on a variety of primary teeth surfaces in two reviews, based on moderate-quality evidence.

We identified two systematic reviews on the topic of crowns for treating cavitated caries in primary teeth. Both reviews examined the use of the Hall Technique to apply crowns on children's carious teeth.^{85,86} There was no overlap of primary studies included in the two reviews. The placement of crowns in primary teeth using the Hall Technique provided signals of successful outcomes, but the quality of the evidence in the reviews was low or very low.

We identified two systematic reviews on comparing direct and indirect restoration materials for restoring cavitated caries in primary teeth.^{87,88} Surprisingly, there was no overlap of primary studies in the two reviews. The findings of both reviews were uncertain as to which restoration materials were superior, and these findings were based on low-quality evidence.

We identified one systematic review on the topic of adhesives that supports resin composite restoration of cavitated caries in primary teeth.⁸⁹ There was low-quality evidence that failure of adhesive restorations in restored cavities of primary teeth was similar with and without the placement of a liner.

We identified four systematic reviews on the topic of restoration processes and techniques that assist restoration of cavitated caries in primary teeth: three on the stages and amount of caries removed⁹⁰⁻⁹² and one on the method of caries removal.⁹³ For the outcomes of survival or failure when examining the stages and amount of caries removed, there was overlap of some primary studies included in the three systematic reviews. Selective caries removal, compared with complete caries removal, was associated with higher restoration failure rates and reduced pulp exposure in two reviews – one based on low-quality evidence and the second based on moderate-quality evidence. The third review on the stages and amount of caries removal did not complete a direct comparison. The review comparing chemomechanical caries removal (Papacarie) with conventional mechanical caries removal provided some evidence of reduced pain and anxiety among children undergoing chemomechanical caries removal, but the dentist required a longer time period to complete the chemomechanical caries removal procedure. These findings were based on low- or very low-quality evidence.

We identified one systematic review on the topic of combining restoration material and technique for restoring cavitated caries in primary teeth.⁹⁴ The authors wanted to identify the best treatment for dentine carious lesion arrestment in primary teeth and the success rate of different treatments for dentine carious lesions.⁹⁴ There was very low-quality evidence that resin composite restoration had a higher success rate than resin sealant. However, when caries arrest was considered as the primary outcome, no difference was observed between the restorative treatments.

5.1.2 Permanent dentition

5.1.2.1 Non-cavitated caries

We identified four systematic reviews on the topic of non-invasive treatment for non-cavitated caries in permanent teeth.⁹⁵⁻⁹⁸ One covered non-invasive treatment of coronal caries⁹⁶ and the other three covered non-invasive treatment of root caries.^{95,97,98} There was very high overlap of primary studies across the three reviews evaluating non-invasive treatment of root caries. All three reviews (one with moderate-quality evidence, one with moderate and low-quality evidence, and one with low-quality evidence) found that silver diamine fluoride provided a higher caries arrest effect than comparators in root carious lesions in adults' permanent teeth. In addition, one of the three reviews reported low-quality evidence that dentifrice containing 5000 ppm fluoride and professionally applied chlorhexidine varnish inactivated existing root carious lesions and/or reduced the initiation of root carious lesions. The fourth review evaluated fluoride monotherapy compared with the combined use of CPP-ACP and fluorides for coronal caries and found low-quality evidence that the combination of CPP-ACP and fluoride treatment was better at decreasing the size of early occlusal carious lesions than fluorides monotherapy. However, there was low-quality evidence that fluoride combined with CPP-ACP achieved the same results as fluorides monotherapy for early carious lesions on smooth surfaces.

The presence or absence of community water fluoridation was not considered as part of the intervention effect in this review.

5.1.2.2 Non-cavitated and cavitated caries

One systematic review by Schwendicke et al.³² compared non-invasive, microinvasive, and minimally invasive treatments with each other, with no active treatment or a placebo treatment, or with standard oral home care for treating pit-and-fissure lesions in permanent posterior teeth in adults. The authors found very low-quality evidence that microinvasive and minimally invasive treatments were potentially effective in avoiding retreatments of pit-and-fissure lesions in permanent posterior teeth. In addition, there was some very low-quality evidence that non-invasive treatments might also be effective in avoiding retreatments of pit-and-fissure lesions in permanent posterior teeth. Based on very low-quality evidence, microinvasively sealed lesions required re-sealing regularly, increasing the overall need for re-interventions compared especially with minimally invasive treatments.³²

5.1.2.3 Cavitated caries

We identified 10 systematic reviews on the topic of direct restoration materials for cavitated caries in permanent teeth. Four systematic reviews examined different forms of composite resin compared with each other and/or glass ionomer.⁹⁹⁻¹⁰² For the outcome of clinical performance, there was overlap of some primary studies included in the four systematic reviews. These four systematic reviews (two with moderate-quality evidence and two with low-quality evidence) that compared newer forms of composite resin with conventional composite resin in patients with direct restorations in posterior permanent teeth found that their clinical performance was similar. Three reviews compared amalgam with composite resin.^{11,13,103} For the study outcome of restoration failure, there was complete overlap of primary RCTs included in two of the three systematic reviews^{11,103} and no overlap of primary studies in the third systematic review, as it included mostly cohort studies.¹³ The three systematic reviews that compared the restoration failure of direct composite resin fillings with amalgam fillings for permanent posterior teeth found low- or very low-quality evidence that resin composite had higher failure rates and higher secondary caries rates than amalgam. In addition, there was low- or very low-quality evidence that restoration fracture was the same for both amalgam and resin composite. Two reviews attempted to evaluate amalgam and composite resin repairs with replacements but identified no studies that met their inclusion criteria.^{14,104} One review evaluated restoration materials for root caries and found insufficient and low-quality evidence to recommend any specific material for routine use in the restoration of root carious lesions; all had high failure rates.¹⁰⁵

We identified seven systematic reviews on the topic of indirect restoration materials for cavitated caries in permanent teeth.^{29,106-111} Six of the seven reviews examined indirect restorations and had overlaps between the interventions and comparators, yet no reviews had the exact same interventions or comparators. The six reviews covering indirect restoration examined survival as an outcome, and three identified complications. However, the time points at which survival was assessed were different. Some of the same primary studies were included in six reviews.^{29,106,108-111} These six reviews revealed that the average survival rate at 3 years was over 94%, at 5 years was over 90%, and at 10–11 years was over 87%. The seventh review compared ceramic -crowns- made by a computer-aided design/computer-aided manufacturing system with those made by a conventional manufacturing (milling) system.¹⁰⁷ There was low-quality evidence that the longevity of tooth-supported ceramic crowns made by the computer-aided design/computer-aided manufacturing system was lower than that of crowns made by a conventional manufacturing (milling) system. This systematic review had no overlap of its primary studies with the other six reviews.¹⁰⁷

We identified four systematic reviews comparing direct and indirect restoration materials for cavitated caries in permanent teeth.^{110,112-114} One review compared all direct and indirect restoration materials with each other,¹¹² while the other three reviews compared direct and indirect resin composite restorations

with each other.^{110,113,114} For the three reviews that compared clinical performance of direct and indirect resin composite restorations, some of the same primary studies were included in each of the three reviews. These three reviews (one based on moderate-quality evidence and two based on low-quality evidence) found no difference with respect to the clinical performance of direct and indirect resin composite restorations in permanent teeth for most parameters. Angeletaki *et al.* found that there was low-quality evidence that direct restorations were statistically significantly less likely to experience marginal discolouration.¹¹³ The single review comparing all direct and indirect restoration materials in permanent teeth, using data from RCTs, found that the best annual failure rate for direct restorations was for amalgam (at 1.9%), and for indirect restorations the best rate was for metal ceramic (at 0.3%).¹¹² However, these findings were based on very low-quality evidence. Based on very low-quality evidence, the highest annual failure rate for any method was for zirconia-based ceramic (at 5.1%). Indirect composite resin (3.5%) had a marginally higher failure rate than direct composite resin (2.7%). The failure rate for gold was 0.75%.

We identified two systematic reviews evaluating restoration support material for cavitated caries in permanent teeth.^{115,116} There was no evidence for children aged under 15 years by 2019. The other review evaluated adhesives used alongside posterior resin composite restorations in permanent teeth and found high-quality evidence that the type of adhesive strategy (etch-and-rinse or self-etch) did not seem to influence the risk and intensity of post-operative sensitivity in posterior resin composite restorations.¹¹⁶

We identified four systematic reviews evaluating restoration processes or techniques for cavitated caries in permanent teeth.¹¹⁷⁻¹²⁰ Each of these four reviews evaluated a different technique. Arcanjo Frota Barros *et al.*¹¹⁷ evaluated the risk or benefit of selective caries removal for the treatment of dentinal caries in permanent teeth compared with non-selective (complete) or stepwise caries removal and found very low-quality evidence that selective removal resulted in greater success of maintaining pulp vitality compared with both non-selective (complete) and stepwise excavation. Göstemeyer *et al.*¹¹⁸ evaluated the efficacy of atraumatic restorative treatment compared with conventional restorative treatment for restoring root carious lesions in older adults and found moderate-quality evidence that there was no significant difference in the failure rates of restorations using atraumatic restorative treatment compared with those using conventional restorative treatment. Solon de Mello *et al.*¹¹⁹ evaluated whether the survival rates of indirect restorations cemented with self-adhesive resin (cement) in permanent teeth were influenced by the presence or absence of selective enamel etching and found moderate-quality evidence of no statistically significant difference in the clinical longevity of indirect restorations cemented with self-adhesive resin cement in permanent teeth, with or without selective enamel etching. Deng *et al.*¹²⁰ evaluated the effects of *direct pulp capping using laser treatment* compared with pulpectomy or pulpotomy in patients who required such treatment for their deep carious lesions, and estimated the success of restorations. There was low-quality evidence that the success rate of pulp capping using the laser treatment (89.9%) was statistically significantly higher than that of control groups (67.2%) who had pulpectomy or pulpotomy.

5.1.3 Mixed dentition

5.1.3.1 Non-cavitated caries

We identified seven systematic reviews on the topic of non-invasive treatment for non-cavitated caries in primary and permanent teeth.¹³⁵⁻¹⁴¹ One review evaluated the remineralisation potential of NovaMin and found low-quality evidence based on one trial that there was no statistically significant difference between the NovaMin group and the control group (Crest toothpaste) in remineralising capacity.¹³⁵ Three reviews examined the remineralisation ability of CPP-ACP, but there was no overlap of primary studies

across the three systematic reviews.^{136,137,141} The authors found that CPP-ACP was as effective for remineralisation as fluoride (moderate- or low-quality evidence),^{136,137,141} and it was better than no intervention in two reviews (moderate- or low-quality evidence).^{136,141} Four reviews evaluated the remineralisation and arresting potential of applied fluoride products. There was very high overlap (40%) of five primary papers across two of the four systematic reviews evaluating the same fluoride intervention.^{139,140} These reviews examined the effectiveness of professionally applied fluoride products. One of the other two reviews compared different remineralisation agents (fluoride products, CPP-ACP, and ICON plc. resin) and techniques with each other, and there was slight overlap (one primary paper) between this systematic review by Paula *et al.*¹⁴¹ and the reviews by Gao *et al.*¹⁴² and Lenzi *et al.*,¹⁴⁰ with one primary study used across all three reviews. There was no overlap with the review by Chong *et al.*¹³⁸ Three reviews (two based on low-quality evidence and one based on moderate-quality evidence) reported that fluoride varnish was an effective remineralising agent for targeting early caries in primary teeth¹³⁹⁻¹⁴¹ and two of the three reviews reported a similar finding for permanent teeth.^{140,141} One review, based on very low-quality evidence, found that silver diamine fluoride was more effective than controls for remineralising and arresting the progression of active caries in both primary and permanent teeth in children and adolescents.¹³⁹ There was low-quality evidence, based on a review with one trial, that slow-release fluoride devices (glass beads) helped reduce dental decay.¹³⁸

We identified eight systematic reviews on the topic of microinvasive treatment for non-cavitated caries in primary and permanent teeth.¹⁴³⁻¹⁵⁰ Five examined infiltration and sealing^{143,147-150} and three examined infiltration only.¹⁴⁴⁻¹⁴⁶ There was very high overlap of primary studies across the eight reviews for the outcome of arresting or slowing caries progression and for the intervention of resin infiltration. There was consistent evidence reported in eight systematic reviews that resin infiltration is effective for reducing and/or arresting the progression of non-cavitated proximal carious lesions in primary and permanent teeth (moderate- or low-quality evidence).¹⁴³⁻¹⁵⁰ Five reviews reported that sealing demonstrated effectiveness for reducing and/or arresting the progression of non-cavitated proximal carious lesions in primary and permanent teeth (moderate- or low-quality evidence).^{143,147-150}

The presence or absence of community water fluoridation was not considered as part of the intervention effect in this review.

5.1.3.2 Non-cavitated and cavitated caries

We identified three systematic reviews on the topic of non-invasive treatment for non-cavitated caries and cavitated caries in primary and permanent teeth – one covering ozone therapy¹⁵¹ and two covering silver diamine fluoride – and there was high overlap of primary studies across the two systematic reviews covering the intervention silver diamine fluoride.^{139,152} One review reported low and very low-quality evidence that ozone therapy was more effective for reducing lesion progression and severity compared with no ozone (compressed air) or no treatment; was as effective as fluoride varnish; and was less effective than chlorhexidine digluconate.¹⁵¹ Two reviews (one with moderate-quality evidence and one with very low-quality evidence) reported that 38% and/or 30% concentrations of silver diamine fluoride arrested caries in primary teeth.^{139,152} The two reviews reported differing findings for permanent teeth: one review concluded there was not enough evidence to assess the effectiveness in permanent molars (no evidence)¹⁵² whereas the other review reported that silver diamine fluoride was not more effective than comparators (very low-quality evidence).¹³⁹

We identified one systematic review on the topic of microinvasive and invasive treatment for non-cavitated caries and cavitated caries in primary and permanent teeth.¹⁵³ de Amorim *et al.*¹⁵³ evaluated the survival rate of atraumatic restorative treatment glass ionomer restorations and atraumatic restorative treatment sealants in primary and permanent posterior teeth. There was very low-quality evidence that

the survival rates of single-surface and multiple-surface atraumatic restorative treatment restorations in primary posterior teeth over the first 2 years were 94.3% and 65.4%, respectively. Additionally, there was very low-quality evidence that single-surface atraumatic restorative treatment restorations in permanent posterior teeth over the first 3 years had a survival rate of 87.1%, and multiple-surface atraumatic restorative treatment restorations in permanent posterior teeth over the first 5 years had a survival rate of 77.0%. Based on very low-quality evidence, the weighted average annual failure rates of completely lost atraumatic restorative treatment sealants in permanent posterior teeth over the first 3 and 4 years were 10.7% and 9.6%, respectively. The average annual failure percentages for dentine carious lesions in previously sealed pits and fissures using atraumatic restorative treatment sealants in permanent posterior teeth were 0.9% at 3 years and 1.9% at 5 years, again based on very low-quality evidence.¹⁵³

We identified one systematic review on the topic of non-invasive and microinvasive treatment for non-cavitated caries and cavitated caries in primary and permanent teeth. Urquhart *et al.*¹⁵⁴ compared non-restorative treatments with other active intervention(s), or with no treatment or a placebo, for the arrest or reversal of non-cavitated and cavitated carious lesions in primary and permanent teeth in children and adults. There was a series of findings from this large-scale systematic review:

- There was low-quality evidence that the combination of sealants with 5% sodium fluoride varnish for arrest or reversal of non-cavitated carious lesions on occlusal lesions in primary and permanent teeth is superior to most other treatments.
- There was very low-quality evidence that the combination of resin infiltration and 5% sodium fluoride varnish was better than no treatment for non-cavitated carious lesions on approximal surfaces in primary and permanent teeth.
- There was very low-quality evidence that sealants or resin infiltration were more effective than no treatment intervention for arrest or reversal of non-cavitated carious lesions on approximal surfaces in primary and permanent teeth.
- There was low-quality evidence that 30% silver diamine fluoride solution, applied annually, is better than 30% silver diamine fluoride solution applied once per week for 3 weeks or 5% sodium fluoride varnish applied once per week for 3 weeks on any coronal surface for arrest or reversal of carious lesions.
- There was low-quality evidence that 38% silver diamine fluoride solution, applied biannually, was better than 38% silver diamine fluoride solution applied annually or 12% silver diamine fluoride solution applied annually on any coronal surface for arrest or reversal of carious lesions.
- There was low-quality evidence that 5% sodium fluoride varnish was more effective than some other non-invasive treatments or no treatment for arresting or reversing carious lesions on any coronal surface of primary and permanent teeth.
- There was low-quality evidence that the use of 1.23% acidulated phosphate fluoride gel on facial/lingual lesions for arresting or reversing such lesions was more effective than oral health education, although only at longer follow-up times.
- There was low-quality evidence to suggest that 5000 ppm fluoride (1.1% sodium fluoride) toothpaste or gel was more effective than no intervention for arresting or reversing non-cavitated and cavitated carious lesions on root surfaces in permanent teeth.

We identified two systematic reviews on the topic of microinvasive and restorative treatment for non-cavitated caries and cavitated caries in primary and permanent teeth, and these reviews dealt with safety. Both covered the release of bisphenol A into the body after the use of composite resins and/or dental

sealants.^{155,156} One review included studies that measured bisphenol A in urine only¹⁵⁵ while the other review included studies that measured bisphenol A in saliva and blood as well as in urine.¹⁵⁶ There was very high overlap of the primary studies measuring urinary bisphenol A across the two reviews. There was low-quality evidence in both reviews that there is bisphenol A exposure in humans from resin-based dental sealants and restorations, but its consequences were not yet known (no evidence).^{155,156} On the other hand, one primary study, in an evaluation of resin use followed immediately by mouthwash, demonstrated an abrupt decrease in bisphenol A levels.¹⁵⁶ The authors do not mention the age cut-off for rinsing with mouthwash.

5.1.3.3 Cavitated caries

We identified two systematic reviews on the topic of direct restoration materials for cavitated caries in primary and permanent teeth.¹⁵⁸⁻¹⁶⁰ Each of the reviews evaluated the clinical performance of different restoration materials, so overlap of primary studies in the two systematic reviews was not an issue. One review examined the performance of bulk-fill direct resin composites and, based on low-quality evidence, reported that there were no significant differences in the clinical performance of bulk-fill resin composites compared with that of conventional resin composites, regardless of the type of restoration, type of tooth restored, or technique used.¹⁵⁸ The second review examined high-viscosity glass ionomer covered with a resinous coating and found low-quality evidence of no difference in survival between high-viscosity glass ionomer and resin composite or other glass ionomer cements.^{159,160}

We identified five systematic reviews on the topic of restoration support materials for cavitated caries in primary and permanent teeth.^{89,161-164} Two systematic reviews examined the usefulness of cavity pretreatment, and there was no overlap of primary studies across these two reviews.^{161,163} The two reviews reported that cavity pretreatment with chlorhexidine (two reviews), ethanol wet-bonding (one review), or quaternary ammonium compounds (one review), compared with no treatment, placebo, or alternative pretreatments, did not increase restoration survival; these findings were based on low- or moderate-quality evidence.^{161,163} Two reviews evaluated the effectiveness of cavity liners, and both examined different outcomes.^{89,162} For primary teeth, one review that evaluated liners (calcium hydroxide) found very low-quality evidence indicating better clinical success using liners for deep carious lesion treatments than using glass ionomer, and low-quality evidence of no difference in success compared with inert materials or adhesive systems.¹⁶² For permanent teeth, there was low-quality evidence from the other review that evaluated liners, based on bacterial counts, that calcium hydroxide liners did not increase the clinical success of carious lesion treatments.⁸⁹ The remaining review attempted to examine the effects of antibacterial agents incorporated into composite restorations, but the review authors did not identify any eligible primary studies.¹⁶⁴

One systematic review by Schwendicke *et al.*²⁵ compared the survival of combinations of adhesive and restorative materials placed in load-bearing posterior cavitated lesions with each other in permanent and primary teeth. There was low-quality evidence that conventional and bulk-fill resin composites seem suitable for load-bearing lesions. Of note, bulk fills had not all been placed in bulk but in increments in included studies, which possibly improved this material class's performance. There was low-quality evidence that etch-and-rinse adhesives might be preferable in permanent teeth, whereas self-etch systems might be suitable for primary teeth.

We identified 11 systematic reviews on the topic of restoration processes or techniques for cavitated caries in primary and permanent teeth.^{30,166-175} Nine reviews evaluated methods of caries removal using one of the following methods: chemomechanical methods, laser, or air- and/or sono-abrasion, and compared the chosen method with the traditional drill method.^{30,166-173} However, there was moderate to very high overlap of primary studies across the nine reviews, varying by outcome of interest. Six of the

nine reviews evaluating chemomechanical methods of caries removal measured procedure time, and all six reported that the alternative treatment methods had longer treatment times compared with the conventional method.^{166,168-170,172,173} The quality of evidence for the six reviews varied: two were based on moderate-quality evidence, one was based on low-quality evidence, and three were based on very low-quality evidence. Only three reviews (one based on moderate-quality evidence, one based on low-quality evidence, and one based on very low-quality evidence) examined the adequacy of caries removal using alternative methods compared with the conventional method, and all three reported no difference.^{166,171,173} One review estimated bacterial counts in the excavated cavity and reported reductions with all methods (very low-quality evidence).¹⁶⁶ Seven reviews (two based on moderate-quality evidence, three based on low-quality evidence, and two based on very low-quality evidence) evaluated pain, and six of the seven reviews reported that the pain experienced was lower for the alternative methods compared with the conventional method.^{166,168-171,173} However, the pain experience during atraumatic restorative treatment and conventional drilling was reported to be similar.³⁰ Four reviews (one based on moderate-quality evidence, one based on low-quality evidence, and two based on very low-quality evidence) documented the need for anaesthesia and reported a reduced need among patients receiving the alternative method of caries removal.^{166,169,171,173} Four reviews explored patient experience.^{166,169,170,173} One review (based on moderate-quality evidence) reported better experiences for patients receiving the alternative caries removal method.¹³⁷ Two reviews (one based on low-quality evidence and one based on very low-quality evidence) reported that laser treatment was associated with an unpleasant smell and taste, which therefore reduced acceptance.^{166,170} The remaining review (based on very low-quality evidence) reported no difference between intervention and comparator with respect to fear and anxiety.¹⁶⁹ Five reviews (one based on moderate-quality evidence, two based on low-quality evidence, and two based on very low-quality evidence) reported similar restoration survival rates across the methods of extraction.^{30,168-171} However, one of these reviews reported lower survival for high-viscosity glass ionomer placed using atraumatic restorative treatment compared with placement using the conventional method.³⁰ One review, based on very low-quality evidence, measured microleakage, and reported that the incidence of microleakage was not statistically significantly higher after employing a traditional bur compared with the Er,Cr:YSGG laser on either the dentine or the whole marginal line.¹⁶⁷

Two reviews compared the effects of different stages and amounts of caries removal in primary and permanent teeth, and one review found no statistically significant differences with respect to risk of complications, pain, time required for excavation, and/or number of bacteria remaining.¹⁷⁴ However, these findings were based on low-quality evidence. Schwendicke *et al.* (2013a)¹⁷⁵ compared *selective and stepwise* incomplete removal with complete (non-selective) caries removal of carious lesions requiring restoration in primary or permanent teeth and found significantly reduced pulpal exposure and no significant differences with respect to risk of post-operative pulpal symptoms, overall failure, and caries progression; however, the authors reported that the evidence was inconclusive and low quality.

5.2 Comparison with other overviews of systematic reviews

We identified only one published overview of systematic reviews on the topic of managing non-cavitated caries and cavitated caries in primary, permanent, and mixed dentition, and this review covered the non-invasive intervention of silver diamine fluoride. Seifo *et al.*¹⁷⁶ concluded that silver diamine fluoride arrested coronal caries in primary teeth and root caries in permanent teeth when compared with fluoride varnish, atraumatic restorative treatment, or placebo, and these findings concur with the findings of this HRB overview of systematic reviews. Eight systematic reviews reported adverse events, seven of which, similar to this HRB review, reported black staining on arrested lesions. One review reported that participants experienced reversible, small, mildly painful white lesions in oral mucosa due to inadvertent

contact with silver diamine fluoride, which healed within 48 hours; the HRB did not identify silver diamine fluoride as an irritant on the oral mucosa.

5.3 Evidence for consensus clinical guidelines

We identified four recently published clinical guideline documents.

The most recent were consensus recommendations – based on two systematic reviews, and a consensus conference followed by an e-Delphi consensus process – identifying best practice on how to intervene in the caries process in adults, specifically in cases of proximal and secondary carious lesions.¹⁷⁷ The consensus conference included academics from 10 countries in Europe (Belgium, Croatia, Denmark, France, Germany, Italy, Lithuania, the Netherlands, Switzerland, and the UK) and 2 countries in the Americas (Chile and the USA). With respect to non-cavitated carious lesions, the overview authors recommend that “non-invasive measures (e.g. interdental cleaning, topical fluoride application) could be applied to arrest proximal lesions. This may be sufficient for lesion arrest in low caries risk/susceptible individuals or for lesions radiographically confined to enamel (weak recommendation, agreement 88%, median: 10).”^{177(p3318)} With respect to individuals classified as high-risk/susceptible or for lesions extending radiographically into dentine, the authors recommend that “microinvasive strategies should be considered additionally (moderate recommendation, agreement 83%, median: 10).”^{177(p3318)} The authors stated that “the decision between sealing and resin infiltration should be guided by individual considerations, including applicability, clinical experience, or costs (moderate recommendation, agreement 88%, median: 10).”^{177(p3318)} For cavitated carious lesions, the authors note that “restorative strategies will often be needed. For restoring proximal lesions, adhesive direct restorations allow minimally invasive, tooth-preserving preparations, are tooth-colored, and hence are already the material of choice in many cases. Amalgams, however, come with a lower risk of secondary lesions and since their placement is less technique-sensitive, they may be preferred in more clinically complex scenarios, dependent on specific national guidelines. According to legal regulations, the use of amalgam may be restricted in some countries or populations [including Ireland], now and in the future (weak recommendation, agreement 84%, median: 10).”^{177(p3318)} The authors also provide guidelines “with respect to structurally compromised teeth, especially when endodontically treated, indirect cuspal coverage restorations may be indicated (weak recommendation, agreement 92%, median: 10).”^{177(p3318)} This HRB review does not address the management of secondary caries.

The 2018 Scottish Dental Clinical Effectiveness Programme evidence review and clinical guidelines examined the prevention and treatment of dental caries in children’s and adolescents’ primary or permanent teeth and made recommendations to the dental profession in the UK based on its findings.⁴³ The guidelines recommend that “for a child with a carious lesion in a primary tooth, choose the least invasive, feasible caries management strategy, taking into account: the time to exfoliation, the site and extent of the lesion, the risk of pain or infection, the absence or presence of infection, preservation of tooth structure, the number of teeth affected, and avoidance of treatment-induced anxiety (strong recommendation; low-quality evidence).”^{43(p59)} The clinical guidelines go on to state that “for a child in pain due to pulpitis in a vital primary tooth with irreversible symptoms and no evidence of dental abscess, consider carrying out a pulpotomy to preserve the tooth and to avoid the need for an extraction (conditional recommendation; low-quality evidence).”^{43(p59)} The guidelines further recommend that “For a child with a carious lesion in a permanent tooth, choose the least invasive, feasible caries management strategy taking into account: the site and extent of the lesion, the risk of pain or infection, preservation of tooth structure and the health of the dental pulp, avoidance of treatment-induced anxiety, lifetime prognosis of the tooth, orthodontic considerations and occlusal development (strong recommendation; low-quality evidence).”^{43(p72)}

The American Dental Association evidence-based clinical practice guidelines, published in 2018, cover non-restorative treatments for carious lesions in primary and permanent teeth.¹⁷⁸ The summary clinical guidelines are presented in a user-friendly slide set that was developed for display in dental clinics to support dental practitioners' clinical decision-making (Appendix O). The American Dental Association evidence-based clinical practice guidelines on non-restorative treatments for carious lesions in primary teeth based on the user-friendly slide set are as follows:

- “To arrest advanced cavitated carious lesions on any coronal surface of primary teeth, the expert panel recommends clinicians prioritize the use of 38% silver diamine fluoride (SDF) solution (biannual application) over 5% sodium fluoride varnish (application once per week for 3 weeks)” (Appendix O); the quality of the evidence is moderate and the recommendation is strong.
- “To arrest or reverse noncavitated carious lesions on occlusal surfaces of primary teeth, the expert panel recommends clinicians prioritize the use of sealants plus 5% sodium fluoride varnish (application every 3–6 months) or sealants alone over 5% sodium fluoride varnish alone (application every 3–6 months)”, and if these interventions are not feasible, then use “1.23% acidulated phosphate fluoride gel (application every 3–6 months), resin infiltration plus 5% sodium fluoride varnish (application every 3–6 months), or 0.2% sodium fluoride mouthrinse (once per week)” (Appendix O); the quality of the evidence is moderate and the recommendation is strong.
- “To arrest or reverse noncavitated carious lesions on facial or lingual surfaces of primary teeth, the expert panel suggests clinicians use 1.23% acidulated phosphate fluoride gel (application every 3–6 months) or 5% sodium fluoride varnish (application every 3–6 months)” (Appendix O); the quality of the evidence is moderate to low and the recommendation is conditional.
- “To arrest or reverse noncavitated carious lesions on approximal surfaces of primary teeth, the expert panel suggests clinicians use 5% sodium fluoride varnish (application every 3–6 months), resin infiltration alone, resin infiltration plus 5% sodium fluoride varnish (application every 3–6 months), or sealants alone” (Appendix O); the quality of the evidence is low to very low and the recommendation is conditional.
- “To arrest or reverse noncavitated carious lesions on coronal surfaces of primary teeth, the expert panel suggests clinicians do not use 10% [CPP-ACP] paste if other fluoride interventions, sealants, or resin infiltration is accessible” (Appendix O); the quality of the evidence is low and the recommendation is conditional.

The American Dental Association evidence-based clinical practice guideline on non-restorative treatments for carious lesions in permanent teeth based on the user-friendly slide set are as follows:¹⁷⁸

- “To arrest advanced cavitated carious lesions on any coronal surface of permanent teeth, the expert panel suggests clinicians prioritize the use of 38% silver diamine fluoride (SDF) solution (biannual application) over 5% sodium fluoride varnish (application once per week for 3 weeks)” (Appendix O); the quality of the evidence is low and the recommendation is conditional.
- “To arrest or reverse noncavitated carious lesions on occlusal surfaces of permanent teeth, the expert panel recommends clinicians prioritize the use of sealants plus 5% sodium fluoride varnish (application every 3–6 months) or sealants alone over 5% sodium fluoride varnish alone (application every 3–6 months), 1.23% acidulated phosphate fluoride gel (application every 3–6 months), or 0.2% sodium fluoride mouthrinse (once per week)” (Appendix O); the quality of the evidence is moderate and the recommendation is strong.

- “To arrest or reverse noncavitated carious lesions on facial or lingual surfaces of permanent teeth, the expert panel suggests clinicians use 1.23% acidulated phosphate fluoride gel (application every 3–6 months) or 5% sodium fluoride varnish (application every 3–6 months)” (Appendix O); the quality of the evidence is moderate to low and the recommendation is conditional.
- “To arrest or reverse noncavitated carious lesions on approximal surfaces of permanent teeth, the expert panel suggests clinicians use 5% sodium fluoride varnish (application every 3–6 months), resin infiltration alone, resin infiltration plus 5% sodium fluoride varnish (application every 3–6 months), or sealants alone” (Appendix O); the quality of the evidence is low to very low and the recommendation is conditional.
- “To arrest or reverse noncavitated and cavitated carious lesions on root surfaces of permanent teeth, the expert panel suggests clinicians prioritize the use of 5,000 ppm fluoride (1.1% sodium fluoride) toothpaste or gel (at least once per day) over 5% sodium fluoride varnish (application every 3–6 months), 38% SDF plus potassium iodide solution (annual application), 38% SDF solution (annual application), or 1% chlorhexidine plus 1% thymol varnish (application every 3–6 months)” (Appendix O); the quality of the evidence is low and the recommendation is conditional.
- “To arrest or reverse noncavitated carious lesions on coronal surfaces of permanent teeth, the expert panel suggests clinicians do not use 10% [CPP-ACP] paste if other fluoride interventions, sealants, or resin infiltration is accessible” (Appendix O); the quality of the evidence is low and the recommendation is conditional.

The clinical guidelines in the USA were informed by the very large systematic review completed by Urquhart *et al.*¹⁵⁴

We also secured guidelines for Denmark (2020),¹⁷⁹ Norway (2011), and Sweden (2008); however, they were in each country’s national language. We translated Denmark’s guidelines using Google Translate, as they were the most recently published guidance. They comprised guidance on the use of dental filling materials in Denmark, under the Authorization Act No. 990 of 18 August 2017, and were prepared based on the Danish Health and Medicines Authority’s report.¹⁷⁹ The guidelines recommended that resin composites can be used for all types of dental fillings. According to the guidelines, glass ionomer is typically used as a filling therapy for fillings in primary teeth. Silver amalgam can be used in filling therapy in permanent molar and premolar teeth in cases where it is obvious that a filling in this material will have the best durability. These amalgam cases are limited to dental treatments where it will not be possible to dry the area, the cavity is difficult to access, the cavity is especially large, or there is a large distance between the affected tooth and the neighbouring tooth. Silver amalgam must not be used as filling therapy in children aged under 15 years or in pregnant or breastfeeding women, unless the dentist deems it strictly necessary based on the patient’s special medical needs.

Schwendicke *et al.*¹⁷⁷ concluded in their consensus recommendations for caries in adults that “Dental clinicians have an increasing number of interventions available for the management of dental caries. Many of them are grounded in the growing understanding of the disease. The best evidence, patients’ expectations, clinicians’ expertise, and the individual clinical scenario all need to be considered during the decision-making process.”¹⁷⁷ (p3315) The American Dental Association’s evidence-based clinical practice guidelines on non-restorative treatments for carious lesions in primary and permanent teeth stated that the concept of informed consent should be employed when managing dental caries, in that all appropriate non-restorative and restorative treatment options and their potential side effects (such as blackened tooth surfaces treated with silver diamine fluoride) should be explained to all patients.¹⁷⁸ The Danish guidelines reiterated the importance of informed consent and of keeping patient records.¹⁷⁹

Based on low- or moderate-quality evidence of the interventions for the treatment of non-cavitated caries and cavitated caries in permanent and primary teeth that the HRB has summarised, there is sufficient data to support implementing similar recommendations in Ireland.

5.4 Strengths and limitations

5.4.1 Search

A significant limitation of the literature search stage of this overview of reviews was the lack of non-English-language databases and resources included in the search. The use of a language limit (in the form of English-language work only) was necessary, as the review team members do not have adequate language skills to interpret complex and technical papers in other languages, and the time frame and competing work commitments did not allow for the professional translation of papers. Based on previous experience, the HRB review team determined that the use of Google Translate software would not be adequate for thorough, detailed extraction and synthesis of these papers. However, it is known that a considerable amount of work has been carried out on this topic in languages other than English. During the title and abstract screening, non-English-language reviews with English-language abstracts or keywords which appeared to be relevant to the topic were excluded, but the records were retained in order to ensure that this wider research was recorded and credited. These records are available in Appendix B and included works in 10 languages, representing a wide geographic span. These records were captured using English-language-based databases, and it is expected that using non-English-language databases or regional databases would capture considerably more of this body of work. There is some research to suggest that omitting languages other than English may not change the direction of findings significantly,^{180,181} but findings may be field- or topic-specific and it may not be possible to extrapolate from the general to the specific in this matter. While the inclusion of an adequate search process in the reviews which make up this overview of reviews was required, the use of non-English-language databases in those searches was not mandatory. The limits of the search methods of those reviews influenced the quality of research included. The inclusion of English-only primary studies in the reviews included in this overview may compound the language bias of only including English-language reviews in the overview. However, 53 of the 107 included systematic review papers stated that there were no language restrictions in their search and therefore non-English-language papers were included in their analyses. Additionally, several other reviews mentioned that they included more than one language in their search. The characteristics of the primary studies indicate that research came from all continents including the Americas and Europe. Over one-third of the systematic reviews included in this overview of reviews searched Latin American and Caribbean Health Sciences Literature database. Dr. Susana Morimoto, one of the peer reviewers, noted “the coverage period determined for this overview will not impact the inclusion of materials and procedures, as the [systematic reviews] should have included primary studies without time and language limits, ensuring that the most established materials and techniques have been included.”

The search for this overview of reviews was based around the concepts of caries and restorations, as other types of interventions were not of interest. It is possible that reviews which dealt with restorations in the context of caries, but which did not include caries-related terms in any of the searchable fields of the resources used, may not have been picked up. While a very broad search using only the concept of dental restoration could have been used, employing the screening process to identify reviews on restorations and caries, it would have resulted in search numbers that would have been unmanageable within the time frame of the review. As can be seen from the search results of the Ovid MEDLINE database alone, the results for just the concept of dental restoration amounted to 165,086 items. The terms used for caries were very broad and it was expected that any study that evaluated restorations for

caries would have included a term for caries in the title, abstract, author keywords, and controlled vocabulary (MeSH, etc.), but not all databases use full-text searching for the search terms. For example, Ovid lists the searchable fields available in Ovid MEDLINE in its database guide; this database searches the record of the article rather than the article itself.¹⁸² Less structured, general searches were used in many of the resources used, which it was hoped would capture a wide range of results. The use of supplemental searching (reference, citation, and protocol follow-up and screening of a previous work by the HRB authors)³³ was also expected to capture as much relevant material as possible, which may limit the number of missed articles.

The final searches were carried out in December 2020 and supplemental searching was carried out in February 2021. Therefore, reviews published after these dates could not be included. As noted in Section 3.8.7, this is a dynamic topic, and a cut-off date was necessary to allow for the analysis and synthesis to be carried out. The final search, including the supplemental searching, was robust when compared with other systematic reviews and clinical guidelines.

A limitation of overviews of systematic reviews is that interventions developed 2–3 years prior to the overview are not included as there would not be adequate primary research investigating the intervention.

5.4.2 Quality of systematic reviews and primary studies

During full-text screening, the HRB authors attempted to reduce the number of systematic reviews with serious shortcomings by screening out papers with inadequate coverage of bibliographic databases and grey or unpublished literature.

As reported in Chapter 4, the quality of some of the systematic reviews included in this overview was lower than desired. For example, 66 (62%) of our 106 systematic reviews were classified as either low or critically low-quality using AMSTAR 2; of these, 31 (29%) were deemed to be of critically low quality. During full-text screening, we attempted to increase the transparency of the quality of primary studies included in systematic reviews by screening out studies that did not complete a quality assessment or provide transparent and detailed quality assessment results to allow us to assign a GRADE level of evidence. The quality of the 106 included systematic reviews was hampered by the large number of primary studies that had an unclear or high risk of bias that could not be or was not controlled for in the meta-analyses via sensitivity or subgroup analysis. Many of our included systematic reviews included RCTs (69/106) only; however, a large proportion of these trials were neither randomised nor blinded, leading to questions about the validity of such trials. For example, 32 (46%) of the systematic reviews that solely included RCTs as their study design presented data indicating that 75% of their included primary studies had inadequate randomisation, and 36 (52%) of these systematic reviews presented data that indicated that 75% of their included primary studies had inadequate blinding when ascertaining the outcome.

Thirty systematic reviews included a combination of different study designs, and less than one-half of these systematic reviews recorded a justification for their decision to include multiple study designs. Where provided, the authors' main justification was to increase the power of the analysis, as there were too few RCTs, which is understandable. However, 11 of the 30 review teams combined the results collected through different study designs in a pooled analysis without controlling for differing study designs through stratification or sensitivity analysis.

Some systematic review teams did not report a feasibility assessment for assessment of clinical or methodological heterogeneity, and 17 systematic review teams did not discuss the effects of heterogeneity on their results.

Forty of the 106 systematic reviews (107 systematic review papers) had an inadequate sample size, based on the number of teeth or restorations included in the analysis, for one or more of the outcomes. Of the 106 systematic reviews, 48 reported including primary papers that treated more than one of an individual participant's teeth, but handling each restored or treated tooth as an individual research subject; however, the majority of papers did not follow through by controlling for this clustering or homogeneity effect in calculating their 95% confidence intervals around their effect size, leading to artificially narrower confidence intervals, and increasing the possibility that a result was statistically significant when it was not.

We dealt with these issues when grading the quality of evidence so that the reported quality of evidence was realistic. We used the adapted algorithm originally developed by Pollock *et al.*⁷³ to grade the quality of evidence in our overview of reviews. We provide a transparent record of downgrades applied to each systematic review in Appendix M. Some systematic review teams had applied GRADE to their outcomes using recommended tools; however, for consistency, we re-graded our outcomes using a systematic approach. This adjusted the GRADE classification for some reviews, and these adjustments are justified at the end of each paper summary in Appendices G to J.

Another issue of note is that only 19 systematic review teams ascertained who funded the primary studies in their review; of these, 17 reported that one or more studies included in their review was industry funded. Any data we have indicate that the dental industry plays a considerable role in funding primary research on the management of dental caries, and declaration of funding sources was not a common journal requirement when publishing primary research papers on this topic. The latter is important for transparency. We did a quick search on MEDLINE and identified 17 papers investigating or discussing dental industry funding of treatment interventions. One systematic review examining the effect of industry sponsorship on dental restorative trials, a topic related to this HRB overview, reported that 62 (54%) of 114 trials were clearly or possibly sponsored by industry sources; 18% were known to be sponsored and 36% were classified as possibly sponsored.¹⁸³ Sponsored trials evaluated restorations of load-bearing cavities significantly more often than non-sponsored trials, had longer follow-up periods, and showed significantly increased risk of detection bias. Schwendicke *et al.* concluded that the effect of industry sponsorship on dental restorative trials seems limited.¹⁸³ High detection bias in primary studies was one of the issues the HRB noted when examining the risk of bias in the systematic reviews included in this overview of reviews.

The points highlighted in this section are issues that need to be considered when using this research for clinical guidelines, and need to be addressed when designing future research. However, it is important to note that when we say that the evidence for an intervention is low or very low quality, it generally means that the research base upon which to evaluate the intervention is inadequate, rather than that the intervention itself is inadequate. There were few cases where the intervention was not useful (such as dental liners for permanent teeth and silver-reinforced glass ionomer cement).

5.4.3 Differences between protocol and review

The protocol specified the inclusion of a final search to be conducted in early 2021, the tight time frame did not allow for this final search to be conducted after the supplemental searches. While this may have excluded some reviews published at the beginning of 2021, this is a dynamic topic, with research regularly published on the area, and it was necessary to impose a cut-off date to allow for comprehensive data synthesis.

5.5 Future research

The research base in Ireland for evidence on restoration materials, techniques and processes could be improved by partnerships with international state-funded trial networks to increase the power of the trials and by employing best practice research techniques to minimise bias. In addition, Ireland could add to restoration survival data by establishing data collection at sentinel sites. There are research gaps that will need to be addressed through additional research including costs of dental treatments in Ireland and synthesis of newer research interventions not yet covered in systematic reviews. Of note, the presence or absence of community water fluoridation was not considered as part of the intervention effect in this review.

6 Conclusion

There are effective alternatives to manage early carious lesions and avoid invasive restorative procedures through non-invasive (fluoride-based and other products), and microinvasive (sealants and resin infiltration) treatments. In addition, there are viable alternatives to using dental amalgam to restore cavitated caries through either direct or indirect restorations. The promising direct alternates to dental amalgam are resin-modified glass ionomer cement, compomers, and different composite resins. In addition, there are promising indirect alternates including ceramics and resin composites. Crowns fabricated from gold, metal ceramic, all ceramic, or zirconia are other alternates in specific situations. Some of these alternatives are not quite as successful as dental amalgam and some are more successful. There are also improved support materials and techniques available to dentists to enhance the effectiveness of interventions and acceptability of their treatments. The techniques include methods (such as selective caries removal as well as chemical or laser caries removal methods) to maximise the conservation of dentine and reduce pain experienced by the patient. The support materials include using the most appropriate adhesive for the specific intervention.

The evidence base provided in this overview of reviews is based on the best available reviews; however, the description 'best' indicates a body of research that is of mainly low-quality evidence, and the quality of research requires improvement particularly in the design and conduct of RCTs. It is important to note that when we say that the evidence for an intervention is low or very low quality, it generally means that the research base upon which to evaluate the intervention is inadequate, rather than that the intervention itself is inadequate. There were few cases where the intervention was not useful (such as dental liners to support restorations of permanent teeth and silver-reinforced glass ionomer cement as a restorative material). The research base in Ireland for evidence on restoration materials, techniques and processes could be improved by partnerships with international state-funded trial networks to increase the power of the trials and by employing best practice research techniques to minimise bias. In addition, Ireland could add to restoration survival data by establishing data collection at sentinel sites.

Another important issue raised in several clinical guideline documents was the consideration, during the decision-making process, of patients' expectations, clinicians' expertise, and the individual clinical scenario alongside the best evidence. In addition, informed consent by patients was a requirement.

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Appendix A: Literature search strategies

Search description table

1. Results from initial searches					
	Database/Resource	Final search date	Results	Deduplicated results	Total included
Clinical databases	Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to December 04, 2020	05 Dec 2020	2,119		
	EBSCO CINAHL	07 Dec 2020	713		
	Scielo	09 Dec 2020	205		
Systematic review/HTA resources	Wiley & Sons Cochrane Library	07 Dec 2020	383		
	Epistemonikos	08 Dec 2020	348		
	Campbell Library	08 Dec 2020	0		
	AHRQ Systematic Review Data Repository	08 Dec 2020	0		
	Database of Abstracts of Reviews of Effects (DARE)	08 Dec 2020	201		
	DoPHER	08 Dec 2020	42		
	JB I Evidence Synthesis	08 Dec 2020	2		
	International Health Technology Assessment (HTA) database	08 Dec 2020	7		
	Health Evidence	09 Dec 2020	37		
	Social Systems Evidence	09 Dec 2020	0		
	Health Systems Evidence	09 Dec 2020	2		
Search engines	Google.com 1 st 100	10 Dec 2020	289		
	DuckDuckgo targeted searches	09 Dec 2020	131		
	Google Scholar 1 st 100	08 Dec 2020	350		
Open access repository/Preprints/Grey literature	Core.ac.uk	08 Dec 2020	150		
	Osf.io	08 Dec 2020	67		
	Researchsquare	08 Dec 2020	0		
	MedRxiv/BioRxiv	10 Dec 2020	33		
	Websites	10 Dec 2020	20		
Total			5,099	3,712	94*
2. Reference chasing and protocol follow-up					
References and citations	Reference chasing	09-12 Feb 2021	5,030		
	Citation chasing	09-12 Feb 2021	2,210		
	Combined and deduplicated		4,760		
Protocols	PROSPERO protocols	Feb 2021	533		
	Follow-up of protocols noted during the screening process		86	12	

Core text search	Screening of Keane <i>et al.</i> 's previous review ³³	Mar 2021	1
			13
3. Final searches (conducted near end of review)			
	Planned but not completed due to time constraints		0
Total number of papers included in final synthesis*			107

*Note: the two papers by Kielbassa *et al.*^{159,160} are two parts of one review published separately, therefore the review synthesis included 107 papers but 106 reviews.

Database search strategies

Ovid Medline search strategy			
Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to December 04, 2020			
Platform: Ovid			
Search date: 05 Dec 2020			
Caries terms	1	exp Dental Caries/ or Tooth Demineralization/	48056
	2	Dental Cavity preparation/ or DMF Index/ or Dental Caries Activity tests/ or Dental Caries Susceptibility/	19214
	3	(Caries or carious or cariogenic or cariology or dental fissure*).mp.	63595
	4	(karie* or "cariës" or carie).mp.	3333
	5	((decay* or lesion* or cavity or cavities or cavitated or "micro-cavity" or "micro-cavities") and (dent\$ or tooth or teeth)).mp.	64525
	6	((proximal or primary or secondary or progressive or progressing or arrested or frank) adj2 (lesion or lesions or defect* or fissure*)).mp.	25357
	7	(cavosurface* or cavitated or "non-cavitated" or noncavitated or "micro-cavitated" or microcavit* or precavitat* or "pre-cavitated").mp.	3953
	8	(active lesion* or inactive lesion* or sticky lesion* or defective filling*).mp.	1795
	9	((Dentine or dentin or enamel or root or pulp or cementum) adj2 (lesion* or decay* or cavit* or defect* or fissure*)).mp.	15563
	10	((Molar* or premolar* or incisor* or canine* or distal or mesial or coronal or "lingual-palatinal" or lingual or palatinal or buccal or "labial-buccal" or labial or occlusal or "incisal-occlusal" or incisal or pit or apical or periapical or approximal or proximal or maxillary or axiopulpal or subsurface or root) adj2 (lesion* or decay* or cavit* or fissure*)).mp.	15587
	11	((root or cervical) adj2 (lesion* or decay* or cavit* or fissure*)) and (dent* or tooth or teeth)).mp.	1637
	12	((decalcif* or demineral* or hypomineral*) adj5 (dent* or tooth or teeth)).mp.	4834
	13	(dent* and (white spot* or "white-spot" or brown spot*)).mp.	941
	14	(ICDAS or ICDAS-II).af.	512

	15	("Decayed, Missing, and Filled" or "Decayed, Missing, Filled" or "decayed-missing-filled" or DMFT or DMF Index).mp.	11741
	16	(lesion severity assessment or lesion activity assessment).mp.	31
	17	or/1-16	149766
Dental restoration methods	18	exp Dental Restoration, Permanent/ or Dental Restoration, temporary/ or Dental atraumatic restorative treatment/ or dental cavity preparation/	29928
	19	((filling or fillings or restoration\$ or restorative or repair\$) and (dental or tooth or teeth or dentist)).mp.	67390
	20	(direct restoration\$ or directly placed restoration\$ or indirect restoration\$ or posterior restoration\$ or first restoration* or permanent restoration* or invisible restoration* or adhesively retained restoration* or provisional restoration* or "Root and crown restoration" or "drill and fill" or "drilling and filling" or "root-end surgery" or "root end surgery" or "root-end treatment" or "root end treatment").mp.	2385
	21	(dental restoration failure/ or Dental Marginal Adaptation/) and filling*.ti,ab,kw,kf.	473
	22	((intracoronaral or extracoronaral) adj2 (preparation\$ or restoration)).mp.	47
	23	((open-sandwich or open sandwich or closed sandwich or closed-sandwich or sandwich technique*) and (dental or restoration or composite* or caries)) or sandwich restoration*).mp.	202
	24	((restorative or restoration or microinvasive or minimally invasive or non-restorative or conservative) adj2 (technique* or treatment or surgery)).mp.	74014
	25	(cavity preparation or prepared cavit* or dental internal adaptation or dental internal fit).mp.	8527
	26	(infiltrat* adj10 (caries or cavit* or teeth or lesion* or dent*)).mp.	13823
	27	(Lasers/ or laser*.mp.) and (dent* or tooth or teeth).ti,ab,kw.	9291
Dental restoration and caries prevention materials	28	((non-surgical adj2 treatment) or secondary prevention).ab,ti,kw,kf. and (dent* or tooth or teeth).ti,ab,kw.	512
	29	or/18-28	165,086
	30	exp Dental Alloys/ or alloy\$.mp.	57513
	31	exp Dental Cements/ or (Cement\$ or Biodentine or Ionomer\$ or Glass-ionomer\$ or Glassionomer\$ or compomer\$ or Polymer\$ or carbomer\$ or ormocer\$ or RMGIC or Cermet or glass-polyalkenoate or Polycarboxylat\$ or polyalkenoat\$ or silicat\$ or Vidrion or Meron or Optiband or Multicure or "Ultra Band Lok" or Heliocore or "Xeno III" or Delton).mp.	1,103,613
	32	exp Resins, Synthetic/ or Photoinitiators, Dental/ or (Resin\$ or Composite\$ or nanocomposite\$ or white filling\$ or Vertise Flow or Filtek or SonicFill or Clearfil or SmartCem2 or Scotchbond or SBMP or Dyract or Heliomolar or Compoglass or Adaptic or "bisphenol A Glycidyl methacrylate" or "Bis-GMA" or BisGMA or TEGDMA or UEDMA or Bulk fill* or nanofill* or Microhybrid or nanohybrid).mp.	30,6274
	33	"Pit and Fissure Sealants"/ or (Sealant\$ or Orthodontic adhesive\$ or dental varnish* or Fluor-Protector or "fluor protector" or durophat or durofluor or Difluorsilane or Difluorosilane or Nuva Seal or Panavia or "Rely X" or Retroplast or Geristore or "Fleck's" or Epoxylite).mp.	11025
	34	Inlays/ or (Inlay\$ or in-lay\$ or onlay\$ or on-lay\$).mp.	22623
	35	exp Dental Bonding/ or (Enamel bond\$ or dentin bond\$ or single bond\$).mp.	28585
	36	exp Crowns/ or (crown\$ or "Hall's technique" or Hall technique).mp.	49517
	37	exp Root Canal Filling Materials/ or root canal filling*.mp.	8491

	38	Dental Porcelain/ or exp Ceramics/ or (porcelain\$ or ceramic\$ or nanoceramic\$).mp.	40592
	39	Dental Pulp Capping/ or Pulpectomy/ or Pulpotomy/ or "Pulp Capping and Pulpectomy Agents"/ or (pulp cap\$ or Pulp therap\$ or pulpptom\$ or pulpect\$ or mineral trioxide aggregate or formocresol).mp.	7594
	40	exp Dental Amalgam/ or dental amalgam.nm. or (amalgam or amalgams or amalgam-free or amalgamfree or amalgamless or post-amalgam or silver filling\$ or mercury filling\$ or amalgaam or amalgama or amalgaami or amalgame or amalgamfyllningar or amalgamfyldninger or amalgamfyllinger or hammasamalgaami).mp. or (amalgamat\$ adj3 (mercury or dent\$)).mp.	11312
	41	(amalgamat\$ adj3 (mercury or dent\$)).mp.	78
	42	Dental Cavity Lining/	1836
	43	Sugar Alcohols/ or (xylitol or erythritol* or sorbitol or mannitol or manitol or polyol*).mp.	46243
	44	Tooth remineralization/ or Hydroxyapatites/ or (reminerali* or Zinc oxide or eugenol or hydroxyapatite* or hydroxylapatite or novamin or Nano-hydroxyapatite or casein phosphopeptide or amorphous calcium phosphate or "CPP-ACP" or "casein phosphopeptide-ACP" or recalden or ACP or "MI Paste" or glucitol or medevac or cervitec or arginine).mp.	186925
	45	Silver Nitrate/ or (silver adj (nitrate or diamine or diamine or ammonical or fluoride or flouride)).mp. or advantage arrest.mp.	6810
	46	exp Cariostatic Agents/ or cariostatic\$.mp.	35910
	47	(Sodium fluoride/ or Acidulated phosphate fluoride/ or Chlorhexidine/ or Calcium Phosphates/ or Calcium Hydroxide/ or Sodium Bicarbonate/) and (dent* or tooth or teeth or caries).ti,ab,kf,hw.	12422
	48	(remineralization agent* or nano hydroxyapatite or carbamide peroxide or chlorhexidine* or peridex or periRx or sodium monofluorophosphate or calcium phosphate or "tri-calcium phosphate" or tricalcium phosphate or calcium sodium phosphosilicate or casein phosphopeptide or calcium hydroxide or "NAHCO3" or "Ca(OH)2" or sodium bicarbonate or hydrogen carbonate or baking soda).mp. and (dent* or tooth or teeth or caries).ti,ab,kf,hw.	15075
	49	((fluorid* or flourid*) adj (stannous or sodium or phosphate or ammonium or silver or nano-silver or varnish or topical)).mp. and (dent* or tooth or teeth or caries).ti,ab,kf,hw.	4925
	50	Prebiotics/ or Probiotics/ or ((prebiotics or probiotics) and (dent* or tooth or teeth)).ti,ab,hw.	19519
	51	or/30-50	1719463
Restoration/ prevention techniques OR methods	52	29 or 51	1828244
Caries AND restoration/ prevention	53	17 and 52	56474
Systematic reviews ⁵⁶⁾	54	((systematic or state-of-the-art or scoping or literature or umbrella) adj (review* or overview* or assessment*)) or "review* of reviews" or meta-analy* or metaanaly* or ((systematic or evidence) adj1 assess*) or "research evidence" or metasynthe* or meta-synthe*).tw. or exp Review Literature as Topic/ or exp Review/ or Meta-Analysis as Topic/ or Meta-Analysis/ or "systematic review"/	2952525
Caries restoration	55	53 and 54	4864

/prevention SRs			
Date limit	56	limit 55 to yr="2009 -Current"	2119

EBSCO CINAHL Complete search strategy

Database: EBSCO CINAHL Complete

Platform: EBSCO

Search date: 07 Dec 2020

S1	(MH "Dental Caries") OR (MH "Tooth Demineralization+") OR (MH "Dental Caries Activity Tests")	13,111
S2	(TX (Caries OR carious OR cariogenic OR cariology OR karie* OR "cariës" OR carie OR "dental fissure" OR "dental fissures"))	46,386
S3	(TX (decay* OR lesion* OR cavity OR cavities OR cavitated OR "micro-cavity" OR "micro-cavities") N4 (dent* OR tooth OR teeth))	10,624
S4	(TX ((proximal OR primary OR secondary OR progressive OR progressing OR Arrested OR frank) N2 (lesion OR lesions OR defect* OR fissure*)) AND (dent* OR tooth OR teeth OR oral))	857
S5	TX (cavosurface* OR Cavitated OR "Non-cavitated" OR Noncavitated OR "Micro-cavitated" OR "Micro-cavity" OR "Micro-cavities" OR Microcavit* OR "Pre-cavitated" OR Precavitat*)	776
S6	TX ("active lesion" OR "active lesions" OR "inactive lesion" OR "inactive lesions" OR "sticky lesion" OR "sticky lesions" OR "defective filling" OR "defective fillings") AND TX (dent* OR tooth OR teeth OR oral)	340
S7	TX ((Dentine OR dentin OR enamel OR root OR pulp OR cementum) N2 (lesion* OR decay* OR cavit* OR defect* OR fissure*)) AND TX (dent* OR tooth OR teeth OR oral)	3,126
S8	TX (((Molar* OR premolar* OR incisor* OR canine* OR distal OR mesial OR coronal OR "lingual-palatinal" OR Lingual OR Palatinal OR buccal OR "labial-buccal" OR labial OR occlusal OR "incisal-occlusal" OR incisal OR pit OR apical OR periapical OR approximal OR proximal OR maxillary OR axiopulpal OR subsurface) N2 (lesion* OR decay* OR cavit* OR fissure*)) AND (dent* OR tooth OR teeth OR oral)	3,021
S9	TX ((Cervical OR root) N2 (lesion* OR decay* OR cavit*)) AND TX (dent* OR tooth OR teeth)	1,047
S10	TX ((decalcif* OR demineral* OR hypomineral*) N5 (dent* OR tooth OR teeth))	1,662
S11	TX ((dent*) AND ("white spot" OR "white spots" OR "white-spot" OR "brown spot" OR "brown spots"))	672
S12	TX (ICDAS or "ICDAS-II")	404
S13	TI ("Decayed, Missing, and Filled" OR "Decayed, Missing, Filled" OR "decayed-missing-filled" OR DMFT OR "DMF Index") OR AB ("Decayed, Missing, and Filled" OR "Decayed, Missing, Filled" OR "decayed-missing-filled" OR DMFT OR "DMF Index") OR KW ("Decayed, Missing, and Filled" OR "Decayed, Missing, Filled" OR "decayed-missing-filled" OR DMFT OR "DMF Index")	1,605
S14	TX ("lesion severity assessment" OR "lesion activity assessment")	15
S15	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14	54,989
S16	(MH "Dental Restoration, permanent+") OR (MH "Dental Restoration, temporary")	8,991
S17	TX ((filling OR fillings OR restoration* OR restorative OR repair*) AND (dental OR tooth OR teeth OR dentist*))	36,358
S18	(TX ("direct restoration" OR "direct restorations" OR "directly placed restoration" OR "directly placed restorations" OR "indirect restoration" OR "indirect restorations" OR "posterior restoration" OR "posterior restorations" OR "first restoration" OR "first restorations" OR "permanent restoration" OR "permanent restorations" OR "invisible restoration" OR "adhesively retained restoration" OR "adhesively retained restorations" OR "provisional restoration" OR "provisional restorations" OR	859

	"Root and crown restoration" OR "drill and fill" OR "drilling and filling" OR "root-end surgery" OR "root end surgery" OR "root-end treatment" OR "root end treatment"))	
S19	TX ((intracoronaral or extracoronaral) N2 (preparation* or restoration))	20
S20	TX (((("open-sandwich" OR "open sandwich" OR "closed sandwich" OR "closed-sandwich" OR "sandwich technique" OR "sandwich techniques") AND (dental OR restoration OR composite* OR caries)) OR ("sandwich restorations" OR "sandwich restoration"))	69
S21	TX ((Restorative OR restoration OR microinvasive OR "minimally invasive" OR "non-restorative" OR conservative) N2 (technique* OR treatment OR surgery))	35,062
S22	TX ("cavity preparation" OR "prepared cavity" OR "prepared cavities" OR "dental internal adaptation" or "dental internal fit")	308
S23	TX ((infiltrat*) N10 (caries or cavit* OR teeth OR lesion* OR dent*))	4,321
S24	((MH "Lasers") OR TX (laser OR lasers)) AND TX (dent* OR tooth OR teeth)	8,717
S25	TX (("non-surgical" N2 treatment) OR "secondary prevention") AND TX (dent* or tooth or teeth)	2,557
S26	S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25	82,454
S27	(MH "Dental Alloys+") OR (MH "Alloys+") OR (TX alloy*)	8,189
S28	MH ("Dental Cements") OR TX (cement* OR Biodentine OR Ionomer* OR "Glass-ionomer" OR "Glass-ionomers" or Glassionomer* OR compomer* OR Polymer* OR carbomer* OR ormocer* OR RMGIC OR Cermet OR "glass-polyalkenoate" OR Polycarboxylat* OR polyalkenoate* OR silicat* OR Vidrion OR Meron OR Optiband OR Multicure OR "Ultra Band Lok" OR Heliaseal OR "Xeno III" OR Delton)	119,281
S29	(MH "Resins, Synthetic+") OR TX (Resin* OR Composite* OR nanocomposite* OR white filling* OR "Vertise Flow" OR Filtek OR SonicFill OR Clearfil OR SmartCem2 OR Scotchbond OR SBMP OR Dyract OR Heliomolar OR Compoglass OR Adaptic OR "bisphenol A Glycidyl methacrylate" OR "Bis-GMA" OR BisGMA OR TEGDMA OR UEDMA OR "Bulk fill" OR nanofill OR Microhybrid OR nanohybrid)	77,615
S30	(MH "Pit and Fissure Sealants") OR TX (sealant* OR "Orthodontic adhesive" OR "orthodontic adhesives" OR "dental varnish" OR "dental varnishes" OR "Fluor-Protector" OR "fluorprotector" OR difluorsilane OR difluorosilane OR "Nuva Seal" OR Panavia OR "Rely X" OR Retroplast OR Geristore OR "Fleck's" OR Epoxylite)	5,261
S31	(MH "Inlays") OR TX (inlay* OR "in-lay" OR "in-lays" OR onlay* OR "on-lays" OR "on-lay"))	57,851
S32	(MH "Dental Bonding+") OR TX ("enamel bond" OR "enamel bonds" OR "enamel bonding" OR "dentin bond" OR "dentin bonds" OR "dentin bonding" OR "dentin-bonded" OR "enamel-dentin-bonded" OR "single bond" OR "single bonded")	4,805
S33	(MH "Crowns") OR TX (crown OR crowns OR "Hall's technique" OR "Hall technique"))	17,419
S34	(MH "Root Canal Filling Materials") OR TX ("root canal filling" OR "Root canal fillings"))	1,400
S35	(MH "Dental Porcelain") OR TX (porcelain* OR ceramic* OR Nanoceramic* OR bioceramic*)	9,600
S36	(MH "Pulpectomy") OR TX ("pulp capping" OR "pulp therapy" OR pulpotom* OR pulpectom* OR "mineral trioxide aggregate" OR formocresol))	996
S37	(MH "dental amalgam") OR TX (amalgam OR amalgams OR "silver filling" OR "silver fillings" OR "mercury filling" OR "mercury fillings" OR "amalgam-free" OR amalgamfree OR amalgamless OR "post-amalgam" OR amalgaam OR amalgama OR amalgaami OR amalgame OR amalgamfyllningar OR amalgamfyldningar OR amalgamfyllinger OR hammasamalgaami)) OR (amalgamat* N3 (mercury OR dent*))	3,496
S38	(MH "Sugar Alcohols+") OR TX (xylitol OR erythritol* OR sorbitol OR mannitol OR manitol OR polyol*)	13,750
S39	(MH "Tooth Remineralization") OR (MH "Hydroxyapatites") OR TX (Reminerali* OR "Zinc oxide" OR Eugenol OR hydroxyapatite* OR hydroxylapatite OR Novamin OR "Nano-hydroxyapatite" OR "casein phosphopeptide" OR "amorphous calcium phosphate" OR "CPP-ACP" OR "casein phosphopeptide-ACP" OR Recalden OR ACP OR "MI Paste" OR Glucitol OR Medevac OR Cervitec OR Arginine))	31,561
S40	(MH "silver nitrate") OR TX ((silver) N1 (nitrate OR diamine or diamine OR ammonical OR fluoride OR flouride))) OR TX ("advantage arrest")	1,589
S41	(MH "Cariostatic Agents") OR TX (cariostatic)	1,417

S42	((MH "Fluorides+") OR (MH "Chlorhexidine") OR (MH "Phosphates") OR (MH "Sodium Bicarbonate") OR (MH "Hydroxides")) AND TX (dent* OR tooth OR teeth OR caries)	6,183
S43	TX ("remineralization agent" OR "remineralization agents" OR "remineralisation agent" OR "remineralisation agents" OR "nano hydroxyapatite" OR "carbamide peroxide" OR chlorhexidine* OR peridex OR periRx OR "sodium monofluorophosphate" OR "calcium phosphate" OR "tri-calcium phosphate" OR "tricalcium phosphate" OR "calcium sodium phosphosilicate" OR "casein phosphopeptide" OR "calcium hydroxide" OR "NAHCO3" OR "Ca(OH)2" OR "sodium bicarbonate" OR "hydrogen carbonate" OR "baking soda") AND (dent* OR tooth OR teeth OR caries)	4,418
S44	TX ((fluorid* OR flourid*) N1 (stannous OR sodium OR phosphate OR ammonium OR silver OR "nano-silver" OR varnish OR topical)) AND TX (dent* OR tooth OR teeth OR caries)	4,212
S45	(MH "Prebiotics") OR (MH "Probiotics") OR (TX (prebiotic* OR probiotic*) AND (dent* OR tooth OR teeth))	8,980
S46	S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45	317,469
S47	S26 OR S46	373,030
S48	S15 AND S47	21,296
S49	TI (((systematic OR state-of-the-art OR scoping OR literature OR umbrella) W0 (review OR reviews OR overview* OR assessment*)) OR "review* of reviews" OR meta-analy* OR metaanaly* OR ((systematic OR evidence) N1 assess*) OR "research evidence" OR metasynthe* OR meta-synthe*) OR AB (((systematic OR state-of-the-art OR scoping OR literature OR umbrella) W0 (review OR reviews OR overview* OR assessment*)) OR "review* of reviews" OR meta-analy* OR metaanaly* OR ((systematic OR evidence) N1 assess*) OR "research evidence" OR metasynthe* OR meta-synthe*) OR KW (((systematic OR state-of-the-art OR scoping OR literature OR umbrella) W0 (review OR reviews OR overview* OR assessment*)) OR "review* of reviews" OR meta-analy* OR metaanaly* OR ((systematic OR evidence) N1 assess*) OR "research evidence" OR metasynthe* OR meta-synthe*) OR MH ("Literature Review+" OR "Meta Analysis" OR "Meta Synthesis" OR "Cochrane Library"))	223,522
S50	PT "systematic review" OR "Meta Analysis" OR "Meta Synthesis"	119,523
S51	S49 OR S50	230,264
S52	S48 AND S51	815
S53	DT 20090101-20201231	5,041,991
S54	S52 AND S53	713

Scielo search strategy

Database: Scielo

Platform: <https://scielo.org/>

Search date: 09 Dec 2020

((ab:(*caries))) AND (review OR systematic OR meta-analysis) 205

Note: an abbreviated search was used for Scielo given the overlap with Medline

Wiley Cochrane Library search strategy

Database: Cochrane Library

Platform: John Wiley & Sons Inc. <https://www.cochranelibrary.com/>

Search date: 07 Dec 2020

#1	MeSH descriptor: [Dental Caries] explode all trees	2,593
#2	MeSH descriptor: [Tooth Demineralization] explode all trees	2,799
#3	MeSH descriptor: [Dental Cavity Preparation] explode all trees	626
#4	MeSH descriptor: [DMF Index] explode all trees	515
#5	MeSH descriptor: [Dental Caries Activity Tests] explode all trees	42
#6	MeSH descriptor: [Dental Caries Susceptibility] explode all trees	100
#7	((Caries or carious or cariogenic or cariology or "dental fissure" or "dental fissures" or cavosurface* or cavitated or "non-cavitated" or noncavitated or "micro-cavitated" or microcavit* or precavitat* or "pre-cavitated" or "active lesion" OR "active lesions" or "inactive lesion" OR "inactive lesions" or "sticky lesion" or "sticky lesions" or "defective filling" or "defective fillings" or "lesion severity assessment" or "lesion activity assessment" or ICDAS or "ICDAS-II" or "Decayed, Missing, and Filled" or "Decayed, Missing, Filled" or "decayed-missing-filled" or DMFT or "DMF Index")):ti,ab,kw	7,464
#8	((((decay* or lesion* or cavity or cavities or cavitated or "micro-cavity" or "micro-cavities") and (dent* or tooth or teeth))):ti,ab,kw	6,637
#9	((proximal or primary or secondary or progressive or progressing or arrested or frank or Dentine or dentin or enamel or root or pulp or cementum or Molar* or premolar* or incisor* or canine* or distal or mesial or coronal or "lingual-palatinal" or lingual or palatinal or buccal or "labial-buccal" or labial or occlusal or "incisal-occlusal" or incisal or pit or apical or periapical or approximal or proximal or maxillary or axiopulpal or subsurface or root) NEAR (lesion or lesions or defect* or fissure*)):ti,ab,kw	7,729
#10	(((((root or cervical) NEAR (lesion* or decay* or cavit* or fissure*)) and (dent* or tooth or teeth))):ti,ab,kw	619
#11	((((decalcif* or demineral* or hypomineral*) NEAR (dent* or tooth or teeth))):ti,ab,kw	604
#12	((dent* and (white spot* or "white-spot" or "brown spot" or "brown spots"))):ti,ab,kw	279
#13	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12	16,675
	Of which Cochrane reviews	419
	Date limit 2009-2020: Cochrane reviews:	383

Epistemonikos search strategy

Database: Epistemonikos

Platform:

Search date: 08 Dec 2020

(title:((title:((Caries OR carious OR cariogenic OR cariology OR "dental fissure" OR "dental fissures" OR "dental decay" OR "dental lesion" OR cavity OR cavities OR cavitated OR "micro-cavity" OR "micro-cavities" OR "non-cavitated" OR noncavitated OR "micro-cavitated" OR precavitat* OR "pre-cavitated" OR cavosurface OR "active lesion" OR "active lesions" OR "inactive lesion" OR "inactive lesions" OR "sticky lesion" OR "sticky lesions" OR "defective filling" OR "defective fillings" OR "proximal lesion" OR "primary lesion" OR "secondary lesion" OR "progressive lesion" OR "progressing lesion" OR "arrested lesion" OR "frank lesion")) OR abstract:((Caries OR carious OR cariogenic OR cariology OR "dental fissure" OR "dental fissures" OR "dental decay" OR "dental lesion" OR cavity OR cavities OR cavitated OR "micro-cavity" OR "micro-cavities" OR "non-cavitated" OR noncavitated OR "micro-cavitated" OR precavitat* OR "pre-cavitated" OR cavosurface OR "active lesion" OR "active lesions" OR "inactive lesion" OR "inactive lesions" OR "sticky lesion" OR "sticky lesions" OR "defective filling" OR "defective fillings" OR "proximal lesion" OR "primary lesion" OR "secondary lesion" OR "progressive lesion" OR "progressing lesion" OR "arrested lesion" OR "frank lesion")))) AND (title:(restoration OR restorative OR filling OR fillings OR "root end surgery" OR microinvasive OR infiltration OR "cavity preparation" OR "dental cement" OR composite OR resin* OR alloy* OR sealant* OR bonding OR crown* OR inlay* OR onlay* OR porcelain* OR amalgam OR "cavity lining" OR reminerali* OR hydroxyapatite OR biodentine OR fluoride OR calcium OR chlorhexidine OR silver) OR abstract:(restoration OR restorative OR filling OR fillings OR "root end surgery" OR microinvasive OR infiltration OR "cavity preparation" OR "dental cement" OR composite OR resin* OR alloy* OR sealant* OR bonding OR crown* OR inlay* OR onlay* OR porcelain* OR amalgam OR "cavity lining" OR reminerali* OR hydroxyapatite OR biodentine OR fluoride OR calcium OR chlorhexidine OR silver)) AND (title:(dental OR dentistry OR dentist OR tooth OR teeth) OR abstract:(dental OR dentistry OR dentist OR tooth OR teeth))) OR abstract:((title:((Caries

OR carious OR cariogenic OR cariology OR "dental fissure" OR "dental fissures" OR "dental decay" OR "dental lesion" OR cavity OR cavities OR cavitated OR "micro-cavity" OR "micro-cavities" OR "non-cavitated" OR noncavitated OR "micro-cavitated" OR precavitated* OR "pre-cavitated" OR cavosurface OR "active lesion" OR "active lesions" OR "inactive lesion" OR "inactive lesions" OR "sticky lesion" OR "sticky lesions" OR "defective filling" OR "defective fillings" OR "proximal lesion" OR "primary lesion" OR "secondary lesion" OR "progressive lesion" OR "progressing lesion" OR "arrested lesion" OR "frank lesion")) OR abstract:((Caries OR carious OR cariogenic OR cariology OR "dental fissure" OR "dental fissures" OR "dental decay" OR "dental lesion" OR cavity OR cavities OR cavitated OR "micro-cavity" OR "micro-cavities" OR "non-cavitated" OR noncavitated OR "micro-cavitated" OR precavitated* OR "pre-cavitated" OR cavosurface OR "active lesion" OR "active lesions" OR "inactive lesion" OR "inactive lesions" OR "sticky lesion" OR "sticky lesions" OR "defective filling" OR "defective fillings" OR "proximal lesion" OR "primary lesion" OR "secondary lesion" OR "progressive lesion" OR "progressing lesion" OR "arrested lesion" OR "frank lesion")) AND (title:(restoration OR restorative OR filling OR fillings OR "root end surgery" OR microinvasive OR infiltration OR "cavity preparation" OR "dental cement" OR composite OR resin* OR alloy* OR sealant* OR bonding OR crown* OR inlay* OR onlay* OR porcelain* OR amalgam OR "cavity lining" OR reminerali* OR hydroxyapatite OR biodentine OR fluoride OR calcium OR chlorhexidine OR silver) OR abstract:(restoration OR restorative OR filling OR fillings OR "root end surgery" OR microinvasive OR infiltration OR "cavity preparation" OR "dental cement" OR composite OR resin* OR alloy* OR sealant* OR bonding OR crown* OR inlay* OR onlay* OR porcelain* OR amalgam OR "cavity lining" OR reminerali* OR hydroxyapatite OR biodentine OR fluoride OR calcium OR chlorhexidine OR silver)) AND (title:(dental OR dentistry OR dentist OR tooth OR teeth) OR abstract:(dental OR dentistry OR dentist OR tooth OR teeth))))

Last 10 years and SRs: 348

Campbell Library search strategy

Database: Campbell Library

Platform: Wiley Campbell Library by the Campbell Collaboration

Search date: 08 Dec 2020

Caries	0
Carious	0
Dental restoration	0
Filling	0

AHRQ Systematic review data repository search strategy

Database AHRQ Systematic review data repository (SRDR)

Platform: AHRQ <https://sdr.ahrq.gov/>

Search date: 08 Dec 2020

Title: caries: 0	0
Description: caries: 0	0
Title dental 0	0
description: dental	0
Title: tooth 0	0
Description: tooth 0	0
Title: teeth 0	0
description teeth 0	0
Title: restoration 0	0
Description: restoration: 0	0

[Note: EPC evidence reports: Caries: 2 results, pre-dating 2009]

DARE/NHS EED/HTA search strategy

Database: The Database of Abstracts of Reviews of Effects (DARE), NHS Economic Evaluation Database (EED) and HTA

Platform: University of York Centre for Reviews and Dissemination <https://www.crd.york.ac.uk/CRDWeb/>

Search date: 08 Dec 2020

Mesh search for Caries:	164 results, of which 82 published 2009- 2020 or no date given	
Any field: (caries OR carious OR dental cavity OR dental cavities OR cavitated OR cavities) OR (dental fissure OR dental fissures OR dental decay OR tooth decay OR dental lesion OR dental lesions) OR (microcavity OR micro-cavity OR micro-cavities OR precavitated OR noncavitated OR non-cavitated) FROM 2009 TO 2020	133	
Any Field: Results for: (lesion* OR decay* OR defect* OR fissure*) AND (proximal OR primary OR secondary OR progressive OR progressing OR arrested OR frank) AND (dent* OR teeth OR tooth) FROM 2009 TO 2020	33	
Any Field: Results for: (Molar* OR premolar* OR incisor* OR canine* OR distal OR mesial OR coronal OR "lingual-palatinal" OR Lingual OR Palatinal OR buccal OR labial-buccal OR labial OR occlusal OR "incisal-occlusal" OR incisal OR pit OR apical OR periapical OR approximal OR proximal OR maxillary OR axiopulpal OR subsurface OR root) AND (lesion* OR decay* OR cavit* OR fissure*) FROM 2009 TO 2020	70	
Results for: (Dentine OR dentin OR enamel OR root OR pulp OR cementum) AND (lesion* OR decay* OR cavit* OR defect* OR fissure*) FROM 2009 TO 2020	50	
Deduplicated	368	201 unique results

DoPHER search strategy

Database: DoPHER

Platform: EPPI-Centre <https://eppi.ioe.ac.uk/webdatabases4/Intro.aspx?ID=9>

Search date: 08.12.2020

		Date range: 2009-2020
Freetext (All but Authors): caries OR carious OR "dental cavity" OR "dental cavities" OR cavitated OR cavities OR "dental fissure" OR "dental fissures" OR "dental decay" OR "tooth decay" OR "dental lesion" OR "dental lesions" OR microcavity OR "micro-cavity" OR "micro-cavities" OR precavitated OR noncavitated OR "non-cavitated"	74	42
Freetext (All but Authors): "proximal OR primary OR secondary OR progressive OR progressing OR arrested OR frank"	0	0
Freetext (All but Authors): dental	4	0
AND Freetext (All but Authors): Molar* OR premolar* OR incisor* OR canine* OR distal OR mesial OR coronal OR "lingual-palatinal" OR Lingual OR Palatinal OR buccal OR labial-buccal OR labial OR occlusal OR "incisal-occlusal" OR		

incisal OR pit OR apical OR periapical OR approximal OR proximal OR maxillary OR axiopulpal OR subsurface OR root		
Freetext (All but Authors): "Dentine OR dentin OR enamel OR root OR pulp OR cementum "	0	0
		42

JB1 Evidence Synthesis search strategy

Database: JBI Evidence Synthesis

Platform: Joanna Briggs Institute <https://journals.lww.com/jbisrir/pages/advancedsearch.aspx>

Search date: 08 Dec 2020

Showing 2 results for: caries OR carious OR "dental cavity" OR "dental cavities" OR cavitated OR cavities OR "dental fissure" OR "dental fissures" OR "dental decay" OR "tooth decay" OR "dental lesion" OR "dental lesions" OR microcavity OR "micro cavity" OR "micro cavities" OR precavitated OR noncavitated OR "non cavitated"; restoration OR repair OR filling* OR resin* OR porcelain* OR inlay* OR onlay* OR composite OR ionomer* OR amalgam OR hydroxyapatites OR xylitol OR fluoride* OR silver* Or infiltrat*	2

International HTA database search strategy

Database: International HTA database

Platform: <https://database.inahta.org/>

Search date: 08 Dec 2020

Dates		2009-2020
"Dental Caries"[mh]	14	7
(caries OR carious OR "dental cavity" OR "dental cavities" OR cavitated OR cavities OR "dental fissure" OR "dental fissures" OR "dental decay" OR "tooth decay" OR "dental lesion" OR "dental lesions" OR microcavity OR "micro-cavity" OR "micro-cavities" OR precavitated OR noncavitated OR "non-cavitated") FROM 2009 TO 2021		15
(cavosurface* or cavitated or "non-cavitated" or noncavitated or "micro-cavitated" or microcavit* or precavitat* or "pre-cavitated") FROM 2009 TO 2021		0
((decalfif* or demineral* or hypomineral*) FROM 2009 TO 2021) AND (dent* OR tooth OR teeth) FROM 2009 TO 2021		0

Google.com search strategy

Search engine: Google

Platform: www.google.com

Search date: 10 Dec 2020

Limits:

Date range: 2009-2020

Ads not included

'Free pdf' or phishing type sites not included

Caries restoration review	First 80 results (following results were advertisements for dental clinics)
Dental cavity operative "review"	First 71 results (following results were advertisements)
Cavities restoration "review"	73 results
Caries management "review"	61 results (following results were advertisements)
285	

DuckDuckGo search strategy

Search engine: DuckDuckGo

Platform: <https://duckduckgo.com/>

Search date: 09 Dec 2020

All Regions

Caries restoration "systematic review" (ad links excluded)	27
All regions Any time Safe search: moderate All formats	
"Review" caries cavities carious fillings restoration restorative microinvasive infiltration	27
Caries review synthesis filetype:pdf ad links excluded)	28
All regions Any time Safe search: moderate All formats	
Dental cavity repair systematic review HTA synthesis	21
Dental fillings systematic review	28
	131

Google Scholar "First 100 results" search strategy

Search engine: Google Scholar

Platform: <https://scholar.google.com/>

Search date: 08 Dec 2020

Limit: First 100 results for each search

Date range: 2009-2021

"Systematic review" caries restoration OR filling OR fillings OR restorative OR microinvasive OR infiltration OR composite	100	
Caries restoration "systematic review"	100	About 17,800 results (0.08 sec)
Caries management systematic review	150	About 18,400 results (0.10 sec)

Core.ac.uk search strategy		
Search repository: Core.ac.uk		
Search date: 08 Dec 2020		
Limit: first 50 results taken for each search set		
Showing results for title:((caries) ""systematic review"" AND (restoration OR repair OR filling OR amalgam OR composite OR resin OR porcelain OR inlay OR onlay OR infiltration OR fluoride OR silver)) abstract:((caries) ""systematic review"" AND (restoration OR repair OR filling OR amalgam OR composite OR resin OR porcelain OR inlay OR onlay OR infiltration OR fluoride OR silver)) AND year:[2009 TO 2020]	37,416 articles found	1 st 50 results
Showing results for title:((caries) ""systematic review"" AND (restoration OR repair OR filling OR amalgam OR composite OR resin OR porcelain OR inlay OR onlay OR infiltration OR fluoride OR silver)) AND year:[2009 TO 2020]	7,261 articles found	1 st 50 results
Showing results for title:(("cavity AND repair") ""systematic review"" AND (dental OR caries OR carious OR teeth OR tooth)) AND year:[2009 TO 2020]	6,166 articles found	1 st 50 results

OSF.io search strategy		
Database: OSF		
Website: Centre for Open Science. https://osf.io/search/		
Search date: 08 Dec 2020		
Tags:("caries") OR tags:("early childhood caries") OR tags:("dental caries")	All OSF results 17	17
Dental Cavity repair review First 50 results	41104	50
Total		67

ResearchSquare search strategy	
Database: ResearchSquare	
Website: https://www.researchsquare.com/	
Search date: 08 Dec 2020	
Search: Abstract	
Date: 2009-present	
Publication type: systematic reviews	
Caries	0
"Dental restoration"	0
Ionomer	0
Filling	0

Amalgam	0
Cavities	0
Carious	0
"Dental lesion"	0

Note: for MedRxiv and BioRxiv, searches were abbreviated, as search results produced thousands of out of scope results

Biorxiv search strategy

Database: BioRxiv

Website: <https://www.biorxiv.org/>

Server: Cold Spring Harbour Laboratory

Founded by Cold Spring Harbour Laboratory

Search date: 10 Dec 2020

Limits: dates 2009-2010

title ""caries"" (match phrase words) and posted between "01 Jan, 2009 and 31 Dec, 2020"	16
title ""dental restoration"" (match phrase words) and posted between "01 Jan, 2009 and 31 Dec, 2020"	1
title ""dental restorations"" (match phrase words)	
title "sealant" (match phrase words)	0
title "silver diamine" (match phrase words)	2
title "dental composite" (match all words)	0
title "ionomer" (match all words)	2
BioRxiv total	21

MedRxiv search strategy

Database: MedRxiv

Website: <https://www.medrxiv.org/>

Server: Cold Spring Harbour Laboratory

Founded by Cold Spring Harbour Laboratory, BMJ, Yale University

Search date: 10 Dec 2020

title "caries" (match all words)	7
title "dental restorations" (match phrase words)	0
title "dental restoration" (match phrase words)	0
abstract or title "dental restoration" (match phrase words)	0
abstract or title "dental composite" (match all words)	2
abstract or title "ionomer" (match all words)	1
abstract or title "silver diamine" (match phrase words)	2
abstract or title "sealant" (match phrase words)	0

MedRxiv total	12
BioRxiv + MedRxiv combined total	33

Websites used to search for systematic reviews

Search date: 10 Dec 2020

<https://www.eudental.eu/about.html> caries

<https://www.adee.org/>

<https://www.eadph.org/?s=caries>

www.dentist.ie

<https://www.fdiworldddental.org/>

<https://www.eapd.eu/index.php/education>

<https://www.bda.org/>

<https://www.ucc.ie/en/ohsrc/>

<https://www.aapd.org/>

<https://www.sdcep.org.uk/>

<https://jcda.ca/>

<https://www.awmf.org>

<https://nam.edu/>

www.nice.org.uk

<https://www.agd.org/>

www.cdc.org

Health Evidence search strategy

Database: Health Evidence

Website: <https://www.healthevidence.org/>

Search date: 09 Dec 2020

Results for: [(caries OR caviti*) AND (restor* OR repair OR sealant* OR composite OR resin OR ionomer* OR filling* OR fluoride*)] AND Limit: Date = Published from 2009 to 2020 37

Social Systems Evidence search strategy

Database: Social Systems Evidence

Website: <https://www.socialsystemsevidence.org/?lang=en>

Search date: 09 Dec 2020

Caries AND "dental restoration"	0
Caries AND Repair	0
Dental cavity AND Repair	0
Caries AND Sealants	0

Caries AND Filling	0
Caries AND Composites	0
Total included	0

Health Systems Evidence search strategy

Database: Health Systems Evidence

Website: <https://www.healthsystemsevidence.org/?lang=en>

Search date: 09 Dec 2020

Caries AND "dental restoration"	0
Caries AND Repair	0
Cavit* AND Restor*	0
Caries AND Sealant	2
Caries AND Filling	0
Caries AND Composite	0
Total included after deduplication	2

National Institute for Health Research

PROSPERO international prospective register of systematic reviews

Brief searches for relevant protocols

Caries AND restor*	263
Cavit* AND Restor*	135
Non-cavit* AND intervention*	15
Caries filling	1
Caries composite	1
Microcavit*	0
Total	533

Appendix B: Relevant non-English language papers excluded at any stage of screening

Note: This list includes non-English language papers excluded from the review process at the title and abstract screening stage that may cover topics relevant to the review, indicating the wider body of relevant literature that was beyond the scope of the review but must be acknowledged.

There were ten languages represented in this group of papers: Chinese, Dutch, French, German, Italian, Norwegian, Persian, Polish, Russian, and Spanish. These papers originated from a range of countries and were captured using English-based databases, suggesting that there is considerable research done on this topic across the globe in many languages other than English. Some of these papers were published with English abstracts or keywords.

Chinese

1. Xiaotong W, Nanquan R, Jing X, *et al.*¹⁸⁴ 酪蛋白磷酸肽-无定型磷酸钙凝胶治疗釉质脱矿效果的系统评价. *Hua Xi Kou Qiang Yi Xue Za Zhi* 2017;35(6):629-35. Available at: <https://doi.org/10.7518/hxkq.2017.06.013>
2. Zhang D, Chen X.¹⁸⁵ [Research on the aging of all-ceramics restoration materials]. *Shengwu Yixue Gongchengxue Zazhi* 2011;28(5):1048-51. Available at: <https://pubmed.ncbi.nlm.nih.gov/22097281/>

Dutch

1. Frencken JE.¹⁸⁶ Hoe zinvol is restauratieve behandeling van het tijdelijk gebit? *Ned Tijdschr Tandheelkd* 2017;124(4):187-92. Available at: <https://doi.org/10.5177/ntvt.2017.04.16207>
2. Frencken JE, Flohil KA, de Baat C.¹⁸⁷ Atraumatic restorative treatment in relatie tot pijn, ongemak en angst voor tandheelkundige behandelingen. *Ned Tijdschr Tandheelkd* 2014;121(7-8):388-93. Available at: <https://doi.org/10.5177/ntvt.2014.07/08.13240>
3. Hollanders ACC, Kuper NK, Opdam NJM, *et al.*¹⁸⁸ Preventieve tandheelkunde 5. Secundaire cariës. *Ned Tijdschr Tandheelkd* 2017;124(5):257-63. Available at: <https://doi.org/10.5177/ntvt.2017.05.16212>
4. van de Sande FH.¹⁸⁹ Hora est 5. Levensduur van composietrestauraties in posterieure gebitsdelen. *Ned Tijdschr Tandheelkd* 2016;123(9):429-31. Available at: <https://doi.org/10.5177/ntvt.2016.09.16182>

German

1. Schwendicke F.¹⁹⁰ Unvollständige kariesentfernung: eine systematische Übersicht und meta-analyse. *Z Evid Fortbild Qual Gesundhwes* 2015;109(1):56-8. Available at: <https://doi.org/10.1016/j.zefq.2015.01.009>

Italian

1. Polesel A.¹⁹¹ Il restauro conservativo del dente singolo posteriore trattato endodonticamente. *G Ital Endod* 2011;25(1):3-21. Available at: <https://doi.org/10.1016/j.gien.2011.05.006>

Norwegian

1. Steiro A, Strøm V, Hafstad E, *et al.*¹⁹² Helseskadelige effekter ved bruk av tannkomposittmaterialer Systematisk oversikt. Oslo: Folkehelseinstituttet, avdeling for kunnskapsoppsummering, 2016:91pp. Available at: <https://www.fhi.no/globalassets/dokumenterfiler/rapporter/2016/helseskadelige-effekter-ved-bruk-av-tannkomposittmaterialer.-systematisk-oversikt.pdf>

Persian

- 1.¹⁹³ Journal of Dental Medicine 2016;29(3):215-22. Available at: <http://jdm.tums.ac.ir/article-1-5566-fa.html>
2. Daneshkazemi A, Ersi M.¹⁹⁴ A review of silorane and methacrylate based composites and effective factors on microleakage of them [م. ضرور و صرف: ی بر کامپوزیت های متاکریلات و سیلوران بیس و عوامل موثر بر ریس نشأت آن ها]. *JSSU* 2020; 28(6).
3. Keshvad MA, Hooshmand T.¹⁹⁵ Evaluation of the theoretical and clinical methods for reducing marginal leakage in resin-based composite restorative materials: A review. [مقاله مروری: بررسی راهکارهای نظری و بالینی موجود برای کاهش Marginal leakage در مواد رزین کامپوزیتی]. *J Dent Med* 2016; 29(2). <http://jdm.tums.ac.ir/article-1-5533-fa.html>.
4. مروری بر جایگاه فلوراید سیستمیک در دندان پزشکی پیشگیری¹⁹⁶. *et al.* محمّدپور م، منصوری م، خادمی ع. *Journal of Isfahan Dental School* 2014;10(6):498-506.

Polish

1. Berczynski P, Gmerek A, Buczkowska-Radlinska J.¹⁹⁷ Remineralizing methods in early caries lesions -- review of the literature. *Pomeranian J Life Sci* 2015;61(1):68-72. Available at: <https://doi.org/10.21164/pomjilifesci.55>

2. Kobierska-Brzoza JM, Dobrzynski M, Fita KA, et al.¹⁹⁸ Aktualnie zalecane materiały odtwórcze w nowoczesnej stomatologii zachowawczej. Currently recommended restorative materials in modern conservative dentistry. *Polim Med* 2015;45(1):37-43. Available at: <http://www.polimery.umed.wroc.pl/en/article/2015/45/1/37/>

Portuguese

1. Aguiar Dias AG.¹⁹⁹ Cimento de ionômero de vidro é melhor do que resina composta em restaurações classe II de dentes decíduos? Uma revisão sistemática com meta-análise [Doctoral thesis]. Universidade Estadual Paulista “Júlio de Mesquita Filho” (UNESP), 2016. Available at: <http://hdl.handle.net/11449/148761>
2. Carrilho E, Marques S, Moreira F, et al.²⁰⁰ Materiais restauradores libertadores de flúor. *Rev Port Estomatol Cir Maxilofac* 2010;51(1):27-34. Available at: [https://doi.org/10.1016/S1646-2890\(10\)70082-0](https://doi.org/10.1016/S1646-2890(10)70082-0)
3. Chaves SCL, Vieira-da-Silva LM.²⁰¹ A efetividade do dentifrício fluoretado no controle da cárie dental: uma meta-análise. *Rev Saude Publica* 2002;36(5):598-606. Available at: <https://doi.org/10.1590/S0034-89102002000600009>
4. de Veras BML, Pires Dos Santos Menezes G, Gomes Filho VV, et al.²⁰² Comportamento clínico de resinas compostas em dentes posteriores – revisão sistematizada da literatura. *Odontol clín-cient* 2015;14(3):689-94. Available at: <http://revodonto.bvsalud.org/pdf/occ/v14n3/a03v14n3.pdf>
5. Monteiro PFA.²⁰³ Lesões de cárie não cavitadas no esmalte: atuação com agentes remineralizantes e infiltrantes [Masters Thesis]. Universidade Fernando Pessoa 2016. Available at: <http://hdl.handle.net/10284/5512>
6. Raggio DP.²⁰⁴ Inspeção do cimento de ionômero de vidro em duas camadas no tratamento restaurador atraumático (Art): estudos in vitro e in vivo. Inspection of the ionomer cement glass in two layers in non-traumatic restorative treatment (ART): in vitro and in vivo studies. Universidade de São Paulo, 2012. Available at: http://143.107.154.240/CRUESP:CRUESP:usp_base03002336240

Russian

1. Kodzaeva ZS, Turkina AY, Doroshina VY.²⁰⁵ Отдаленные результаты реставрации зубов композитными материалами светового отверждения: обзор литературы. The long-term results of teeth restoration with composite resin materials: a systematic literature review. *Stomatologiya* 2019;98(3):117-22. Available at: <https://doi.org/10.17116/stomat201998031117>

Spanish

1. Garchitorena MI, Strehl A.²⁰⁶ Abordaje biológico de la caries profunda de dentina: el tratamiento por etapas. *Odontostomatología* 2010;12(15):4-12. Available at: <http://www.scielo.edu.uy/pdf/ode/v12n15/v12n15a02.pdf>
2. Uribe Espinoza SA.²⁰⁷ Prevalencia y factores de riesgo de caries temprana de la infancia en población urbano-rural de Panguipulli [Tesis doctoral]. Universidad Austral de Chile, 2017. Available at: <https://osf.io/utwce/>
3. Vargas JP, Uribe M, Ortuno D, et al.²⁰⁸ Fluoruro diamino de plata comparado con técnica de restauración atraumática para el tratamiento de caries cavitadas en dentición primaria y mixta primera fase. Silver diamine fluoride compared to atraumatic restorative technique for the treatment of caries in primary and mixed first phase dentition. *Medwave* 2020;20(7):e8003. Available at: <https://doi.org/10.5867/medwave.2020.07.8002>

Appendix C: Studies excluded at full text and extraction screening stages

Papers excluded on full-text screening, with reasons (n=91)

Reasons for exclusion	Brief explanation
Excluded on inadequate risk of bias analysis (n=28)	If no risk of bias is presented, or if the risk of bias presented is incomplete or is an inappropriate measure
Excluded on inadequate search strategy (n=3)	If the search strategy is not presented, if at a minimum no keywords/outline or full search strategies are presented, if no supplemental searches are described, if no PICO is presented as a table or as a description
Excluded on inadequate risk of bias analysis AND inadequate search strategy (n=14)	Both risk of bias and search strategy are inadequate
Excluded on study type (n=21)	The study is not a systematic review, e.g., narrative reviews, overviews, primary studies, opinion pieces etc.
Excluded on intervention (n=8)	A dental/caries intervention was examined but not specifically dealing with restorations
Excluded on topic (n=12)	The topic of the paper was not dental in nature
Excluded on duplicate (n=1)	Where two records were noted for the same paper (assessed by DOI and/or text comparison), one was selected for inclusion and the other was excluded
Excluded on language (n=4)	The language used was not English

Excluded on inadequate risk of bias analysis (n=28)

1. Abduo J, Sambrook RJ.²⁸ Longevity of ceramic onlays: A systematic review. *J Esthet Restor Dent* 2018;30(3):193-215. Available at: <https://doi.org/10.1111/jerd.12384>
2. Araujo NS, Moda MD, Silva EA, Zavanelli AC, Mazaro JV, Pellizzer EP.²⁰⁹ Survival of all-ceramic restorations after a minimum follow-up of five years: A systematic review. *Quintessence Int* 2016;47(5):395-405. Available at: <https://doi.org/10.3290/j.qi.a35699>
3. Astvaldsdottir A, Dagerhamn J, van Dijken JW, Naimi-Akbar A, Sandborgh-Englund G, Tranaeus S, et al.²¹⁰ Longevity of posterior resin composite restorations in adults - A systematic review. *J Dent* 2015;43(8):934-54. Available at: <https://doi.org/10.1016/j.jdent.2015.05.001>
4. Boruziniat A, Gharaee S, Sarraf S, Majidinia S, Vatanpour M.²¹¹ Evaluation of the efficacy of flowable composite as lining material on microleakage of composite resin restorations: A systematic review and meta-analysis. *Quintessence Int* 2016;47(2):93-101. Available at: <https://doi.org/10.3290/j.qi.a35260>
5. Dawson VS, Amjad S, Fransson H.²¹² Endodontic complications in teeth with vital pulps restored with composite resins: a systematic review. *Int Endod J* 2015;48(7):627-38. Available at: <https://doi.org/10.1111/iej.12364>
6. Demarco FF, Collares K, Coelho-de-Souza FH, Correa MB, Cenci MS, Moraes RR, et al.²¹³ Anterior composite restorations: A systematic review on long-term survival and reasons for failure. *Dent Mater* 2015;31(10):1214-24. Available at: <https://doi.org/10.1016/j.dental.2015.07.005>
7. Duangthip D, Jiang M, Chu CH, Lo ECM.²¹⁴ Restorative approaches to treat dentin caries in preschool children: systematic review. *Eur J Paediatr Dent* 2016;17(2):113-21.
8. Duangthip D, Jiang M, Chu Chun H, Lo Edward CM.²¹⁵ Non-surgical treatment of dentin caries in preschool children – systematic review. *BMC Oral Health* 2015;15(1):44. Available at: <https://doi.org/10.1186/s12903-015-0033-7>
9. Ferreira J, Pinheiro S, Sampaio F, Menezes VA.²¹⁶ Caries removal in primary teeth--a systematic review. *Quintessence Int* 2012;43:e9-15.

10. Gluzman R, Katz RV, Frey BJ, McGowan R.²¹⁷ Prevention of root caries: a literature review of primary and secondary preventive agents. *Spec Care Dentist* 2013;33(3):133-40. Available at: <https://doi.org/10.1111/j.1754-4505.2012.00318.x>
11. Jacobsen T, Norlund A, Englund GS, Tranaeus S.²¹⁸ Application of laser technology for removal of caries: a systematic review of controlled clinical trials. *Acta Odontol Scand* 2011;69(2):65-74. Available at: <https://doi.org/10.3109/00016357.2010.536901>
12. Kantovitz KR, Pascon FM, Nobre-dos-Santos M, Puppini-Rontani RM.²¹⁹ Review of the effects of infiltrants and sealers on non-cavitated enamel lesions. *Oral Health Prev Dent* 2010;8(3):295-305. Available at: <https://doi.org/10.3290/j.ohpd.a19581>
13. Maru Viral P, Shakuntala BS, Nagarathna C.²²⁰ Caries removal by chemomechanical (Carisolv™) vs. rotary drill: a systematic review. *Open Dent J* 2015;9:462-72. Available at: <https://doi.org/10.2174/1874210601509010462>
14. Mickenautsch S, Tyas MJ, Yengopal V, Oliveira LB, Bonecker M.²²¹ Absence of carious lesions at margins of glass-ionomer cement (GIC) and resin-modified GIC restorations: a systematic review. *Eur J Prosthodont Restor Dent* 2010;18(3):139-45.
15. Mickenautsch S, Yengopal V.²²² Absence of carious lesions at margins of glass-ionomer cement and amalgam restorations: An update of systematic review evidence. *BMC Res Notes* 2011;4:58. Available at: <https://doi.org/10.1186/1756-0500-4-58>
16. Mickenautsch S, Yengopal V.²²³ Failure rate of atraumatic restorative treatment using high-viscosity glass-ionomer cement compared to that of conventional amalgam restorative treatment in primary and permanent teeth: a systematic review update. *J Minimum Interv Dent* 2012;5(5):63-124. <https://journals.co.za/doi/abs/10.10520/EJC121702>
17. Mickenautsch S, Yengopal V.²²⁴ Failure rate of high-viscosity GIC based ART compared with that of conventional amalgam restorations--evidence from an update of a systematic review. *SADJ* 2012;67(7):329-31.
18. Mickenautsch S, Yengopal V.²²⁵ Failure rate of direct high-viscosity glass-ionomer versus hybrid resin composite restorations in posterior permanent teeth - a systematic review. *Open Dent J* 2015;9:438-48. Available at: <https://doi.org/10.2174/1874210601509010438>
19. Mickenautsch S, Yengopal V, Banerjee A.²²⁶ Atraumatic restorative treatment versus amalgam restoration longevity: a systematic review. *Clin Oral Investig* 2010;14(3):233-40. Available at: <https://doi.org/10.1007/s00784-009-0335-8>
20. Ntovas P, Doukoudakis S, Tzoutzas J, Lagouvardos P.²²⁷ Evidence provided for the use of oscillating instruments in restorative dentistry: a systematic review. *Eur J Dent* 2017;11(2):268-73. Available at: https://doi.org/10.4103/eid.ejd_232_16
21. Opdam NJ, van de Sande FH, Bronkhorst E, Cenci MS, Bottenberg P, Pallesen U, et al.²²⁸ Longevity of posterior composite restorations: a systematic review and meta-analysis. *J Dent Res* 2014;93(10):943-9. Available at: <https://doi.org/10.1177/0022034514544217>
22. Ortiz-Ruiz AJ, Perez-Guzman N, Rubio-Aparicio M, Sanchez-Meca J.²²⁹ Success rate of proximal tooth-coloured direct restorations in primary teeth at 24 months: a meta-analysis. *Sci Rep* 2020;10(1):6409. Available at: <https://doi.org/10.1038/s41598-020-63497-4>
23. Pakdaman A, Montazeri A, Evans RW.²³⁰ Deciduous dentition approximal caries lesion progression and regression following preventive treatment: literature review. *Aust Dent J* 2018;63(4):422-8. Available at: <https://doi.org/10.1111/adj.12646>
24. Senthilkumar V, Ramesh S.²³¹ Systematic review on alternative methods for caries removal in permanent teeth. *J Conserv Dent* 2020;23(1):2-9. Available at: https://doi.org/10.4103/JCD.JCD_263_19
25. Tellez M, Gomez J, Kaur S, Pretty IA, Ellwood R, Ismail AI.³¹ Non-surgical management methods of noncavitated carious lesions. *Community Dent Oral Epidemiol* 2013;41(1):79-96. Available at: <https://doi.org/10.1111/cdoe.12028>
26. Twetman S, Dhar V.²³² Evidence of effectiveness of current therapies to prevent and treat early childhood caries. *Pediatr Dent* 2015;37(3):246-53.
27. van de Sande FH, Collares K, Correa MB, Cenci MS, Demarco FF, Opdam NJM.²³³ Restoration survival: revisiting patients' risk factors through a systematic literature review. *Oper Dent* 2016;41(S7):S7-S26. Available at: <https://doi.org/10.2341/15-120-LIT>
28. Zhao IS, Gao SS, Hiraishi N, Burrow MF, Duangthip D, Mei ML, et al.²³⁴ Mechanisms of silver diamine fluoride on arresting caries: a literature review. *Int Dent J* 2018;68(2):67-76. Available at: <https://doi.org/10.1111/idj.12320>

Excluded on inadequate search (n=3)

1. Bahader S.²³⁵ Arresting caries using silver diamine fluoride: a systematic review [Masters thesis]. University of North Carolina at Chapel Hill, 2016.
2. Jiang M, Fan Y, Li KY, Lo ECM, Chu CH, Wong MCM.²³⁶ Factors affecting success rate of atraumatic restorative treatment (ART) restorations in children: A systematic review and meta-analysis. *J Dent* 2021;104:103526. Available at: <https://doi.org/10.1016/j.jdent.2020.103526>
3. Tedesco TK, Calvo AF, Lenzi TL, Hesse D, Guglielmi CA, Camargo LB, et al.²³⁷ ART is an alternative for restoring occlusoproximal cavities in primary teeth - evidence from an updated systematic review and meta-analysis. *Int J Paediatr Dent* 2017;27(3):201-9. Available at: <https://doi.org/10.1111/ipd.12252>

Excluded on inadequate risk of bias AND search strategy (n=14)

1. Alvanforoush N, Palamara J, Wong RH, Burrow MF.²³⁸ Comparison between published clinical success of direct resin composite restorations in vital posterior teeth in 1995-2005 and 2006-2016 periods. *Aust Dent J* 2017;62(2):132-45. Available at: <https://doi.org/10.1111/adj.12487>
2. Beck F, Lettner S, Graf A, Bitriol B, Dumitrescu N, Bauer P, et al.²³⁹ Survival of direct resin restorations in posterior teeth within a 19-year period (1996-2015): A meta-analysis of prospective studies. *Dent Mater* 2015;31(8):958-85. Available at: <https://doi.org/10.1016/j.dental.2015.05.004>
3. Contreras V, Toro Milagros J, Elías-Boneta Augusto R, Encarnación-Burgos A.²⁴⁰ Effectiveness of silver diamine fluoride in caries prevention and arrest: a systematic literature review. *Gen Dent* 2017;65(3):22-9. Available at: [https://www.agd.org/docs/default-source/self-instruction-\(gendent\)/gendent_mj17_contreras.pdf?sfvrsn=90e174b1_0](https://www.agd.org/docs/default-source/self-instruction-(gendent)/gendent_mj17_contreras.pdf?sfvrsn=90e174b1_0)
4. de Assuncao IV, da Costa Gde F, Borges BC.²⁴¹ Systematic review of noninvasive treatments to arrest dentin non-cavitated caries lesions. *World J Clin Cases* 2014;2(5):137-41. Available at: <https://doi.org/10.12998/wjcc.v2.i5.137>
5. Demarco FF, Correa MB, Cenci MS, Moraes RR, Opdam NJ.²⁴² Longevity of posterior composite restorations: not only a matter of materials. *Dent Mater* 2012;28(1):87-101. Available at: <https://doi.org/10.1016/j.dental.2011.09.003>
6. Domejean S, Ducamp R, Leger S, Holmgren C.²⁴³ Resin infiltration of non-cavitated caries lesions: a systematic review. *Med Princ Pract* 2015;24(3):216-21. Available at: <https://doi.org/10.1159/000371709>
7. Fernandes JM, Massoni AC, Ferreira JM, Menezes VA.²⁴⁴ Use of calcium hydroxide in deep cavities of primary teeth. *Quintessence Int* 2013;44(6):417-23. Available at: <https://doi.org/10.3290/j.qi.a29503>
8. Heintze SD, Rousson V, Hickel R.²⁴⁵ Clinical effectiveness of direct anterior restorations--a meta-analysis. *Dent Mater* 2015;31(5):481-95. Available at: <https://doi.org/10.1016/j.dental.2015.01.015>
9. Heintze SD, Ruffieux C, Rousson V.²⁴⁶ Clinical performance of cervical restorations--a meta-analysis. *Dent Mater* 2010;26(10):993-1000. Available at: <https://doi.org/10.1016/j.dental.2010.06.003>
10. Lai G, Lara C, Cocco F, Cagetti MG, Lingstrom P, Almhojd U, et al.²⁴⁷ Comparison of Carisolv system vs traditional rotating instruments for caries removal in the primary dentition: A systematic review and meta-analysis. *Acta Odontol Scand* 2015;73(8):569-80. Available at: <https://doi.org/10.3109/00016357.2015.1023353>
11. Marks LA, Faict N, Welbury RR.²⁴⁸ Literature review: restorations of class II cavities in the primary dentition with compomers. *Eur Arch Paediatr Dent* 2010;11(3):109-14. Available at: <https://doi.org/10.1007/BF03262725>
12. Meyer-Lueckel H, Machiulskiene V, Giacaman RA.²⁴⁹ How to intervene in the root caries process? Systematic review and meta-analyses. *Caries Res* 2019;53(6):599-608. Available at: <https://doi.org/10.1159/000501588>
13. Naganandini S.²⁵⁰ Atraumatic restorative treatment for the management of dental caries: a systematic review. *Int J Oral Health Med Res* 2015;2(2):80-4. Available at: <http://ijohmr.com/page.php?page=volume-2-issue-2>
14. Peumans M, De Munck J, Mine A, Van Meerbeek B.²⁵¹ Clinical effectiveness of contemporary adhesives for the restoration of non-carious cervical lesions. A systematic review. *Dent Mater* 2014;30(10):1089-103. Available at: <https://doi.org/10.1016/j.dental.2014.07.007>

Excluded on study type (n=21)

1. Allen PF, Da Mata C, Hayes M.²⁵² Minimal intervention dentistry for partially dentate older adults. *Gerodontology* 2019;36(2):92-8. Available at: <https://doi.org/10.1111/ger.12389>
2. Almubarak NAA.²⁵³ Marginal integrity of composite resin and glass ionomer as a restoration for non-carious cervical Lesions: a mixed systematic review and cumulative meta-analysis in pursuance of the best evidence base [Masters thesis]. University of California, , 2016.
3. AlQranei MS, Balhaddad AA, Melo MAS.²⁵⁴ The burden of root caries: Updated perspectives and advances on management strategies. *Gerodontology* 2020;24 Available at: <https://doi.org/10.1111/ger.12511>
4. Cazzaniga G, Ottobelli M, Ionescu A, Garcia-Godoy F, Brambilla E.²⁵⁵ Surface properties of resin-based composite materials and biofilm formation: A review of the current literature. *Am J Dent* 2015;28(6):311-20.
5. Cury JA, de Oliveira BH, dos S, A P, Tenuta LM.²⁵⁶ Are fluoride releasing dental materials clinically effective on caries control? *Dent Mater* 2016;32(3):323-33. Available at: <https://doi.org/10.1016/j.dental.2015.12.002>
6. Farmer JW, Singhal S, Dempster L, Quiñonez C.²⁵⁷ Effectiveness, safety, and acceptance of silver diamine fluoride therapy and its implications for dental hygiene practice: Position paper and statement from the Canadian Dental Hygienists Association. *Can J Dent Hyg* 2018;52(3):192-207.
7. Ferracane JL, Lawson NC.²⁵⁸ Probing the hierarchy of evidence to identify the best strategy for placing class II dental composite restorations using current materials. *J Esthet Restor Dent* 2020 Available at: <https://doi.org/10.1111/jerd.12686>
8. Fontana M.²⁵⁹ Enhancing fluoride: clinical human studies of alternatives or boosters for caries management. *Caries Res* 2016;50(Suppl. 1):22-37. Available at: <https://doi.org/10.1159/000439059>
9. Frohlich TT, Rocha RO, Botton G.²⁶⁰ Does previous application of silver diamine fluoride influence the bond strength of glass ionomer cement and adhesive systems to dentin? Systematic review and meta-analysis. *Int J Paediatr Dent* 2020;30(1):85-95. Available at: <https://doi.org/10.1111/ipd.12571>
10. Heintze SD, Rousson V, Mahn E.²⁶¹ Bond strength tests of dental adhesive systems and their correlation with clinical results - A meta-analysis. *Dent Mater* 2015;31(4):423-34. Available at: <https://doi.org/10.1016/j.dental.2015.01.011>
11. Isolani CP, Sarkis-Onofre R, Lima GS, Moraes RR.²⁶² Bonding to sound and caries-Affected dentin: a systematic review and meta-analysis. *J Adhes Dent* 2018;20(1):7-18. Available at: <https://doi.org/10.3290/j.jad.a39775>
12. Kampanas NS, Antoniadou M.²⁶³ Glass ionomer cements for the restoration of non-carious cervical lesions in the geriatric patient. *J Funct Biomater* 2018;9(3):42. Available at: <https://doi.org/10.3390/jfb9030042>

13. Ludovichetti FS, Stellini E, Signoriello AG, Di Fiore A, Gracco A, Mazzoleni S.²⁶⁴ Zirconia vs stainless steel pediatric crowns: a literature review. *Minerva Stomatol* 2020 Available at: <https://doi.org/10.23736/S0026-4970.20.04432-5>
14. Luk K, Zhao IS, Yu OY, Zhang J, Gutknecht N, Chu CH.²⁶⁵ Effects of 10,600 nm carbon dioxide laser on remineralizing caries: a literature review. *Photobiomodul Photomed Laser Surg* 2020;38(2):59-65. Available at: <https://doi.org/10.1089/photob.2019.4690>
15. Mangani F, Marini S, Barabanti N, Preti A, Cerutti A.²⁶⁶ The success of indirect restorations in posterior teeth: a systematic review of the literature. *Minerva Stomatol* 2015;64(5):231-40. Available at: <https://www.minervamedica.it/en/journals/minerva-stomatologica/article.php?cod=R18Y2015N05A0231>
16. Ricketts D, Lamont T, Innes NP, Kidd E, Clarkson JE.²⁶⁷ Operative caries management in adults and children. *Cochrane Database Syst Rev* 2013(3):CD003808. Available at: <https://doi.org/10.1002/14651858.CD003808.pub3>
17. Schwendicke F, Blunck U, Paris S, Gostemeyer G.²⁶⁸ Choice of comparator in restorative trials: A network analysis. *Dent Mater* 2015;31(12):1502-9. Available at: <https://doi.org/10.1016/j.dental.2015.09.021>
18. Verdugo-Paiva F, Zambrano-Achig P, Simancas-Racines D, Viteri-Garcia A.²⁶⁹ Selective removal compared to complete removal for deep carious lesions. *Medwave* 2020;20(1):e7758. Available at: <https://doi.org/10.5867/medwave.2020.01.7758>
19. Yeung SST, Argaez C.²⁷⁰ Silver diamine fluoride for the prevention and arresting of dental caries or hypersensitivity: a review of clinical effectiveness, cost-effectiveness and guidelines. CADTH Rapid Response Reports. Ottawa: Canadian Agency for Drugs and Technologies in Health, 2017:27pp.
20. Zafar S, Siddiqi A.²⁷¹ Biological responses to pediatric stainless steel crowns. *J Oral Sci* 2020;62(3):245-9. Available at: <https://doi.org/10.2334/josnusd.20-0083>
21. Zakizade M, Davoudi A, Akhavan A, Shirban F.²⁷² Effect of resin infiltration technique on improving surface hardness of enamel lesions: a systematic review and meta-analysis. *J Evid Based Dent Pract* 2020;20(2):101405. Available at: <https://doi.org/10.1016/j.jebdp.2020.101405>

Excluded on intervention (n=8)

1. Boutsiouki C, Frankenberger R, Kramer N.²⁷³ Relative effectiveness of direct and indirect pulp capping in the primary dentition. *Eur Arch Paediatr Dent* 2018;19(5):297-309. Available at: <https://doi.org/10.1007/s40368-018-0360-x>
2. Rovai ES, Ambrosio LMB, Morillo CMR, Villar CC, Holzhausen M, Santamaria MP, et al.²⁷⁴ Root coverage procedures in noncarious cervical lesions with and without restoration: a systematic review and meta-analysis. *Int J Periodontics Restorative Dent* 2020;40(3):e127-e35. Available at: <https://doi.org/10.11607/prd.4284>
3. Silva Barroso de Oliveira D, Barreiros D, Assed Bezerra da Silva L, Assed Bezerra da Silva R, Nelson-Filho P, Calvano Kuchler E.²⁷⁵ The effect of polymer burs on microbiological reduction of carious dentin in deciduous teeth: a systematic review. *Dentistry 3000* 2016;4(1):17-24. Available at: <https://doi.org/10.5195/d3000.2016.56>
4. Twetman S, Keller MK.²⁷⁶ Fluoride rinses, gels and foams: an update of controlled clinical trials. *Caries Res* 2016;50 38-44. Available at: <https://doi.org/10.1159/000439180>
5. Wang Y, Li J, Sun W, Li H, Cannon RD, Mei L.²⁷⁷ Effect of non-fluoride agents on the prevention of dental caries in primary dentition: A systematic review. *PLoS One* 2017;12(8):e0182221. Available at: <https://doi.org/10.1371/journal.pone.0182221>
6. Wright JT, Crall JJ, Fontana M, Gillette EJ, Novy BB, Dhar V, et al.²⁷⁸ Evidence-based clinical practice guideline for the use of pit-and-fissure sealants: A report of the American Dental Association and the American Academy of Pediatric Dentistry. *J Am Dent Assoc* 2016;147(8):672-82.e12. Available at: <https://doi.org/10.1016/j.adaj.2016.06.001>
7. Wright JT, Tampi MP, Graham L, Estrich C, Crall JJ, Fontana M, et al.²⁷⁹ Sealants for preventing and arresting pit-and-fissure occlusal caries in primary and permanent molars: A systematic review of randomized controlled trials—a report of the American Dental Association and the American Academy of Pediatric Dentistry. *J Am Dent Assoc* 2016;147(8):631-45.e18. Available at: <https://doi.org/10.1016/j.adaj.2016.06.003>
8. Zhang Y, Wang Y, Chen Y, Chen Y, Zhang Q, Zou J.²⁸⁰ The clinical effects of laser preparation of tooth surfaces for fissure sealants placement: a systematic review and meta-analysis. *BMC Oral Health* 2019;19(1):203. Available at: <https://doi.org/10.1186/s12903-019-0892-4>

Excluded on topic (n=12)

1. Figuero E, Nobrega DF, Garcia-Gargallo M, Tenuta LM, Herrera D, Carvalho JC.²⁸¹ Mechanical and chemical plaque control in the simultaneous management of gingivitis and caries: a systematic review. *J Clin Periodontol* 2017;44 S116-34. Available at: <https://doi.org/10.1111/jcpe.12674>
2. Garrocho-Rangel A, Esparza-Villalpando V, Pozos-Guillen A.²⁸² Outcomes of direct pulp capping in vital primary teeth with cariously and non-cariously exposed pulp: A systematic review. *Int J Paediatr Dent* 2020;30(5):536-46. Available at: <https://doi.org/10.1111/ipd.12633>
3. Hayashi M, Fujitani M, Yamaki C, Momoi Y.²⁸³ Ways of enhancing pulp preservation by stepwise excavation—a systematic review. *J Dent* 2011;39(2):95-107. Available at: <https://doi.org/10.1016/j.jdent.2010.10.012>
4. Hoefler V, Nagaoka H, Miller CS.²⁸⁴ Long-term survival and vitality outcomes of permanent teeth following deep caries treatment with step-wise and partial-carries-removal: A systematic review. *J Dent* 2016;54:25-32. Available at: <https://doi.org/10.1016/j.jdent.2016.09.009>
5. Innes NPT, Schwendicke F.²⁸⁵ Restorative thresholds for carious lesions: systematic review and meta-analysis. *J Dent Res* 2017;96(5):501-8. doi: <https://doi.org/10.1177/0022034517693605>

6. Konradsson K, Lingstrom P, Emilson CG, Johannsen G, Ramberg P, Johannsen A.²⁸⁶ Stabilized stannous fluoride dentifrice in relation to dental caries, dental erosion and dentin hypersensitivity: A systematic review. *Am J Dent* 2020;33(2):95-105.
7. Li J, Huang Z, Mei L, Li G, Li H.²⁸⁷ Anti-caries effect of arginine-containing formulations in vivo: A systematic review and meta-analysis. *Caries Res* 2015;49(6):606-17. Available at: <https://doi.org/10.1159/000435894>
8. Li T, Zhai X, Song F, Zhu H.²⁸⁸ Selective versus non-selective removal for dental caries: a systematic review and meta-analysis. *Acta Odontol Scand* 2018;76(2):135-40. Available at: <https://doi.org/10.1080/00016357.2017.1392602>
9. Lo YF, Crispin A, Kessler A, Hickel R, Kuhnisch J.²⁸⁹ What is an appropriate etching time for sealant application on permanent molars? Results from a meta-analysis. *J Adhes Dent* 2019;21(6):487-95. Available at: <https://doi.org/10.3290/j.jad.a43181>
10. Mickenautsch S, Yengopal V.²⁹⁰ Demineralization of hard tooth tissue adjacent to resin-modified glass-ionomers and composite resins: a quantitative systematic review. *J Oral Sci* 2010;52(3):347-57. Available at: <https://doi.org/10.2334/josnusd.52.347>
11. Silva EJNL, Pinto KP, Ferreira CM, Belladonna FG, De-Deus G, Dummer PMH, et al.²⁹¹ Current status on minimal access cavity preparations: a critical analysis and a proposal for a universal nomenclature. *Int Endod J* 2020;53(12):1618-35. Available at: <https://doi.org/10.1111/iej.13391>
12. Tedesco TK, Reis TM, Volpi Mello-Moura AC, Seabra da Silva G, Scarpini S, Floriano I, et al.²⁹² Management of deep caries lesions with or without pulp involvement in primary teeth: a systematic review and network meta-analysis. *Brazil Oral Res* 2020;35:e004. Available at: <https://doi.org/10.1590/1807-3107bor-2021.vol35.0004>

Excluded on duplicate (n=1)

1. Szesz A, Parreiras S, Martini E, Reis A, Loguercio A.¹²³ Effect of restorations using a flowable resin composite in non-carious cervical lesions: a systematic review and meta-analysis. *J Dent* 2017;65:11-21. Available at: <https://doi.org/10.1016/j.jdent.2017.07.007>

Excluded on language (n=4)

1. Aguiar Dias A. G.¹⁹⁹ Cimento de ionômero de vidro é melhor do que resina composta em restaurações classe II de dentes decíduos? Uma revisão sistemática com meta-análise. Is glass ionomer cement better than composite resin in Class II restorations of deciduous teeth? A systematic review with meta-analysis [Doctoral thesis]. Universidade Estadual Paulista "Júlio de Mesquita Filho" (UNESP), 2016.
2. de Veras BML, dos Santos Menezes GP, Gomes Filho VV, et al.²⁰² Comportamento clínico de resinas compostas em dentes posteriores – revisão sistematizada da literatura. Clinical behavior of composite resins in posterior teeth- systematic literature review. *Odontol clín-cient* 2015;14(3):689-94. doi: <http://revodonto.bvsalud.org/pdf/occ/v14n3/a03v14n3.pdf>.
3. Steiro A, Strøm V, Hafstad E, Reinart LM.¹⁹² Helsekadelige effekter ved bruk av tannkomposittmaterialer. Systematisk oversikt. Oslo: Folkehelseinstituttet, 2016:91pp. Available at: <https://www.fhi.no/globalassets/dokumenterfiler/rapporter/2016/helsekadelige-effekter-ved-bruk-av-tannkomposittmaterialer.-systematisk-oversikt.pdf>
4. Vargas JP, Uribe M, Ortuno D, Verdugo-Paiva F.²⁰⁸ Fluoruro diamino de plata comparado con técnica de restauración atraumática para el tratamiento de caries cavitadas en dentición primaria y mixta primera fase. Silver diamine fluoride compared to atraumatic restorative technique for the treatment of caries in primary and mixed first phase dentition. *Medwave* 2020;20(7):e8003. Available at: <https://doi.org/10.5867/medwave.2020.07.8002>

Papers excluded at extraction stage, with reasons (n=10)

- Excluded on study type (n=6)
- Excluded on intervention (n=1)
- Excluded on topic (n=2)
- Excluded on inadequate quality assessment (n=1)

Excluded on study type (n=6)

1. Asokan S, Geethapriya PR, Vijayasankari V.²⁹³Effect of nonfluoridated remineralizing agents on initial enamel carious lesions: A systematic review. <i>Indian J Dent Res</i> 2019;30(2):282-90. Available at: https://doi.org/10.4103/ijdr.IJDR_200_18	A descriptive account of the outcomes of a small number of studies is provided with little in-depth discussion of the implications of trying to group these

	outcomes in this review. Important decisions in review stages are not accounted for by the authors. Most notable exception: the authors do not describe the actual design of the included studies so it is not possible to tell if they are randomised or non-randomised.
2. de Melo Avila WM, Hesse D, Bonifacio CC. ²⁹⁴ Surface conditioning prior to the application of glass-ionomer cement: A systematic review and meta-analysis. <i>J Adhes Dent</i> 2019;21(5):391-9. Available at: https://doi.org/10.3290/j.jad.a43183	Mainly laboratory studies. Unable to conclude on human studies as too little information.
3. Fakhruddin KS, Egusa H, Ngo HC, <i>et al.</i> ²⁹⁵ Clinical efficacy and the antimicrobial potential of silver formulations in arresting dental caries: a systematic review. <i>BMC Oral Health</i> 2020;20(1):160. Available at: https://doi.org/10.1186/s12903-020-01133-3	Randomised clinical trials with a follow-up period of at least two years were eligible. A list of studies excluded at full text were not provided but their reasons for exclusion were reported. The approach to analysis was not described in the methods
4. Schwendicke F, Meyer-Lueckel H, Dörfer C, <i>et al.</i> ²⁹⁶ Failure of incompletely excavated teeth--a systematic review. <i>J Dent</i> 2013;41(7):569-80. Available at: https://doi.org/10.1016/j.jdent.2013.05.004	Randomised and non-randomised, controlled and uncontrolled, prospective and retrospective clinical studies published between 1982 and 2013 were included. Twelve studies were randomised controlled trials, two studies were nonrandomised but controlled trials, and five studies were case series or retrospective studies. This then did not fit the inclusion criteria.
5. Shaalan OO, Abou-Auf E, El Zoghby AF. ²⁹⁷ Clinical evaluation of flowable resin composite versus conventional resin composite in carious and noncarious lesions: Systematic review and meta-analysis. <i>J Conserv Dent</i> 2017;20(6):380-5. Available at: https://doi.org/10.4103/JCD.JCD_226_17	The authors do not report on the type of studies included; risk of bias not adequately dealt with in the meta-analysis or the interpretation of the results. No consideration given to assessing the heterogeneity in the included studies so the meta-analysis is incomplete.
6. Subbiah GK, Gopinathan NM. ²⁹⁸ Is silver diamine fluoride effective in preventing and arresting caries in elderly adults? A systematic review. <i>J Int Soc Prev Community Dent</i> 2018;8(3):191-9. Available at: https://doi.org/10.4103/jispcd.JISPCD_99_18	This review consists of a brief summary of the included studies. Their reporting of the risk of bias is inconsistent and their treatment of the studies overall is poor.

Excluded on intervention (n=1)

1. Jabin Z, Vishnupriya V, Agarwal N, <i>et al.</i> ²⁹⁹ Effect of 38% silver diamine fluoride on control of dental caries in primary dentition: A systematic review. <i>J Family Med Prim Care</i> 2020;9(3):1302-7. Available at: https://doi.org/10.4103/jfmpc.jfmpc_1017_19	Wrong intervention examined. Emphasis on prevention

Excluded on topic (n=2)

1. Abdullah Z, John J. ³⁰⁰ Minimally invasive treatment of white spot lesions--a systematic review. <i>Oral Health Prev Dent</i> 2016;14(3):197-205. Available at: https://doi.org/10.3290/j.ohpd.a35745	On close reading, the white spot lesions referred to in the PICO related to post-orthodontic treatment
2. Dutra D, Pereira G, Kantorski KZ, <i>et al.</i> ³⁰¹ Does finishing and polishing of restorative materials affect bacterial adhesion and biofilm formation? A systematic review. <i>Oper Dent</i> 2018;43(1):E37-E52. Available at: https://doi.org/10.2341/17-073-L	The two clinical studies cover titanium abutments (implants) which are outside the scope of this review.

Excluded on inadequate quality assessment (n=1)

1. Afrashtehfar KI, Emami E, Ahmadi M, <i>et al.</i> ³⁰² Failure rate of single-unit restorations on posterior vital teeth: A systematic review.	The Cochrane risk of bias tool was employed to assess the risk of bias in the

J Prosteth Dent 2017;117(3):345-53.e8. Available at:
<https://doi.org/10.1016/j.prosdent.2016.08.003>

five trials. For the observational studies, the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement was used to assess the nine prospective and retrospective studies. However this is a set of guidelines for writing up an observational study rather than a quality assessment tool.

Appendix D: Included studies

Papers included in final synthesis (n=107)

1. Aiem E, Joseph C, Garcia A, et al.⁹⁰ Caries removal strategies for deep carious lesions in primary teeth: Systematic review. *Int J Paediatr Dent* 2020;30(4):392-404. Available at: <https://doi.org/10.1111/ipd.12616>
2. Aiem E, Smail-Faugeron V, Muller-Bolla M.⁸⁸ Aesthetic preformed paediatric crowns: systematic review. *Int J Paediatr Dent* 2017;27(4):273-82. Available at: <https://doi.org/10.1111/ipd.12260>
3. Ammari MM, Soviero VM, da Silva Fidalgo TK, et al.¹⁵⁰ Is non-cavitated proximal lesion sealing an effective method for caries control in primary and permanent teeth? A systematic review and meta-analysis. *J Dent* 2014;42(10):1217-27. Available at: <https://doi.org/10.1016/j.jdent.2014.07.015>
4. Ancira-Gonzalez L, Esparza-Villalpando V, Garrocho-Rangel A, et al.⁷⁸ White spot lesion remineralisation agents in primary teeth: A systematic review. *Oral Health Prev Dent* 2018;16(5):391-400. Available at: <https://doi.org/10.3290/j.ohpd.a41404>
5. Angeletaki F, Gkogkos A, Papazoglou E, et al.¹¹³ Direct versus indirect inlay/onlay composite restorations in posterior teeth. A systematic review and meta-analysis. *J Dent* 2016;53:12-21. Available at: <https://doi.org/10.1016/j.jdent.2016.07.011>
6. Antonelli da Veiga AM, Carneiro Cunha A, Masterson Tavares Pereira Ferreira D, et al.¹¹⁴ Longevity of direct and indirect resin composite restorations in permanent posterior teeth: A systematic review and meta-analysis. *J Dent* 2016;54:1-12. Available at: <https://doi.org/10.1016/j.jdent.2016.08.003>
7. Aparecida Silva Martins D, Silva Moreira KM, Soares Swerts Pereira M.⁹² Partial removal of carious in primary teeth: A systematic review of the literature. *Oral Health Dent Manage* 2018;17(1):1-5. Available at: <https://www.longdom.org/abstract/partial-removal-of-carious-in-primary-teeth-a-systematic-review-of-the-literature-41629.html>
8. Arbildo-Vega HI, Lapinska B, Panda S, et al.¹⁵⁸ Clinical effectiveness of bulk-fill and conventional resin composite restorations: systematic review and meta-analysis. *Polymers (Basel)* 2020;12(8):1786. Available at: <https://doi.org/10.3390/polym12081786>
9. Badar SB, Tabassum S, Khan FR, et al.⁸⁵ Effectiveness of Hall technique for primary carious molars: A systematic review and meta-analysis. *Int J Clin Pediatr Dent* 2019;12(5):445-52. Available at: <https://doi.org/10.5005/jp-journals-10005-1666>
10. Barros MMAF, de Queiroz Rodrigues MI, Muniz FWMG, et al.¹¹⁷ Selective, stepwise, or nonselective removal of carious tissue: which technique offers lower risk for the treatment of dental caries in permanent teeth? A systematic review and meta-analysis. *Clin Oral Investig* 2020;24(2):521-32. Available at: <https://doi.org/10.1007/s00784-019-03114-5>
11. Becker Rodrigues SS, Franken P, Keller Celeste R, et al.¹⁰⁷ CAD/CAM or conventional ceramic materials restorations longevity: a systematic review and meta-analysis. *J Prosthodont Res* 2019;63(4):389-95. Available at: <https://doi.org/10.1016/j.jpor.2018.11.006>
12. Bezerra IM, Brito ACM, de Sousa SA, et al.¹²² Glass ionomer cements compared with composite resin in restoration of noncarious cervical lesions: A systematic review and meta-analysis. *Heliyon* 2020;6(5):e03969. Available at: <https://doi.org/10.1016/j.heliyon.2020.e03969>
13. Boing TF, de Geus JL, Wambier LM, et al.²⁶ Are glass-ionomer cement restorations in cervical lesions more long-lasting than resin-based composite resins? A systematic review and meta-analysis. *J Adhes Dent* 2018;20(5):435-52. Available at: <https://doi.org/10.3290/j.jad.a41310>
14. Bustamante-Hernández N, Montiel-Company JM, Bellot-Arcís C, et al.¹⁰⁶ Clinical behavior of ceramic, hybrid and composite onlays. A systematic review and meta-analysis. *Int J Environ Res Public Health* 2020;17(20):7582. Available at: <https://doi.org/10.3390/ijerph17207582>
15. CADTH.¹⁰³ Composite resin versus amalgam for dental restorations: a health technology assessment Ottawa: CADTH; 2018. Available from: https://www.cadth.ca/sites/default/files/pdf/ht0021_dental_amalgam_report_final.pdf
16. Cardoso M, Coelho A, Lima R, et al.¹⁶⁶ Efficacy and patient's acceptance of alternative methods for caries removal-a systematic review. *J Clin Med* 2020;9(11):23. Available at: <https://doi.org/10.3390/jcm9113407>
17. Chatzimarkou S, Koletsis D, Kavvadia K.¹⁴⁶ The effect of resin infiltration on proximal caries lesions in primary and permanent teeth. A systematic review and meta-analysis of clinical trials. *J Dent* 2018;77:8-17. Available at: <https://doi.org/10.1016/j.jdent.2018.08.004>
18. Chee B, Rickman LJ, Satterthwaite JD.¹²⁹ Adhesives for the restoration of non-carious cervical lesions: a systematic review. *J Dent* 2012;40(6):443-52. Available at: <https://doi.org/10.1016/j.jdent.2012.02.007>
19. Chen Y, Chen D, Lin H.¹⁴³ Infiltration and sealing for managing non-cavitated proximal lesions: a systematic review and meta-analysis. *BMC Oral Health* 2021;21(1):13. Available at: <https://doi.org/10.1186/s12903-020-01364-4>
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Appendix E: HRB-adapted AMSTAR 2 instrument

- HRB-adapted AMSTAR 2 instrument
- HRB-adapted AMSTAR 2: Critical domains
- Rating overall confidence in the results of the review
- Guidelines for extraction tables

HRB-adapted AMSTAR 2 instrument

AMSTAR 2: Critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. The HRB-adapted version of AMSTAR 2 for use in this overview of reviews is below.

The notation for the HRB adapted version of AMSTAR 2 is as follows:

- An asterisk * following a number denotes a critical factor.
- Text in red indicates an exclusion factor.
- Text in purple indicates agreed adaptations and interpretation.

These factors will be included in the screening criteria. Any systematic review that searched less than two databases and/or has not completed any quality assessment or risk of bias assessment will be excluded.

We piloted AMSTAR 2 on four systematic reviews and following this we made several adjustments to the tool (See table below: Appendix E Table 1 HRB Adapted AMSTAR 2). We have retained the text of the questions as per AMSTAR 2. We have adjusted the scoring of Question 1, Question 4, and Question 8 to provide consistent and more stringent judgement of the parameter being scrutinised. We have added text to further explain what is required when assessing Questions 1 to 4, Questions 8 and 9, and Questions 11 to 16 to ensure all reviewers are making decisions using the same parameters.

Appendix E: Table 1 HRB-adapted AMSTAR 2 instrument

HRB-adapted AMSTAR 2 instrument		
1*	Did the research questions and inclusion criteria for the review include the components of PICO?	• Yes • No
	Four of five components must be in the introduction or methods to be awarded a YES	
For Yes to PICO:		
	• Population	
	• Intervention	-
	• Comparator group	

- Outcome
- Time frame for follow-up

2*	Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol? The protocol must be accessible to check that the parameters below are covered.	• Yes • Partial Yes • No

For Partial Yes: **Protocol must be reported as prepared and accessible**

The authors state that they had a written protocol or guide that included ALL the following:

- review question(s)
- a search strategy
- inclusion/exclusion criteria
- a risk of bias assessment

For 'full' Yes: **Protocol must be registered and accessible**

As for partial yes, plus the protocol should be registered and should also have specified:

- a meta-analysis/synthesis plan, if appropriate, *and*
- a plan for investigating causes of heterogeneity
- justification for any deviations from the protocol

3	Did the review authors explain their selection of the study designs for inclusion in the review?	• Yes • No
	Must have justified their rationale for selecting the study design to be awarded a YES	
	They provide the study design a-priori but not an explanation NO	

For Yes, the review should satisfy ONE of the following:

- *Explanation for* including only RCTs
- OR *Explanation for* including only NRSI
- OR *Explanation for* including both RCTs and NRSI

4*	Did the review authors use a comprehensive literature search strategy?	• Yes • Partial Yes • No

For Partial Yes (all the following):

- searched at least two databases
(relevant to research question) (**Less than two fatal flaws and exclude**)
- provided keyword and/or search strategy
- justified publication restrictions (e.g., language and/or duration of search)

For 'full' Yes, should have (**two or more** of the following):

- searched the reference lists/bibliographies of included studies (moved from below and considered necessary step)
- searched trial/study registries
- where relevant, searched for grey literature
- conducted search within 24 months of completion of the review
- included/consulted experts in the field

5	Did the review authors perform study selection in duplicate?	• Yes • No

For Yes, either ONE of the following:

- at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include
- OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 per cent), with the remainder selected by one reviewer

6	Did the review authors perform data extraction in duplicate?	• Yes • No

For Yes, either ONE of the following:

- at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include
- OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 per cent), with the remainder selected by one reviewer

7	Did the review authors provide a list of excluded studies and justify the exclusions?	• Yes • Partial Yes • No

For Partial Yes:

- provided a list of all potentially relevant studies that were read in full text form but excluded from the review

For 'full' Yes, must also have:

- Justified the exclusion from the review of each potentially relevant study

8	Did the review authors describe the included studies in adequate detail?	• Yes
		• Partial Yes
		• No

For Partial Yes (ALL the following):

- adequately described populations
- adequately described interventions
- described comparators
- described outcomes
- described research designs

For 'full' Yes, should also have ALL the following:

- described study's setting
- time frame for follow-up

Removed points on detailed description as overlap with criteria above.

9*	Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? No quality assessment or risk of bias completed on primary studies (fatal flaw and exclude) Did the authors use the correct instrument for the included study design(s)? Did the authors assess the relevant points, see below? Randomised controlled or clinical trials	• Yes
		For Partial Yes, must have assessed RoB from
		• unconcealed allocation (randomization and blinding combined when allocating the intervention), <i>and</i>
	• lack of blinding assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality or admission to hospital)	• No
		• Includes only

For 'full' Yes, must have assessed RoB from:

- allocation sequence that was not truly random (individual randomisation versus group randomization), *and*
- selection of the reported result from among multiple measurements or analyses of a specified outcome, known as selective reporting (using only the outcomes or measurements that provide the researchers with their desired answer and ignoring other outcomes that may contradict the desired findings)

Non-randomised epidemiological studies.

For Partial Yes, must have assessed RoB:

- from confounding, *and*
 - from selection bias
- Yes
- Partial Yes

For Yes, must also have assessed RoB:

- methods used to ascertain exposures and outcomes, *and*
 - selection of the reported result from among multiple measurements or analyses of a specified outcome, known as selective reporting using only the outcomes or measurements that provide the researchers with their desired answer and ignoring other outcomes that may contradict the desired findings)
- No
- Includes only
- RCTs
NRSI

- 10
- Did the review authors report on the sources of funding for the studies included in the review?**
- Yes
 - No

For Yes,

- Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information, but it was not reported by study authors also qualifies

- 11* **If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?**
- Randomised controlled or clinical trials**
- Yes

For Yes:

- The authors justified combining the data in a meta-analysis
 - AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present
 - AND investigated the causes of any heterogeneity conducted
- No
- No meta-analysis

If heterogeneity present: completed feasibility analysis to decide what studies to include (PICO for clinical heterogeneity) and what type of meta-analysis to use (pairwise [2 arm trials and two competing interventions] versus network [three or more arm trials])

and more than two competing interventions]), used a random effects model if statistical heterogeneity is greater than an pre-agreed level (25%, 50% or 75%), estimate statistical heterogeneity (Q or I² test), determine influence of highly weighted studies (any one study influencing the outcome), high risk or unclear risk of bias studies (removed from analysis), or studies with different populations, comparators and intervention formats through sensitivity or subgroup analysis

Non-randomised epidemiological studies

- The authors justified combining the data in a meta-analysis
- AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present
- AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available
- AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review

If heterogeneity present: completed feasibility analysis to decide what studies to include (PICO for clinical heterogeneity) and what type of meta-analysis to use (pairwise [2 arm trials and two competing interventions] versus network [three or more arm trials and more than two competing interventions]), studied controls for confounding, used confounding adjusted risk or odds ratios, used a random effects model if statistical heterogeneity is greater than an pre-agreed level (25%, 50% or 75%), estimate statistical heterogeneity (Q or I² test), determine influence of highly weighted studies (any one study influencing the outcome), high risk or unclear risk of bias studies (removed from analysis), or studies with different populations, comparators and intervention formats through sensitivity or subgroup analysis

12*	If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	• Yes • No • No meta-analysis

For Yes:

- included only low risk of bias RCTs (**sensitivity analysis**)

Note: **It is not good practice to combine RCT and NRSI, therefore separate results should be provided, and their similarities or differences discussed**

13*	Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?	• Yes • No

For Yes:

- included only low risk of bias RCTs in the review
- included only low risk of bias RCTs (in meta-analysis or a sensitivity analysis and discuss differences)
- OR, if RCTs with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results **and quality of evidence or limitations in conclusions or summary**

Generally, NRSI have more positive results than RCTs because of self-selection bias and lack of randomization and readers should be reminded of this. Confounding should be controlled for in the meta-analysis by using adjusted odds ratios. Loss to follow-up should be controlled for in the inclusion criteria. Loss to follow-up of over 20% introduces a serious bias to longitudinal studies.

Risk of bias should also be discussed for narrative analysis

Risk of bias should concentrate on the areas that were at high risk or unclear risk of bias its effect on the direction of the results.

14*	Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	• Yes • No

For Yes:

- There was no significant heterogeneity in the results
- OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results (feasibility assessment, random effects model, sensitivity and subgroup analysis) and discussed the impact of this on the results of the review and the quality of evidence

If narrative analysis completed, the effects of clinical heterogeneity on the results and quality of evidence should be discussed.

15	If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	• Yes • No • No meta-analysis

For Yes:

- performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias

Publication bias occurs when results of published studies are systematically different from unpublished or grey literature studies. Publication bias is trying to estimate the influence of unpublished studies on the results of the systematic review. Publication bias can be controlled for through a good comprehensive search strategy that includes unpublished studies, yet to be published studies, or studies published in grey literature and a wide selection of databases.

Publication bias can be measured using a funnel plot and its p-value. A funnel plot is a scatter plot of estimates of the treatment effects of

each study against the measure of its precision (1/Standard Error). In the absence of publication bias, plot will look like symmetric inverted funnel. A minimum of ten studies are required to run the funnel plot analysis.

The effect of publication bias should be considered in the GRADE quality of evidence

16	Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	• Yes • No

For Yes:

- The authors reported no competing interests OR
- The authors described their funding sources and how they managed potential conflicts of interest

In this case, the industry producing dental products are may main source of conflict of interest

HRB-adapted AMSTAR: Critical domains

We selected eight rather than seven critical factors. We highlight the critical items that are selected by us and the original **AMSTAR 2** authors and we justify domain exclusions and inclusions in Appendix C Table 1.

Table 1 HRB-adapted AMSTAR: Critical domains

Original Shea AMSTAR 2 critical domains	Pollock AMSTAR Critical domains	HRB authors selected critical domains	Agreement or justification for inclusion or exclusion
	Did the research questions and inclusion criteria for the review include the components of PICO (Item 1)?	Did the research questions and inclusion criteria for the review include the components of PICO (Item 1)?	We thought that this item is critical as overviews indicate that clarity in the PICO leads to a better research objective, search strategy, clear inclusion and exclusion criteria, and a planned

			approach to analysis
Protocol registered before commencement of the review (item 2)		Protocol registered before commencement of the review (item 2)	We agree that this item is critical.
Adequacy of the literature search (item 4)	Adequacy of the literature search (item 4)	Adequacy of the literature search (item 4)	We agree that this item is critical. In addition, the inclusion of this item may help deal with excluding items 7 [excluded primary studies] and 15 [publication bias] as critical, and we agree that trials or cohort studies excluded at full-text screening should be listed with a reason for exclusion.
		Was there duplicate study selection and data extraction? (item 5)	We think this item is standard practice nowadays
Justification for excluding individual studies (item 7)	Justification for excluding individual studies (item 7)		We thought that this overlapped with items 1 [PICO], 4 [search strategy] and Item 9 [risk of bias] did not need to be included
Risk of bias from individual studies being included in the review (item 9)	Risk of bias and publication bias based on primary studies being included in the systematic review (item 9)		We agree that this item is critical.

Appropriateness of meta-analytical methods (item 11)	Appropriateness of meta-analytical methods (item 11)	We agree that this item is critical.
	If meta-analysis was performed, did the review authors assess the potential impact of risk of bias in individual studies on the results of the meta-analysis or other evidence synthesis? (item 12)	We thought that item 12 [risk of bias in doing meta-analysis] is critical. We think dealing with bias openly is key to avoiding misleading results
Consideration of risk of bias when interpreting the results of the review (item 13)	Consideration of risk of bias when interpreting the results of the review (item 13)	We agree that this item is critical.
	Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? (item 14)	We think the clinical and statistical homogeneity or consistency [item 14] are key to a trustworthy analysis and must be dealt with the authors before and after meta-analysis.
Assessment of presence and likely impact of publication bias (item 15)		We thought other items more critical, and that Item 9 could include this issue.

Rating overall confidence in the results of the review

Appendix B:Table 2 Rating overall confidence in the results of the review

Score	Criteria

High	No or one non-critical weakness: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest
Moderate	More than one non-critical weakness*: the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review
Low	One critical flaw with or without non-critical weaknesses: the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest
Critically low	More than one critical flaw with or without non-critical weaknesses: the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies
*Downgrade	*Multiple non-critical weaknesses may diminish confidence in the review, and it may be appropriate to move the overall appraisal down from moderate to low confidence.

Summary quality assessment results

Appendix B: Table 3. Summary quality assessment results

Author (Year)	1*PICO	2*Protocol prior to review and report deviations	3 Justify primary study design for inclusion	4*Comprehensive literature search	5 Duplicate screening	6 Duplicate data extraction	7 List of excluded studies	8 Detailed characteristics of primary studies

Author (Year)	9* Method for assessment of bias	10 Source of funding for primary studies	11 *Methods for meta- analysis	12 *Discussed heterogeneity	13*Meta- analysis and risk of bias in analysis	14 *Risk of bias in discussion of results	15 Publication bias (search, measure [10 sources], and GRADE)	16 Conflicts of interest and funding	Overall rating

Appendix F: Joanna Briggs Institute data extraction form for systematic reviews and research syntheses

We extracted information from each full text systematic review into the JBI tabular format.³⁰⁴ The extracted data comprised citation details, objectives of the review, participants, setting, interventions, comparators, search information, study date range, number of primary studies, study design, risk of bias tool used, risk of bias assessment including publication bias, analysis methods, outcomes assessed, and results by outcome(s).

Parameter	Study 1 Extraction
First Author and year of publication (e.g. Jones <i>et al.</i> 2020)	See example (author year)
Objectives (report exact review question(s) and page number	PICOT
Participants (characteristics and numbers) The defining characteristics of the participants in studies included in the research syntheses/review should be detailed, for example this may include diagnostic criteria, age, or ethnicity. The total number of participants that inform the outcomes relevant to the umbrella review question from all studies included studies should be presented.	Generation, type, and surfaces of teeth as exact as possible Number of participants and teeth Age Gender
Setting/context Details of the setting of interest such as acute care, primary health care, or the community or a geographical location should be included. For some umbrella reviews, particularly those that draw upon qualitative research syntheses, the context that underpins the review question will be important to clearly reveal to the reader and may include but is not limited to consideration of cultural factors such as geographic location and specific racial or gender based interests.	Countries (alphabetic order) and setting (university, public or private clinic)
Description of Interventions/ phenomena of interest Clear, succinct details of the interventions or phenomena of interest should be presented as described by systematic review author(s), including the type of intervention, the frequency,	Authors exact definition of the intervention Comparator

Parameter	Study 1 Extraction
and/or intensity of the intervention. A statement of the phenomena of interest is also required where applicable.	
Databases and sources searched The number of sources searched should be reported. Although this will have been considered during critical appraisal of the research synthesis, reporting to the reader of the review will allow rapid and easy comparison between differences across included reviews and also consideration of potential for publication bias in the event that no formal analysis has been conducted. Where possible the names of databases and sources should be listed (i.e. if <5-10). The search range of each database should also be included.	Based on previous search by: Number and names of databases and other sources Dates Search limits Other searches Protocol prepared Yes/No, Published Yes/No and If yes Number Extraction and screening were completed were completed in duplicate. Funding Conflicts of interest.
Date Range (years) of included studies The date range spanning from the earliest study that informs the included research synthesis to the latest should be reported. This is important information that allows for consideration of the currency of the evidence base not necessarily reflected in the year of publication of the research synthesis. If this is not readily identifiable in the table of study characteristics provided by the included synthesis, it should be discerned by scanning the date range of publications through the results section of the included systematic review.	Exact years for included studies
Number of primary studies included in the systematic review Summary descriptive details of the included studies in the research synthesis should be reported. This includes the number of studies in the included research synthesis, the types of study designs included in the research synthesis, for example randomized controlled trials, prospective cohort study, phenomenology, ethnography etc., and also the country of origin of the	Number of studies and (if required) number of studies by study design Research design Study years Study funding

Parameter	Study 1 Extraction
included studies. The latter is important to allow the reader of the review to consider the external validity and generalizability of the results presented.	
Types of studies included	Planned study design to be included List of excluded studies and reason for exclusion
Country of origin of included studies	Country names in alphabetic order
Appraisal instruments used The instrument or tool used to assess risk of bias, rigour or study quality should be reported along with some summary estimate of the quality of primary studies in the included research synthesis. For example, for umbrella reviews that use the Jadad Scale, a mean score for quality may be reported whereas for checklist appraisals, reporting of cut-off score or any ranking of quality should be reported. An example of the latter would be exclusion of studies that score <3/10, and inclusion of four moderate quality studies (4-6/10) and two high quality studies (7-10/10).	The full name of the tool used
Appraisal rating	Number of studies by high risk of bias, medium and low Number of studies out of total number of studies that were at low risk of bias for randomisation and at low risk of bias for outcome ascertainment Authors exact comments on risk of bias and how it affected analysis and quality of evidence Comment of how author dealt with publication bias
Method of analysis The type of research synthesis as stated by the authors of the included review should be detailed. The method of analysis or synthesis used by the included research synthesis should be reported. For example, this may include narrative synthesis, vote counting, random effects meta-analysis, fixed effect meta-analysis, network meta-analysis, thematic synthesis, meta-aggregative synthesis, or meta-ethnography.	Description as per author Justification for narrative or meta-analysis
Outcome assessed Included here should be the outcomes of interest to the umbrella review	List of outcomes assessed and intended time frames Actual timeframes Primary studies by outcome

Parameter	Study 1 Extraction
question reported on by the research synthesis, i.e. the names or labels of the outcomes (see below for presentation of results).	
Results/findings The relevant findings or results presented by the included research syntheses must be extracted. For quantitative reviews, this will ideally be an effect estimate with 95% CIs or measure from a presented meta-analysis. Measures of heterogeneity should also be extracted where applicable. In the absence of this a statement indicating the key result relevant to an outcome may be inserted in the required field. For qualitative syntheses, the key synthesized finding should be extracted.	Findings by outcome Use metaanalysis results if available (relative risk, odds ratio, standardised mean difference, 95% confidence intervals, I ² , number of trials or studies, number of participants or teeth, random or fixed effects, GRADE) Use relative risk, odds ratio, standardised mean difference, 95% confidence intervals and p-value for individual studies where meta-analysis is not available, GRADE)
Significance/direction	See above if results listed by outcome
Heterogeneity	See above if I ² listed above Authors comment on heterogeneity
Comments There should be provision to extract and present in the table of included study characteristics any relevant details or comments on the included research synthesis by the authors of the Umbrella Review. These comments may be relevant details regarding the included research synthesis, for example, the congruence between the review results and conclusions, and for highlighting any potential methodological differences between the individual included reviews.	

Appendix G: Data extraction for studies on primary dentition

Non-cavitated caries

Non-invasive treatment

Ancira-González *et al.* (2018)

Parameter	Extraction
First author and year of publication	Ancira-González <i>et al.</i> (2018) ⁷⁸
Objectives	Compared the effectiveness of fluoride varnishes, gels, casein phosphopeptide-amorphous calcium phosphate, and other remineralisation agents with each other in the management of white spot lesions in children's primary teeth.
Participants	Primary dentition, non-cavitated caries, non-invasive management. Population: Children's primary teeth. Nine randomised controlled trials (six parallel trials, two split-mouth trials, and one quasi-experimental trial) published between 2001 and 2016 were included in this review, with the age of the participating 5,115 children in the trials ranging from 1 to 8 years. Gender was not reported.
Setting/context	The study settings varied; two studies were in school settings and another two in community settings; a further study was in a paediatric clinic. The clinical settings of four studies were not available. The study countries were available for four of the nine studies, and these were the Netherlands, Sweden, Thailand, and the USA.
Description of interventions/phenomena of interest	As the focus of this review was comparing the effectiveness of different remineralising agents, it is important to describe what precisely the process of remineralising enamel in the human tooth involves. According to Ancira-González <i>et al.</i> , "remineralisation is the process whereby calcium and phosphate ions are supplied from a source external to the tooth to promote ion deposition into crystal voids in demineralised enamel to produce net mineral gain". ^{78 (p392)} This review also stated that "topical fluoride-containing varnishes consist of highly concentrated fluoride (around 22,000 ppm [parts per million]) with a resin or synthetic base and casein phosphopeptide-amorphous calcium phosphate can be delivered as a paste." ^{78 p(392)} Comparator: Each other.
Databases and sources searched	A search of three electronic databases (Embase, the Cochrane Library, EBSCOhost) and three other sources (Latin Index, Scielo, and Google Scholar). The search included all available dental articles written in the English or Spanish languages and published in these sources between January 2000 and April 2018. Keywords and search terms were provided. The preparation or publication of a protocol was not mentioned. Search and screening of references and abstracts were performed independently by two authors. The authors do not report extraction in duplicate. Information on funding or conflict of interest was not provided.
Date range (years) of included studies	Nine randomised controlled trials (six parallel trials, two split-mouth trials, and one quasi-experimental trial) published between 2001 and 2016 were included in this review.
Number of primary studies included in the systematic review	Nine randomised controlled trials (six parallel trials, two split-mouth trials, and one quasi-experimental trial) published between 2001 and 2016 were included in this review. The review authors did not report the sources of funding for primary studies.
Types of studies included	Nine randomised controlled trials (six parallel trials, two split-mouth trials, and one quasi-experimental trial) published between 2001 and 2016 were included in this review. The reasons for excluding 86 full-text articles were provided; these were: in vitro studies, not focused on remineralisation as outcome measure, and incomplete data. However, a list of references was not provided.
Country of origin of included studies	The study countries were available for four of the nine studies, and these were the Netherlands, Sweden, Thailand, and the USA.

Parameter	Extraction
Appraisal instruments used	The authors used the Centre for Evidence-Based Medicine guidelines, along with additional bespoke evaluation criteria, to assess the risk of bias in the included trials.
Appraisal rating	The authors used the Centre for Evidence-Based Medicine guidelines, along with additional bespoke evaluation criteria, to assess the risk of bias in the nine included trials. The authors reported that studies had “low to moderate degree of methodological bias”. ^{78 (p393)} However, seven trials had at least one high risk of bias score and the other two studies had at least one unclear risk of bias score. Three of the nine studies were judged to have adequate randomisation techniques. All studies completed laboratory testing for outcome ascertainment. Publication bias was not measured.
Method of analysis	The authors found high heterogeneity among potentially comparable response variables, and this prevented the grouping of the studies and therefore the performance of a meta-analysis. Different comparisons were made between the main remineralising agents using the information extracted from the selected articles.
Outcome assessed	Outcome by primary study: Effectiveness (remineralising) Remineralisation: Anderson 2016; Autio-Gold and Courts 2001; Truin and Vant’t Hof 2005; De Amorim 2008; Juárez-López 2014; Memarpour 2015. Laser: De Amorim 2008; Raucci-Neto 2013. Sealants: De Amorim 2008; Raucci-Neto 2013. Chlorhexidine: De Amorim 2008; Raucci-Neto 2013. Casein phosphopeptide-amorphous calcium phosphate tooth mousse: Sitthisettapong 2012 and 2015. Time frame: Follow-up times varied greatly, ranging from 3 months to 4 years. They were not predetermined or reported by individual comparison.
Results/findings	The analysis was narrative due to heterogeneity between study interventions, comparators, and outcomes. There was low-quality evidence from six studies that fluoride varnishes were better remineralisation agents than any control (placebo or no intervention) when applied on primary tooth enamel. Two studies reported low-quality evidence of no improvement in remineralisation after casein phosphopeptide-amorphous calcium phosphate was combined with fluoride toothpaste, compared with fluoride toothpaste alone. One study reported that remineralisation capacity of fluoride varnish was not superior to that of pit-and-fissure resin sealants or Nd:YAG laser. Another study reported that fluoride varnishes were superior to chlorhexidine. Two of the studies compared fluoride varnish alone with fluoride varnish plus chlorhexidine or Nd:YAG laser, as control interventions, on the enamel of primary teeth, and found low-quality evidence that fluoride varnishes as a monotherapy were less effective than the comparator combined treatment. Based on this analysis of low-quality evidence, there appears to be a slight preference for the performance of fluoride varnish used alone and in combination with other agents. There was no added advantage when casein phosphopeptide-amorphous calcium phosphate was added to treatments. Ancira-González <i>et al.</i> reported that “there is limited evidence indicating an outstanding remineralising capacity among the most wide-spread topical therapies used currently on primary tooth enamel with white spot lesion. However, a difference among these therapies is evident, mainly in favour of fluoride varnish”. ^{78 p(393)}
Significance/direction	Results listed by outcome.
Heterogeneity	The analysis was narrative due to heterogeneity between study interventions, comparators, and outcomes.
Comments	GRADE was not used by the review authors. Seven trials had at least one high risk of bias score and the other two studies had at least one unclear risk of bias score. Three (33%) of the nine studies were judged to have adequate randomisation. All studies completed laboratory testing for outcome ascertainment. The analysis was narrative due to heterogeneity between study interventions, comparators, and outcomes. The quality of the review was rated as low using AMSTAR 2 as the authors did not discuss the

Parameter	Extraction
	implication of high or unclear risk of bias scores on their narrative analysis. The HRB grades the quality of the evidence as low for the different outcomes.

Microinvasive treatment

Lam *et al.* (2020)

Parameter	Extraction
First author and year of publication	Lam <i>et al.</i> (2020) ⁷⁹
Objectives	Evaluated the effectiveness of different types of pit-and-fissure sealants, as compared with no treatment measures among children and adolescents, to arrest of pit-and-fissure occlusal caries. The HRB is only interested in the findings on arresting pit-and-fissure occlusal caries in primary molars of children rather than prevention, and has excluded the prevention aspect of this study.
Participants	Primary dentition, non-cavitated lesions, microinvasive treatments. Pit-and-fissure occlusal caries in primary molars of children. Children and adolescents from the general population younger than 18 years whose primary molars had incipient occlusal carious lesions, or non-cavitated carious lesions were included. Only two of the seven included studies measured caries arrest, and both were published in 2015. The two studies had 197 participants (with 667 primary molars) with an age range of 4–7 years. The proportion of the population classified as being at high risk of caries was between 27% and 60%. Gender was not reported.
Setting/context	One study was conducted in a public dental clinic and the other in an outreach facility. The two study countries were Greenland and Kuwait.
Description of interventions/phenomena of interest	Intervention: Any type of pit-and-fissure sealants have been placed on any primary molars. Comparator: The control teeth or control groups were those that did not receive sealant or received professional topical fluoride application alone. However, when making a comparison between conventional sealants and new types of sealants or caries arrest measures, the conventional types of sealants were used as a control group.
Databases and sources searched	Four electronic databases were searched from inception to March 2018: Cochrane Central Register of Controlled Trials (CENTRAL), Ovid Embase, Ovid MEDLINE, and Web of Science. The authors used broad keywords and MeSH terms in their search strategies, which were published in an appendix. Only studies with full text available in English were included. A hand-search was performed, and reference lists of the included studies and relevant previous systematic reviews were screened to ensure that no relevant studies were omitted. The authors did not reference a protocol. Two reviewers independently selected studies and then extracted data. The authors reported that they received no funding for the review and had no conflicts of interest.
Date range (years) of included studies	Seven randomised clinical trials, published between 1998 and 2015, were included in the qualitative and quantitative syntheses. Only two of the seven studies measured caries arrest, and both were published in 2015.
Number of primary studies included in the systematic review	Only two of the seven included studies measured caries arrest, and both were published in 2015. The two studies had 197 participants (667 primary molars) with an age range of 4–7 years. The proportion of the population classified as being at high risk of caries was between 27% and 60%. Gender was not reported. The longest follow-ups were 12 and 34 months. One study was conducted in a public dental clinic and the other in an outreach facility. The two study countries were Greenland and Kuwait. The sources of funding for the primary studies were not reported. Data comparing the effectiveness of resin-based sealants with topical fluoride varnishes or with resin infiltration were reported. For caries progression, only two studies specifically evaluated the outcome in the International Caries Detection and Assessment System (ICDAS) so that subgroup analysis of caries arrest could be compared.
Types of studies included	Randomised or quasi-randomised controlled trials with follow-up after at least 6 months were eligible. A list of studies excluded at full-text screening were not provided, but their reasons for exclusion were reported.

Parameter	Extraction
Country of origin of included studies	The two study countries were Greenland and Kuwait.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	The two studies were judged to have a high risk of bias. Neither of the two studies were judged to have adequate randomisation, although one study had adequate blinding of outcome assessment. Bias arising from the randomisation process was due to an imbalanced distribution of caries severity between the treatment arms. The only study which also used bitewings as an adjunct to outcome assessment was rated as being of low risk of bias for outcome ascertainment. Risk of bias across studies in terms of publication bias could not be assessed because of a limited number of studies found for each outcome.
Method of analysis	Stata version 13.1 was used to perform the meta-analysis. Pairwise meta-analysis with fewer than five studies was handled with a fixed-effects model, while the random-effects model was adopted for analysis with five or more studies. Subgroup analyses were conducted to evaluate the treatment effects for sealants placed on sound occlusal surfaces (ICDAS code 0), incipient occlusal carious lesions (ICDAS code 1–2), occlusal surfaces with localised enamel breakdown and without clinical signs of dentinal involvement (ICDAS code 3), and non-cavitated occlusal carious lesion progressed to the outer one-third of the dentine (ICDAS code 4). Assessment of heterogeneity was conducted based on the guidelines in the <i>Cochrane Handbook for Systematic Reviews of Interventions</i>.
Outcome assessed	Outcomes: Caries arrest (positive) or caries progression (negative), at 6 months or longer follow-up, was considered as any increase in the extent of caries – for instance, from localised enamel breakdown to progression to dentine (ICDAS code 3 or 4) or from non-cavitated dentine lesion to cavitated lesion with the exposure of dentine (ICDAS code 4, 5 or 6). The longest follow-ups were 12 and 34 months. Outcome by primary study: Caries arrest and new caries incidence post-application: Bakhshandeh and Ekstrand (2015); Honkala (2015);
Results/findings	Two split-mouth studies provided the results for the comparison between resin-based sealants and application of 5% sodium fluoride varnish compared with fluoride varnish alone. Both studies included primary molars with sound occlusal surfaces, incipient lesions, localised enamel lesions, and non-cavitated carious lesions with ICDAS scores ranging from 0 to 4. None of the follow-up time points were similar, and therefore the study results could not be pooled for analysis. Both studies found no significant differences in overall effects in caries prevention and arrest between the two groups (1 year: OR: 0.65, 95% CI: 0.39–1.08, $p=0.095$, 1 trial; 2 years: OR: 0.42, 95% CI: 0.16–1.07, $p=0.069$, 1 trial). In subgroup analyses, a significantly lower caries incidence rate was found in the sealant group than in the varnish group at 1-year follow-up (529 teeth). Significantly fewer primary molars with sound occlusal surfaces or incipient carious lesions (ICDAS code 0–2) had progressed to ICDAS code 3 or above after 1 year (OR: 0.52; 95% CI: 0.29–0.96; $p=0.035$; 1 trial). No significant difference in caries incidence between the two groups was found at 2 years (OR: 0.54; 95% CI: 0.23–12.78; $p=0.7$; 1 trial). When evaluating caries arrest in studies which placed sealants on ICDAS code 3–4 lesions at baseline, significantly fewer carious lesions were found to have progressed at 1-year follow-up with increased ICDAS coding (OR: 0.01; 95% CI: 0.02–0.50; $p=0.02$; 10 teeth; 1 trial), although no difference was found at 2-year follow-up (OR: 0.06; 95% CI: 0.20–1.52; $p=0.245$; 80 teeth; 1 trial). The authors reported that “the body of evidence at 1 year was determined to be low in accordance with GRADE assessment criteria. Despite the fact that the study was somehow well conducted, the lack of blinding in the assessment of caries prevention and minimum sample size raised some concerns regarding the certainty and precision of the results...At 2–3 years, the certainty in the evidence was also assessed as low. It was downgraded twice because of high risk of overall bias and imprecision (only 47 analysed participants).”⁷⁹ (p13) There was no study identified that performed a head-to-head comparison of resin infiltration with sealant in preventing occlusal caries. However, one split-mouth study was found to provide data indirectly for comparison. The study design had three treatment arms: resin infiltration and topical fluoride varnish, resin-based

Parameter	Extraction
	sealant and fluoride varnish, and topical fluoride varnish alone. No difference was found in the overall effectiveness of caries prevention and arrest between the sealants plus fluoride varnish group when compared with the resin infiltration with fluoride varnish group (OR: 1.35; 95% CI: 0.46–4.00; $p=0.58$; 1 trial). When conducting subgroup analyses, resin infiltration with topical fluoride varnish was found to be significantly more effective in arresting non-cavitated dentinal caries of ICDAS code 4 than resin-based sealant with topical fluoride varnish (OR: 9.26; 95% CI: 1.06–80.94; $p=0.044$; 42 teeth; 1 trial), while no difference was found in caries prevention or arrest when the baseline caries level was of ICDAS code 3 (OR: 0.82; 95% CI: 0.05–14.39; $p=0.47$; 33 teeth) or below (OR: 0.13; 95% CI: 0.00–3.52; $p=0.22$; 8 teeth). As the evidence was contributed by one small-scale split-mouth study with topical fluoride varnish applied in all groups, the evidence was considered as having low certainty because of the high risk of overall bias and high risk of bias in the domain of bias arising from randomisation process. With respect to indirectness, there was no direct head-to-head comparison of resin infiltration and sealant due to the potential interference of topical fluoride; regarding imprecision, the total number of events is less than 100. The authors concluded that “There are currently insufficient well-controlled randomized controlled clinical trials to determine whether sealants are beneficial in preventing or arresting non-cavitated occlusal caries in the primary molars.”⁷⁹ (p19)
Significance/direction	No difference between interventions and any differences are based on small numbers.
Heterogeneity	The evidence was not pooled where there was clinical or methodological heterogeneity.
Comments	GRADE was used by the review authors. The two studies were judged to have a high risk of bias. Neither of the two studies were judged to have adequate randomisation, although one study had adequate blinding of outcome assessment. The evidence was not pooled where there was clinical or methodological heterogeneity. The quality of the review was rated as low using AMSTAR 2 as the authors did not control for high risk of bias scores in their meta-analysis. The HRB grades the quality of the evidence as low for the different outcomes, which corresponds with the review authors ratings.

Cavitated caries

Non-invasive treatment

Tolba *et al.* (2019)

Parameter	Extraction
First author and year of publication	Tolba <i>et al.</i> (2019) ⁸¹
Objectives	Evaluated the effectiveness (in arresting caries) of the application of 12% silver diamine fluoride compared with 38% silver diamine fluoride in cavitated dentine caries in children's primary teeth.
Participants	Primary dentition, cavitated caries, non-invasive treatment. Children with cavitated dentine caries in their primary teeth. The number of patients in the two trials was 1,864 children. The three publications involved only primary teeth, but the number of teeth treated was not reported. The mean age range of the patients was 3.8–5.2 years. Gender was not reported. The longest follow-up periods were between 24 and 30 months.
Setting/context	The clinical settings and study countries were not reported.
Description of interventions/phenomena of interest	Twelve per cent silver diamine fluoride compared with 38% silver diamine fluoride. The protocol of silver diamine fluoride application in the first publication was one application for 2 minutes at baseline. In the two more recent publications, the study subjects were treated every 6 months. For the annual groups, SDF was applied alternating with normal saline as a placebo.
Databases and sources searched	Six databases were searched with no restrictions up to 1 February 2018: PubMed, Scopus, Latin American and Caribbean Health Sciences Literature database (LILACS), the Cochrane Library, TRIP database, and National Institute for Health and Care Excellence (NICE Evidence Search) database. The search strategy was based on controlled vocabulary (Medical Subject Headings [MeSH] terms) searches of the PubMed database along with free keywords, and was reported in the text. A manual search was performed on the reference lists of all primary studies for additional relevant publications. Grey Literature Report and ClinicalTrials.gov were also searched. The preparation of a protocol was not reported. Two reviewers screened the literature and extracted the data. The authors declare that they have no competing interests and no funding was sought for the review.
Date range (years) of included studies	Two randomised clinical trials published in three papers from 2009 to 2018 were included.
Number of primary studies included in the systematic review	Two randomised clinical trials published in three papers from 2009 to 2018 were included. The sources of funding for primary studies were not reported.
Types of studies included	Only randomised clinical trials were eligible for inclusion. There were no studies excluded during full-text screening.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	One study was judged to have a high risk of bias, another to have an unclear risk of bias, and the third study had a low risk of bias. All three studies were judged to have adequate randomisation and adequate blinding for outcome ascertainment. Publication bias is not measured or discussed. The results for the risk of bias were not discussed.
Method of analysis	The data analysis plan is not described. However, the authors did a narrative analysis, although the rationale for this is not explained.
Outcome assessed	Dentine caries arrest: Yee 2009; Fung 2016, 2018 The longest follow-up periods were between 24 and 30 months (not predetermined).
Results/findings	The protocol for the application of silver diamine fluoride was different in the two studies, and the follow-up times were also diverse. The mean number and standard deviation for one study and the proportion for the other two studies of caries arrested was lower in the 12% silver diamine

Parameter	Extraction
	fluoride group compared with the 38% silver diamine fluoride group at each time point, and all differences were statistically significant. The black discolouration of the carious dentine after silver diamine fluoride treatment was the most notable side effect. There were no other adverse effects observed or reported.
Significance/direction	Favours silver diamine fluoride.
Heterogeneity	Statistical heterogeneity was not considered for measurement, although the presence of clinical heterogeneity was discussed but not named.
Comments	GRADE was not used by the review authors. Two of the three studies were judged to have a high or unclear risk of bias. All three studies were judged to have adequate randomisation and adequate blinding for outcome ascertainment. The quality of the review was rated as low using AMSTAR 2 because the risk of bias was not discussed. The presence of clinical heterogeneity prevented the pooling of results. The HRB judges the evidence to be moderate.

Trieu *et al.* (2019)

Parameter	Extraction
First author and year of publication	Trieu <i>et al.</i> (2019) ⁸⁰
Objectives	Evaluated dentine caries arrest capabilities of silver diamine fluoride compared with those of sodium fluoride in the carious teeth of children aged 12 years and under.
Participants	Primary dentition [only evidence for primary teeth], cavitated caries (dentine), non-invasive treatment The review authors stated that "The [two] included studies recruited a total of 746 [679 in table] pre-school children with a mean age of 3.4 years [in the Duangthip <i>et al.</i> study] and 4.0 years [in the Lo <i>et al.</i> study]. [Over half (56-60%) were male.] Of the studies, the randomised trial by Lo <i>et al.</i> and its follow-up article focused on carious lesions of upper anterior primary teeth only, while the other RCT [randomised controlled trial] by Duangthip <i>et al.</i> and its follow-up article included both anterior and posterior primary teeth." ⁸⁰ (p2)
Setting/context	The primary studies were conducted in China, China, specifically in Guangzhou and in 16 kindergarten schools in Hong Kong.
Description of interventions/phenomena of interest	Intervention The authors described the intervention as follows: "silver diamine fluoride (38% Ag(NH ₃) ₂ F) is a colourless liquid composed of 24–29% silver and 5–6% fluoride. It is also an alkaline reagent with pH 10.9, which provides an unfavorable environment for dentine collagen enzyme activation. Also, silver has been used as a medical antimicrobial since the 17th century and in dentistry during 1917." ⁸⁰ (p2) Comparator The comparator sodium fluoride treatments were defined as follows: "Topical fluorides, such as sodium fluoride varnish, are used as preventive reagents because of their remineralization and antimicrobial abilities." ⁸⁰ (p2) "[The trial by] Lo <i>et al.</i> and its follow-up article used 38% silver diamine fluoride, while [the trial by] Duangthip <i>et al.</i> and its follow-up article used 30% silver diamine fluoride, but all randomised clinical trials compared the silver diamine fluoride intervention to 5% sodium fluoride varnish." ⁸⁰ (p2)
Databases and sources searched	The authors searched four databases up to 31 March 2018: Ovid, PubMed, Web of Science, and the Cochrane Library. They restricted their search to articles published in English and studies performed in humans. The authors also hand-searched through relevant journals and reviews in order to identify additional relevant studies. The authors did not report preparing a protocol. Extraction and screening were completed in duplicate. Funding: This study was funded by the University of Nevada, Las Vegas, School of Dental Medicine. The authors declared no competing interests.
Date range (years) of included studies	The included studies were published in 2001, 2002, 2005, 2011, 2016, and 2018.

Parameter	Extraction
Number of primary studies included in the systematic review	Six articles, published in 2001, 2002, 2005, 2011, 2016, and 2018, met the inclusion criteria. The authors describe the included articles thus: "Four RCTs [randomised controlled trials] and two [other] studies which were secondary statistical analyses of RCTs. However, the four identified RCTs consist of two individual studies, while the remaining two RCTs were their follow-up articles reporting results at later time points." ^{80 (p2)} The funding sources for primary studies were not reported.
Types of studies included	A list of excluded studies was not provided although reasons for exclusion were reported. Cohort, case-control, controlled, or randomised control study designs were eligible for inclusion.
Country of origin of included studies	The studies were completed in China, specifically in Guangzhou and Hong Kong.
Appraisal instruments used	The quality of the included studies was assessed by the Critical Appraisal Skills Programme checklist for randomised controlled trials. This protocol consists of a set of 11 questions addressing key aspects of the quality of randomised controlled trials, including: question formulation, type of study, relevancy, quality, results, precision of results, application of results to populations, outcomes, and the evaluation between benefits over harms and costs.
Appraisal rating	All six articles had one score of unclear risk of bias and so the studies had an overall unclear risk of bias score. All six articles were judged to have a low risk of bias for randomisation, and all six articles were judged to have an unclear risk of bias for considering all clinically important outcomes. Blinding of outcome ascertainment was not measured as a single domain although it may be included in a more general question on blinding participants, health workers, and researchers. The six articles were judged low risk of bias for blinding. In terms of commenting on risk of bias and how it affected analysis and quality of evidence, the authors stated that "All RCTs [randomised controlled trials] developed PICO [population, intervention, comparator, and outcome] formulated question(s) involving caries arrest by the use of SDF [silver diamine fluoride] intervention compared to sodium fluoride. Sample size calculations were performed in Duangthip <i>et al.</i> (and also reported in the follow-up article by Duangthip <i>et al.</i>), but were not performed in Lo <i>et al.</i> or any of its follow-up articles. Patients were allocated into groups by stratified block randomization in the two papers by Duangthip <i>et al.</i>, while Chu <i>et al.</i> and Lo <i>et al.</i> utilized sequential allocation. All RCTs utilised blinding protocols. While the study by Duangthip <i>et al.</i> and its follow-up article adopted a triple-blind protocol where the... .. treatment providers, sole examiner and participants were blind to the intervention/control, the study by Lo <i>et al.</i> and its follow-up article (Chu <i>et al.</i>) employed a double-blind protocol where an independent examiner was recruited in the study. However, due to the difference in physical appearance between intervention and comparison reagents, patients, providers and/or examiners were likely able to distinguish between the intervention and comparison reagents. Otherwise, all groups were treated equally during the treatment time including the number of exams and/or treatment visits each group attended." ^{80 p3–5} Regarding publication bias, the authors stated that "Publication bias was evaluated with funnel graphs. Duangthip <i>et al.</i> and its follow-up article reported a larger sample size and thus increased precision, but both meta-analysis 1 and meta-analysis 2 showed acceptable symmetry. No publication bias was detected." ^{80 (p5)}
Method of analysis	According to the authors, "Pooled measurements were calculated (OR with 95% CI) by random-effects models to assess the strength of association between SDF [silver diamine fluoride] and NaF [sodium fluoride] to arrest caries. A study of heterogeneity was performed in order to assess the variability between included studies using Cochran's Q test and I² inconsistency index. Consistency of results from different authors were explored with Galbraith's graphs. The funnel graphs have also been created to assess potential publication bias. The software R 3.0.2 and its 'metafor' package was used to perform the meta-analyses. The level of significance used in the analysis has been 5%." ^{80 (p9)} Only four articles (comprising two randomised controlled trials) were considered for meta-analyses, both of which reported results at 18- and 30-month time points.

Parameter	Extraction
	Articles were excluded from the meta-analysis due to different reported effect measures and different group comparisons.
Outcome assessed	All RCTs [randomised controlled trials] utilized the decayed, missing, and filled surfaces protocol to record outcomes by tactile examination. Lesions were classified as active caries or arrested caries using sharp sickled probes or ball-ended probes. Oral hygiene at home was evaluated by parental questionnaire in all RCTs, and clinically examined and recorded by using a visible plaque index in one RCT and its follow-up article.”^{80 (p2)} Outcomes: Decayed, missing, and filled teeth (planned) Caries arrest was measured and reported. Caries arrest: Lo 2001; Chu 2002; Wong 2005; Wong 2011; Duangthip 2016; Duangthip 2018.
Results/findings	The authors reported that “Two meta-analyses were conducted...In meta-analysis 1, arrested caries by treatment group were analyzed in the 18-month trials...while meta-analysis 2 compared the 30-month results. Data between studies was harmonized to determine the odds ratio (OR). Individual estimated ORs and the pooled ORs were generated and revealed a significant increased probability of SDF [silver diamine fluoride] arresting caries as compared to NaF [sodium fluoride] at both 18 months (OR=2.51; 95% CI: 1.2–5.10; $p=0.011$) and 30 months (OR=2.03; 95% CI: 1.5–2.77; $p<0.001$).”^{80 (p5)} According to the authors, “The results of these meta-analyses found that SDF [silver diamine fluoride], when compared to NaF [sodium fluoride], was a more effective fluoride containing reagent for dentine caries arrest in children.”^{80 (p5)}
Significance/direction	In summary, silver diamine fluoride is more effective as a dentine caries-arresting reagent than sodium fluoride and has many implications for paediatric dentistry.
Heterogeneity	Regarding heterogeneity, the authors stated that “Heterogeneity was evaluated with Cochran’s Q Test and the I^2 inconsistency index. A higher level of heterogeneity was found at 18 months ($I^2=90.3\%$, Q test =10.29, $p=0.001$) than at 30 months ($I^2=44.3\%$, Q test =1.79; $p=0.180$). Galbraith graphs were also generated to establish heterogeneity of the meta-analyses. Both meta-analysis 1 and meta-analysis 2 fell within confidence levels suggesting distance, but lay within the confidence intervals.” ^{80 (p5)}
Comments	Trieu <i>et al.</i> noted that “The findings of this systematic review need to be viewed with caution as the study encountered limiting factors. For instance, all RCTs [randomised controlled trials] were conducted in Guangzhou, China and Hong Kong, China, which represent a very specific demographic with a diet, hygiene regimen, and water fluoridation different from the western culture...Although six articles were identified, all included studies are based on two clinical trials. It would be ideal to conduct further clinical trials to formulate stronger clinical recommendations.” ^{80 (p7–8)}

Direct restoration material

Dias *et al.* (2018)

Parameter	Extraction
First author and year of publication	Dias <i>et al.</i> (2018) ²³
Objectives	Compared failure and clinical performance of glass ionomer cement with composite resin in Class II restorations in primary teeth.
Participants	Primary dentition, cavitated caries, direct restorations. Population: Class II restorations in primary teeth. The 592 children (with their 1,425 restorations) participating in the trials were aged 3–11 years. Gender was not reported.
Setting/context	The clinical settings or countries where the studies were completed were not provided
Description of interventions/phenomena of interest	According to Dias <i>et al.</i> , glass ionomer cements “are adhesive materials that release fluoride to the oral environment, and their insertion technique is faster

Parameter	Extraction
	compared to composite resin, making this material an important resource for the treatment of children."²³ (p313) Comparator: Composite resin.
Databases and sources searched	The authors searched seven sources (PubMed, Scopus, Web of Science, Virtual Health Library, the Cochrane Library, ClinicalTrials.gov, and OpenGrey) and did not apply date or language limits. The searches were completed on 6 February 2018. Hand-searching was also performed. The search terms were presented in the article. This search strategy was adapted to each database. This study protocol was registered in the PROSPERO international prospective register of systematic reviews. Two reviewers independently analysed the titles and abstracts of papers found on the databases. Potential papers were read in full to clearly determine their eligibility. Data were extracted using an extraction sheet previously used in other systematic reviews, but it is not stated whether two independent researchers extracted the data. There was no information on review funding or conflict of interest.
Date range (years) of included studies	Ten randomised controlled trials published between 1992 and 2016 were included in this review.
Number of primary studies included in the systematic review	Ten randomised controlled trials published between 1992 and 2016 were included in this review. The sources of funding for primary studies was not reported.
Types of studies included	Randomised controlled trials were included in this review. Fifteen studies were excluded at full-text screening for the following reasons: lack of adequate control (studies without a control group) (n=2), retrospective study (n=1), sample overlapping (n=1), microorganisms count as the main response variable (n=1), study protocols without results (n=2), presentation of the results of Class I and Class II restorations without distinction between the two types of cavities (n=2), presentation of the results of permanent and primary teeth without distinction between the two dentitions (n=1), and restorations in permanent teeth (n=5). The studies themselves were not listed or referenced.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the 10 trials.
Appraisal rating	The authors reported that six trials were classified as having a low risk of bias and four as having an unclear risk of bias. However, all trials had at least one high risk of bias score and five had at least two high risk of bias scores. The overall results appear to be a misinterpretation of Cochrane Collaboration guidance. Seven out of 10 trials had adequate randomisation and four had adequate blinding of outcome assessors. Publication bias was not measured or discussed.
Method of analysis	Pairwise random effect meta-analysis was used and heterogeneity was evaluated by the I² Inconsistency Index. Sensitivity analysis was conducted to estimate and verify the influence of studies, one by one, on the pooled results when the heterogeneity was moderate or considerable (30–100%). For studies reporting the use of more than one composite resin, both resins were considered. No study used more than one type of glass ionomer cement. A random effect pairwise meta-analysis model was applied, and a confidence interval (CI) of 95% was calculated for each outcome. In meta-analyses evaluating the percentage of failures, the heterogeneity ranged from 0% to 81%. To reduce heterogeneity, the selective removal of studies, one by one, was performed. However, given that the removal of studies did not influence the results, no study was removed from the final meta-analyses.
Outcome assessed	Outcome: Failure and clinical performance (comprising marginal adaptation, marginal discolouration, anatomical form, and secondary carious lesions) Time frame: 6–48 months Outcome measured by primary studies Failure: Andersson-Wenckert 2006; Casagrande 2013; Donmez 2016; Ersin 2006; Fuks 2000; Ostlund 1992; Santos 2010; Sengul 2015; Serpa 2016 Secondary carious lesions: Andersson-Wenckert 2006; Donmez 2016; Ersin 2006; Fuks 2000; Ostlund 1992; Santos 2010; Sengul 2015

Parameter	Extraction
	Marginal adaptation: Andersson-Wenckert 2006; Donmez 2016; Ersin 2006; Fuks 2000; Ostlund 1992; Sengul 2015 Marginal discolouration: Donmez 2016; Ersin 2006; Fuks 2000; Ostlund 1992; Pereira 2002 Anatomical form: Andersson-Wenckert 2006; Donmez 2016; Ersin 2006; Fuks 2000; Ostlund 1992; Pereira 2002; Sengul 2015
Results/findings	Meta-analyses using random-effects models were used to assess all outcomes. Glass ionomer cement compared with composite resin in Class II restorations in primary teeth presented similar failure patterns (risk difference: -0.04; 95% CI: -0.11 to 0.03; $p=0.25$; I^2: 51%; 768 restorations; 9 trials). Glass ionomer cement compared with composite resin in Class II restorations in primary teeth also presented similar clinical performance (risk difference: 0.03; 95% CI: -0.00 to 0.06; $p=0.27$; I^2: 0%; 1,857 restorations; 8 trials). When glass ionomer cement was compared with composite resin on marginal discolouration (risk difference: 0.07; 95% CI: -0.08 to 0.21; $p=0.38$; I^2: 77%; 344 restorations; 5 trials), marginal adaptation (risk difference: 0.00; 95% CI: -0.05 to 0.05; $p=1.00$; I^2: 0%; 457 restorations; 6 trials), and anatomical form (risk difference: 0.01; 95% CI: -0.03 to 0.06; $p=0.58$; I^2: 0%; 554 restorations; 7 trials) in Class II restorations in primary teeth, the results were similar for both interventions and the 95% CI for differences all crossed zero. This assessment renders the evidence from this review inconclusive regarding whether glass ionomer cement or composite resin is better for these outcomes. However, there is adequate evidence that glass ionomer cements were significantly better than composite resins at preventing the occurrence of secondary carious lesions in primary teeth (risk difference: 0.06; 95% CI: 0.02-0.10; $p=0.008$; I^2: 0%; 502 restorations; 7 trials). According to Dias <i>et al.</i>, "regarding the occurrence of secondary carious lesions, GIC [glass ionomer cement] presented superior clinical performance, and this effect was more evident for the resin-modified GIC, and either forms of GIC used with rubber dam isolation"^{23 (p12)}
Significance/direction	Varied by outcome.
Heterogeneity	Another aspect considered in the present review was the follow-up period of restorations. The studies included presented follow-up periods ranging from 6 to 48 months, which could contribute to the heterogeneity of studies. However, following subgroup analysis by time (24 months), Dias <i>et al.</i> concluded that "the great variation in the follow-up periods in the present review had little or no influence on the outcomes."^{23 (p9)} In the present study, besides the aspects previously discussed, some factors may also have contributed to the heterogeneity among the studies, especially the individual characteristics of participants and populations of the studies included, as well as the clinical skills and calibration of operators and examiners. Additionally, inherent differences in each type of restorative material may have had some influence on the results. Thus, considering that the included studies were published between 1992 and 2016, it is likely that the more recently studies published used materials with better physical, mechanical, and biological properties, given that restorative materials are in constant evolution.
Comments	GRADE was not used by review authors. All studies were judged to have at least one high risk of bias score. Seven (70%) out of 10 trials had adequate randomisation and four (40%) had adequate blinding of outcome assessors. The quality of the review was rated as moderate using AMSTAR 2. The HRB judges the evidence to be moderate quality.

Weber Pires *et al.* (2018)

Parameter	Extraction
First author and year of publication	Weber Pires <i>et al.</i> (2018) ⁸²
Objectives	Evaluated the clinical performance of different conventional restorative materials placed in posterior primary teeth.
Participants	Primary dentition, cavitated caries, direct restorations.

Parameter	Extraction
	Children's posterior primary teeth; that is, occlusal or occlusoproximal restorations placed in primary molars. Seventeen randomised clinical trials, published between 1980 and 2016, with more than 863 participants (2,867 restorations, of which 41% were Class I and II restorations) were included; one trial did not report its number of participants. The age range was children aged 3–11 years; three studies did not report age range. Gender was not reported.
Setting/context	The settings were not reported. The study countries were Brazil, Greece, India, Japan, Sweden, the Netherlands, Turkey, the United Kingdom (UK), and the United States of America (USA).
Description of interventions/phenomena of interest	Conventional restorative materials available for restoring posterior primary teeth include amalgam, conventional glass ionomer cement, resin-modified glass ionomer cement, high-viscosity glass ionomer cement, compomer, and composite resin. Compared with each other.
Databases and sources searched	A comprehensive literature search was undertaken in January 2017 using PubMed/MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, and TRIP databases to identify studies that evaluated the clinical performance of conventional dental materials placed in primary molars. The search was conducted with no publication year or language restriction using a combination of controlled vocabulary and free-text terms based on the search strategy for the PubMed/MEDLINE database. To reduce publication bias, unpublished documents through the ClinicalTrials.gov database were screened. The authors published a protocol on PROSPERO. Two reviewers independently selected the studies and extracted the data. The authors certify that they have no commercial or associative interest that represents a conflict of interest in connection with the manuscript.
Date range (years) of included studies	Seventeen randomised clinical trials published between 1980 and 2016 were included.
Number of primary studies included in the systematic review	Seventeen randomised clinical trials, published between 1980 and 2016. The sources of funding for primary studies were not reported.
Types of studies included	Randomised clinical trials were eligible for inclusion. The reasons for exclusion were provided, but not a list of the excluded studies.
Country of origin of included studies	The study countries were Brazil, Greece, India, Japan, Sweden, the Netherlands, Turkey, the UK, and the USA.
Appraisal instruments used	The Cochrane risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	All 17 studies were judged to have a high risk of bias. Eleven of the 17 studies were at low risk of bias for randomisation and none were at low risk of bias for outcome ascertainment. Weber Pires <i>et al.</i> reported that "Risk of bias was low in most studies (45.38% of all items across studies)". ^{82 (p4)} The overall results appear to be a misinterpretation of Cochrane Collaboration guidance. The authors subsequently acknowledge: "Our review included clinical studies from the 1980s to 2016, and thus, some of the restorative materials evaluated are no longer available. Moreover, the majority of the studies showed unclear or high risk of bias. Some parameters that could interfere in risk of bias analysis were not reported." ^{82 (p9)} Publication bias was not measured but the authors did a comprehensive search.
Method of analysis	The data were analysed using traditional pairwise meta-analysis followed by network meta-analysis. The network meta-analysis was based on a binomial model with log link function. The effect size measure estimated was relative risk. Glass ionomer cement restoration was considered the baseline treatment. Both fixed-effect and homogeneous variance random-effects models were considered. The choice of model and 'goodness of fit' was made based on the deviance information criterion. Models were adjusted using Markov chain Monte Carlo methods with non-informative priors. Convergence was assessed by trace plots and inconsistency by split node method.
Outcome assessed	Failure rate (number of restorative failures based on clinical criteria). The longest follow-up periods for the studies ranged between 12 and 60 months (not predetermined).

Parameter	Extraction
	Outcome (failure rate) by primary studies: Tonn (1980); Oldenburg (1987); Barr-Agholme (1991); Welbury (1991); Hse and Wei (1997); Marks (1999); Welbury (2000); Dutta (2001); Duggal (2002); Hübel and Mejäre (2003); Kavvadia (2004); Andersson-Wenckert and Sunnegardh-Grönberg (2006); Pascon (2006); Alves dos Santos (2010); Casagrande (2013); Sengul and Gurbuz (2015); Bektas Donmez (2016).
Results/findings	A network meta-analysis of evidence comparing the five restorative materials (glass ionomer cement, resin-modified glass ionomer cement, composite resin, amalgam, and compomer) was performed for all comparison pairs. Results of the network meta-analysis model found that the relative risk of failure is significantly higher for glass ionomer cement when compared with compomer (relative risk: 2.64; 95% credible intervals: 1.29–6.27), resin-modified glass ionomer cement (relative risk: 3.25; 95% credible intervals: 1.58–7.96), amalgam (relative risk: 2.25; 95% credible intervals: 1.17–5.35), and composite resin (relative risk: 3.27; 95% credible intervals: 1.55–8.13). For example, glass ionomer cement is 164% more likely to fail than compomer. The <i>p</i> -value is for inconsistencies between direct and indirect evidence for each comparison pair in a closed loop of evidence, and all the <i>p</i> -values are high, indicating no inconsistency justifying the use of the mixed-treatment comparison model. The material with the highest probability of failure was glass ionomer cement (0.99), followed by amalgam, with a much lower probability (0.008); compomer (0.004); resin-modified glass ionomer cement (0.0009); and composite resin (0.0008). Weber Pires <i>et al.</i> Concluded: “Our network meta-analysis found that GIC [glass ionomer cement] had a higher risk of failure compared to all the other conventional restorative materials. This is an important finding since GIC has been widely used for restoration of primary teeth because of its several advantages including fluoride release, chemical bonding to enamel and dentine, tooth preparation with minimal removal of sound structure, biocompatibility and being user-friendly. Nevertheless, this material presents disadvantages such as low wear resistance and flexural strength. To overcome the brittle nature of this cement and improve its physical properties, modifications on its original composition were developed, such as the RMGIC [resin-modified glass ionomer cement].” ^{82 (p8)}
Significance/direction	Results listed by outcome.
Heterogeneity	Homogeneity was measured and consistency was not an issue.
Comments	GRADE was not used by the review authors. All 17 studies were judged to have a high risk of bias. Eleven (65%) of the 17 studies were at low risk of bias for randomisation and none were at low risk of bias for outcome ascertainment. The quality of the review was rated as critically low using AMSTAR 2 as the authors were unable to control for the high risk of bias in the analysis and did not discuss its implications. The HRB grades the quality of the evidence as low quality.

Raggio *et al.* (2016)

Parameter	Extraction
First author and year of publication	Raggio <i>et al.</i> (2016) ⁸³
Objectives	Compared glass ionomer cements with other restorative materials (amalgam, resin composite, or polyacid-modified resin composite) to prevent adjacent (secondary) carious lesions in the margins of occlusal and occlusoproximal restorations in primary teeth.
Participants	Primary dentition, cavitated caries, direct restoration. Population: Children’s margins of occlusal and occlusoproximal restorations in primary teeth. Eight randomised clinical trials published between 1999 and 2014 with 1,644 children aged 5–8 years were included in this review. Gender was not reported. Each child in the study had at least two carious lesions. The longest follow-up period was 36 months.
Setting/context	The study countries or settings were not provided.

Parameter	Extraction
Description of interventions/phenomena of interest	Fluoride-releasing glass ionomer cements may be capable of preventing caries. The intervention group received either resin-modified glass ionomer cement or high-viscosity glass ionomer cement, and these were compared with amalgam, resin composite, or polyacid-modified resin composite.
Databases and sources searched	The authors conducted a literature search in two very similar databases (PubMed and MEDLINE) up to August 2014. The authors provide a search strategy and searched the reference lists of included studies. The authors prepared a protocol and registered it on PROSPERO. Literature screening and data extraction were performed independently by at least two reviewers. None of the authors reported any disclosures. This study was supported by a grant from the Brazilian National Council for Scientific and Technological Development and the São Paulo Research Foundation, and scholarships from the same Council.
Date range (years) of included studies	Eight randomised clinical trials published between 1999 and 2014 were included.
Number of primary studies included in the systematic review	Eight randomised clinical trials published between 1999 and 2014 with 1,644 children aged 5–8 years were included in this review. The sources of funding for primary studies were not reported.
Types of studies included	The inclusion criteria specified clinical trials with a follow-up period. The reasons for exclusion of studies were presented, but not a list of study references.
Country of origin of included studies	The study countries were not provided.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included trials.
Appraisal rating	All eight trials were assessed using the Cochrane Collaboration's risk of bias instrument and all eight trials had two or more unclear risk of bias scores. All eight trials reported adequate randomisation and five reported adequate blinding of outcome assessor. The authors state that the "lack of information could interfere in the quality analyses of these studies. Likewise, there is no information about the sample size calculated, which may not be representative of the population, limiting the extrapolation of results."⁸³ (p183) Results from the Egger test showed no publication bias in all meta-analyses.
Method of analysis	The authors performed all meta-analyses using statistical software (MedCalc Version 12.5.0.0; Microsoft Partner). The authors considered the secondary caries rate of occlusal and occlusoproximal restorations that were shown as the reason for failure reported in the clinical trials. For both types of restored cavity, they performed meta-analysis using the longest follow-up of each study. They used pairwise random-effects models for all calculations. For the pooled studies, they used an Egger test to aid the analysis of publication bias. It was not possible to perform a meta-analysis of high-viscosity glass ionomer cement compared with other materials and of resin-modified glass ionomer cement compared with other restorative materials in different follow-up periods, because there was insufficient information which precluded pooling. The authors analysed these data descriptively.
Outcome assessed	Outcome: Secondary caries Time frame: Follow-up period of at least 12 months Outcome by primary studies: Prevent secondary caries in margins of occlusal restorations: Taifour 2002; Ersin 2006; dos Santos 2009; Hilgert 2014. Prevent caries in margins of occlusoproximal restorations: Donly 1999; Dutta 2001; Taifour 2002; Andersson-Wenckert and Sunnegardh-Grönberg 2006; Ersin 2006; dos Santos 2009; Hilgert 2014.
Results/findings	The authors completed random-effects pairwise meta-analyses. They did not do any sensitivity or subgroup analysis, although it may have been possible. For the secondary caries rate of occlusal surfaces, it was verified that there were no differences between the materials – glass ionomer cements compared with amalgam or resin composite (odds ratio: 1.2; 95% CI: 0.5–3.1; 4 trials) using the longest follow-up of all included studies (12–36 months).

Parameter	Extraction
	For the prevention of carious lesions in the margins of occlusoproximal restorations, glass ionomer cements were associated with significantly better ability than that of amalgam and resin composite (odds ratio: 1.7; 95% CI: 1.2–2.5; 7 trials) using the longest follow-up of all included studies (12–36 months). The authors reported that they observed no significant heterogeneity in the two meta-analyses. According to Raggio <i>et al.</i>, “there is moderate strength of evidence for a positive association between GIC [glass ionomer cement] and the prevention of carious lesions only in the margins of occlusoproximal restorations of primary teeth”⁸³ (p184), but not in occlusal surfaces.
Significance/direction	See above as listed by outcome.
Heterogeneity	The authors reported that they observed no significant heterogeneity in the two meta-analyses.
Comments	GRADE was not used by the review authors. All eight trials had two or more unclear risk of bias scores. All eight trials reported adequate randomisation and five (63%) reported adequate blinding of outcome assessor. The quality of the review was rated as low using AMSTAR 2 as the authors were unable to control for high or unclear risk of bias in their analysis. The HRB grades the quality of the evidence as moderate quality.

Santos *et al.* (2016)

Parameter	Extraction
First author and year of publication	Santos <i>et al.</i> (2016) ⁸⁴
Objectives	Compared glass ionomer cements, composite resins, and compomers, known as adhesive restorations, in order to determine which is superior in terms of restoration survival in the primary (molar) teeth of children.
Participants	Primary dentition, cavitated caries, direct restorations. Population: Children’s primary (molar) teeth. Eleven clinical trials published between 1999 and 2015, including randomised and non-randomised trials, with 483 children aged 3–10 years, were included in this review. Gender was not reported.
Setting/context	Seven studies reported their setting and all reported that the study took place in a university-based clinic. The remaining four studies did not report their setting. The studies were completed in Brazil, Germany, Norway, Pakistan, Sweden, Turkey, the UK, and the USA.
Description of interventions/phenomena of interest	Glass ionomer cements included conventional glass ionomer cements, resin-modified glass ionomer cement, and silver-reinforced glass ionomer cement. Comparator: Each other (glass ionomer cements, composite resins, and compomers), as well as amalgam and composite resin.
Databases and sources searched	The authors searched five major databases up to November 2015: MEDLINE through PubMed; Web of Science; the Cochrane Library; Latin American and Caribbean Health Sciences Literature database (LILACS); ClinicalTrials.gov; and National Institute for Health and Care Excellence (NICE Evidence Search) database. There were no language restrictions imposed. The search strategy is provided in a table in the article text. A manual search was conducted of the reference lists of included studies. The authors prepared a protocol and registered it on the PROSPERO register. The authors independently read 20% of the studies retrieved to determine inter-examiner agreement. After a good degree of agreement was achieved, the reviewers then independently selected the remaining studies. Data were extracted by three authors. The review does not say that this was independent of each other, but the extraction was verified by a fourth author. This study was supported by the Coordination for the Improvement of Higher Education Personnel, Minas Gerais State Research Foundation, the National Counsel of Technological and Scientific Development, and Pró-Reitoria de Pesquisa da Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, in Brazil. The authors do not provide a conflict of interest statement.

Parameter	Extraction
Date range (years) of included studies	Eleven clinical trials published between 1999 and 2015.
Number of primary studies included in the systematic review	Eleven clinical trials published between 1999 and 2015, including randomised and non-randomised trials, were included in this review. The sources of funding for the primary studies were not provided.
Types of studies included	The inclusion criteria specified clinical trials and/or randomised controlled trials. The option to include only clinical trials and randomised controlled trials was due to the fact that such designs have a higher level of scientific evidence than observational studies. The reasons for exclusion of studies were presented, but not a list of excluded full-text studies.
Country of origin of included studies	The studies were completed in Brazil, Germany, Norway, Pakistan, Sweden, Turkey, the UK, and the USA.
Appraisal instruments used	A modified version of the Jadad scale for reporting controlled trials was used to assess the risk of bias in the included trials.
Appraisal rating	A modified version of the Jadad scale for reporting controlled trials was used to assess the risk of bias in the included trials. The authors say that “no deductions were made for lack of randomisation or blinding”. ^{84 (p371)} Eight of the 11 trials were judged to be at a high risk of bias. Only 3 of the 11 trials reported adequate randomisation, and 3 reported adequate blinding of outcome assessments. The authors report that “the divergent results of the studies included indicated no publication bias”. ^{84 (p375)}
Method of analysis	Six studies were included in meta-analysis. Meta-analysis was performed using the Comprehensive Meta-Analysis software. Heterogeneity was evaluated using the I^2 statistic. A random-effects model was used when heterogeneity was equal to or greater than 25%, and a fixed-effects model was used when heterogeneity was less than 25%. Categorical data were extracted for each material (absolute number of restorations that survived in a time period by the total number of restorations that entered the trial). Summary effect measures were calculated using risk ratios and respective 95% confidence intervals (CIs). Comparisons were made between two different types of materials. Subgroup analysis was performed for duration of evaluation of 18 and 24 months when comparing composite resin and resin-modified glass ionomer cement. A random-effects model was used for the subgroup analysis.
Outcome assessed	Outcome: Survival and clinical performance up to 48 months Time frame: 24–48 months Outcomes by primary studies: Survival of Class I and II composite resin restoration compared with resin-modified glass ionomer cement, 18–24 months: Casagrande 2013; Santos 2009; Santos 2010; Sengul and Gurbuz 2015; Survival of Class I and II composite resin restoration compared with compomer restoration, 24 months: Santos 2009; Santos 2010; Sengul and Gurbuz 2015; Attin 2000; Attin 2001. Survival of Class I and II compomer restoration with resin-modified glass ionomer cement restoration, 24 months: Santos 2009; Santos 2010; Sengul and Gurbuz 2015. Survival of Class II composite resin restoration compared with compomer restoration, 24 months: Sengul and Gurbuz 2015; Attin 2000; Attin 2001.
Results/findings	Two of the 11 studies found that the median survival time of silver-reinforced glass ionomer cement was less than that of glass ionomer cement and resin-modified glass ionomer cement ($p < 0.005$), and 2 studies found that glass ionomer cement had a lower median survival time than both resin-modified glass ionomer cement and compomer ($p < 0.05$). Meta-analysis for composite resin, compomer, and resin-modified glass ionomer cement was conducted using six studies. The number of participants or restorations was not provided in the meta-analysis table. The materials did not differ significantly regarding the number of restorations that survived up to 24 months: composite resin compared with resin-modified glass ionomer cement (random effects; relative risk: 1.12; 95% CI: 0.96–1.31; I^2 : >25%; 7 studies); composite resin compared with compomer (fixed effect; relative risk: 1.04; 95% CI: 0.96–1.13; I^2 : 0%; 4 studies); and compomer compared with resin-modified glass ionomer cement (fixed effect; relative risk: 1.03; 95% CI: 0.84–1.27; I^2 : 0%; 2

Parameter	Extraction
	studies). Subgroup analysis for composite resin compared with resin-modified glass ionomer cement by time indicated no heterogeneity and similar results. The present systematic review has limitations, such as the absence of subgroup analysis between newer and older materials (it was not possible to compare silver-reinforced glass ionomer cements with newer materials), the lack of analysis comparing single- and multi-surface restorations, and some methodological heterogeneity and methodological bias, which hinders definite conclusions. The overall conclusion is that there is very low-quality evidence that any of the adhesive-based materials are superior to each other for restoring primary teeth in children, excluding silver-reinforced glass ionomer cement, which is inferior and not recommended for use in primary teeth. According to Santos <i>et al.</i>, “composite resin, compomers, resin-modified glass ionomer cement and glass ionomer cement are suitable for the restoration of primary teeth in children”.⁸⁴ (p377) The combination of Class I and Class II restorations “could indicate some degree of bias that could compromise the results of the meta-analysis and interpretation of findings, since one material may work well in one situation but not in another, and survival may be different, depending on the number of surfaces involved in the restoration.”⁸⁴ (p376)
Significance/direction	Results listed by outcome.
Heterogeneity	These main meta-analysis indicated heterogeneity but subgroup analysis for composite resin compared with resin-modified glass ionomer cement by time indicated no heterogeneity and similar results.
Comments	GRADE was not used by the review authors. The review includes both randomised and non-randomised trials. Eight of the 11 trials were judged to be at a high risk of bias. Only 3 (27%) of the 11 trials reported adequate randomisation, and 3 (27%) reported adequate blinding of outcome assessments. The quality of the review was rated as low using AMSTAR 2 as the authors were unable to control for high risk of bias in their analysis. The HRB grades the quality of the evidence as low quality.

Indirect restoration material: Crowns

Badar *et al.* (2019)

Parameter	Extraction
First author and year of publication	Badar <i>et al.</i> (2019)⁸⁵
Objectives	Assessed the outcomes (retention and absence of pulpal symptoms) of placement of a crown using the Hall technique on primary carious molars in children and compared it with conventional dental restorations or stainless steel crowns.
Participants	Primary dentition, cavitated caries, crown restoration technique Children with asymptomatic carious primary molar teeth were included in the review. Across the five studies included in this review, the total number of teeth assessed was 1,775. Of these, 1,325 teeth were restored using the Hall technique and the rest were restored using other techniques, including conventional restorations or non-restorative care. The three clinical trials had 280 teeth managed with the Hall technique, whereas 1,045 teeth were restored with the Hall technique in the two retrospective studies. The follow-up period for the evaluation of teeth restored using the Hall technique varied from 15 months to 5 years.
Setting/context	The study countries were: Germany (one study), New Zealand (one study), Scotland (two studies), and the USA (one study). The clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: Placement of a crown using the Hall technique Comparison: Caries removal followed by standard control restorations or stainless steel crown The authors provided the following definition of the intervention: “The placement of a stainless steel crown is sometimes challenging as it requires patient

Parameter	Extraction
	cooperation, which is difficult to achieve in pediatric patients. For the purpose of simplifying the procedure and making it receptive to the patients, Dr Hall devised a technique of stainless steel crown placement in children that does not require local anesthesia, or caries removal or any sort of tooth preparation. This technique is based on the scientific evidence that caries progression gets arrested once an effective marginal seal is achieved. A properly placed stainless steel crown denies the cariogenic bacteria of an environment that is conducive for acidic demineralization of the inorganic and proteolytic disintegration of the organic component of the tooth structure."⁸⁵ (p446) Of the included studies, three compared a stainless steel crown placed with the Hall technique with various control restorations.
Databases and sources searched	Five databases and other sources were searched: PubMed, CINAHL Plus, the Cochrane Library, <i>Journal of Dentistry and Oral Sciences</i>, and Scopus. Searches were limited to articles written in the English language and covering male and female populations. The range of dates for the search were not reported. The most recent included paper was published in 2017. Hand-searching was performed in clinical trial registries (ClinicalTrials.gov and the BioMed Central trial registry), the International Association for Dental Research database, Cochrane databases, and Google Scholar. Furthermore, in the search of grey literature, the databases OpenSIGLE and Grey Literature Report were explored, which also contained articles and theses in languages other than English. For the registered trial protocols cited in the trial registries, authors were contacted regarding the estimated time remaining for the results. A systematic review protocol was prepared and registered with PROSPERO. Extraction and screening were completed in duplicate. The authors reported that this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors, and they had no conflict of interest to declare.
Date range (years) of included studies	The included studies were published in 2006, 2011, 2014, 2017, and 2018.
Number of primary studies included in the systematic review	Five studies – a split-mouth randomised controlled trial, a randomised controlled trial, a quasi-experimental study, a retrospective analysis study, and a retrospective charts review – were included in this review. The studies were published in 2006, 2011, 2014, 2017, and 2018. The sources of funding for primary studies were not reported.
Types of studies included	Randomised controlled trials, quasi-experimental studies, cohort studies, and retrospective studies were eligible for inclusion. The studies excluded at full-text with their reason for exclusion are provided in the text.
Country of origin of included studies	The study countries were Germany, New Zealand, Scotland (two studies), and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included trials. The risk of bias for the retrospective studies was also evaluated using the Agency for Healthcare Research and Quality (AHRQ) criteria.
Appraisal rating	According to Badar <i>et al.</i>, "two randomized controlled trials...showed low risk of bias...the quasi-experimental study lacked randomization of the participants and therefore showed medium risk of bias. Owing to the nature of the intervention, blinding of the participants and care providers was not possible in the trials".⁸⁵ (p449) The two randomised controlled trials were at low risk of bias for randomisation. Risk of bias for outcome assessment was not undertaken. The quality assessment of the included retrospective studies using the Agency for Health Research and Quality criteria found that one study scored 5/11 and one study scored 8/11. The authors do not provide any interpretation of the overall quality of the two cohort studies. It appears that the two cohort studies were representative of their population, but neither controlled for confounding. One of the two cohort studies had inadequate outcome data. The authors do not make any comment on the influence of bias on the analysis in the discussion. Publication bias was not reported on due to the small number of included studies.

Parameter	Extraction
Method of analysis	The random-effects model was adopted as the method of analysis, as it was assumed that the trials had variability in the conduct and reporting of outcomes. Heterogeneity was determined with I^2 statistics.
Outcome assessed	The primary outcomes were retention of deciduous tooth and/or absence of pulpal symptoms. Retention was measured as success, major failure, minor failure, survival of preformed metal crown, and success of preformed metal crown crown. Retention of deciduous tooth and/or absence of pulpal symptoms: Innes 2006; Ludwig 2014; Boyd 2018; Innes 2018; Santamaria 2017.
Results/findings	Five studies were included: two randomised controlled trials, one quasi-experimental trial, and two retrospective studies. A total of 1,775 teeth were assessed, of which 1,325 teeth were restored using the Hall technique. The retrospective studies showed no difference between using the Hall technique and using other methods, whereas the randomised controlled trials and quasi-experimental trial favoured the Hall technique over other treatment modalities. The meta-analysis conducted with three trials on the comparison of the Hall technique with conventional methods of restoring primary carious teeth showed that the Hall technique is far more successful than the comparative treatment modalities (risk ratio: 5.55; 95% CI: 3.31–9.30; $p < 0.001$; I^2 : 0%; 227 restorations; 3 trials). In conclusion, the authors stated the following: “Within the limitation of the present systematic review, it can be concluded that the Hall technique is not only a predictable restorative option but it has significantly outperformed the conventional method of treatment of carious primary molars. The success rate of the Hall technique is 5 times that of the conventional restorative techniques”. ⁸⁵ (p450)
Significance/direction	The meta-analysis conducted with three trials on the comparison of the Hall technique with conventional methods of restoring primary carious teeth showed that the Hall technique is far more successful than the comparative treatment modalities
Heterogeneity	Heterogeneity was measured but the authors did not comment on heterogeneity, however the Forest plot indicates no heterogeneity.
Comments	GRADE was not used by the review authors.

Innes *et al.* (2015)

Parameter	Extraction
First author and year of publication	Innes <i>et al.</i> (2015)⁸⁶ (Cochrane Review)
Objectives	Compared the effectiveness and safety of all types of preformed crowns (using the Hall technique) with conventional filling materials for restoring primary molar teeth in children. Preformed crowns were fitted using the Hall technique, which is a simplified method where the crown is placed on the tooth without the need for local anaesthesia, or for carious lesion or tooth tissue removal.
Participants	Primary dentition, cavitated caries, and restoration materials direct compared with indirect, and one technique. Population: Children’s decayed primary molar teeth Five randomised controlled trials published between 2003 and 2014, which included 438 children (and 693 primary molar teeth) with an age range of 2.6–10 years, were included in this review. The mean age range was 5.1–6.8 years. Just over one-half (53%) were male.
Setting/context	Three studies were set in university-based dental clinics and two were in general dental clinics. The studies were completed in Germany, Israel, Saudi Arabia, the UK, and the USA.
Description of interventions/phenomena of interest	According to Innes <i>et al.</i> , “traditionally, preformed crowns have been made of metal and referred to as either preformed metal crowns or stainless-steel crowns. They are silver in colour. More recently, aesthetic preformed crowns have been developed and used for primary teeth; these crowns are white in colour. Placement of a preformed crown is intended to provide a more durable

Parameter	Extraction
	restoration compared to a conventional filling.”^{86 (p6)} All types of preformed crowns were considered in this Cochrane Review. Comparator: Conventional filling materials included amalgam, composite resin, glass ionomer cement, resin-modified glass ionomer cement, compomers, non-restorative caries treatment, and no treatment.
Databases and sources searched	Four electronic databases were searched: Cochrane Oral Health Group Trials Register (to 21 January 2015), Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library, 2014, Issue 12), MEDLINE via Ovid (1946 to 21 January 2015), and Embase via Ovid (1980 to 21 January 2015). No restrictions were placed on the language or date of publication when searching the databases. The search strategies were presented in appendices. The authors searched ClinicalTrials.gov and the World Health Organization’s (WHO’s) International Clinical Trials Registry Platform for ongoing trials, and OpenGrey for grey literature (to 21 January 2015). The authors requested information about unpublished studies or studies published in the grey literature from relevant companies, relevant investigators, and relevant professional organisations. Literature screening and data extraction were performed independently by at least two reviewers. The authors prepared a protocol. There was no conflict of interest for one of the review authors. Two of the review authors received partial sponsorship in 2000 from a member of the dental products industry for a clinical trial investigating the use of preformed metal crowns to seal carious tissues into primary molar teeth using the Hall technique. These two authors have not taken part in the decision to include the study in the review or assessment of risk of bias of the study. Funding was provided by the University of Manchester, the National Institute for Health Research, and the Cochrane Collaboration.
Date range (years) of included studies	Five randomised controlled trials published between 2003 and 2014 were included.
Number of primary studies included in the systematic review	Five randomised controlled trials published between 2003 and 2014. Two of the five primary studies reported their source of funding; one was partially funded by industry and the other was funded by a university.
Types of studies included	The inclusion criteria specified randomised controlled trials. Full-text articles, references, and reason for exclusion were provided for the eight full-text exclusions.
Country of origin of included studies	The studies were completed in Germany, Israel, Saudi Arabia, the UK, and the USA.
Appraisal instruments used	The Cochrane Collaboration’s risk of bias instrument was used.
Appraisal rating	As this was a Cochrane Review, the Cochrane Collaboration’s risk of bias instrument was used, and all five trials were judged to have a high risk of bias. All five were judged to have adequate randomisation and none had a blinded outcome assessment. There was an insufficient number of trials (more than 10 required) to assess publication bias. The authors assessed reporting bias as between-study publication bias or within-study reporting bias. They completed a comprehensive search. Publication bias was considered as part of the GRADE assessment.
Method of analysis	For dichotomous data, the estimate of effect of an intervention was expressed as risk ratios, together with 95% CIs using a random-effects model. The authors combined data from split-mouth studies with data from parallel group trials using a method outlined by Elbourne (2002), using the generic inverse-variance method in RevMan. The authors assessed clinical heterogeneity by examining the types of participants (e.g. age), interventions (e.g. method of restoration), and outcomes (e.g. pain relief) in each study. The authors assessed heterogeneity by inspection of the point estimates and CIs on the forest plots. The variation in treatment effects was assessed by means of Cochran’s Q test for heterogeneity and quantified by the I² statistic. Sensitivity and subgroup analysis were planned, but only one subgroup analysis was done.
Outcome assessed	Outcome: Reduction in the risk of major clinical or radiological failure or pain in the primary tooth in the long term compared with using fillings. Time frame: Long term (12–48 months)

Parameter	Extraction
	Outcome by primary study: Major failure: Hutcheson 2012; Innes 2011; Santamaria 2014. Pain: Hutcheson 2012; Innes 2011. Satisfaction with treatment: No studies Time to restoration failure/retreatment: No studies Discomfort associated with procedure: Innes 2011; Santamaria 2014. Gingival bleeding: Atieh 2008; Hutcheson 2012. Cost: No studies Adverse events: No studies
Results/findings	The main findings suggest that crowns placed on primary teeth with carious lesions, or where pulp treatment has been carried out, are likely to reduce the risk of major failure (random effects; relative risk: 0.18; 95% CI: 0.06–0.56; 346 teeth; 3 studies; I^2: 0%) or pain (fixed effects; relative risk: 0.15; 95% CI: 0.04–0.67; 312 teeth; 2 studies; I^2: 0%) in the primary tooth in the long term compared with using fillings. The review authors report that evidence supporting this finding is judged to be of moderate quality based on the GRADE criteria and suggests that crowns are more effective than fillings in managing dental decay in primary teeth. Crowns fitted using the Hall technique may reduce discomfort at the time of treatment compared with using other fillings (fixed effects; relative risk: 0.56; 95% CI: 0.36–0.87; 381 participants; 2 studies; I^2: 0%; moderate-quality evidence). The evidence supporting this finding is judged to be of moderate quality based on the GRADE criteria and suggests that crowns fitted using the Hall technique are less likely to cause abscesses and pain. Both findings suggest that there is adequate evidence to support the view that preformed crowns (fitted using the Hall technique) are superior to conventional fillings for managing tooth decay in primary teeth. The incidence of gingival bleeding was not different (relative risk: 1.74; 95% CI: 0.99–3.06; I^2: 0%; 2 trials; 195 participants; low-quality evidence). In reflecting on the generalisability of these findings, Innes <i>et al.</i> point out that “crowns seemed to perform better than fillings, and the variability between the studies reinforces the applicability of this finding to different settings.”⁸⁶p22
Significance/direction	Results listed by outcome.
Heterogeneity	The authors assessed both clinical and statistical heterogeneity. Statistical heterogeneity was not an issue in the meta-analyses.
Comments	GRADE was used by the review authors. As this was a Cochrane Review, the Cochrane Collaboration’s risk of bias instrument was used, and all five trials were judged to have a high risk of bias. All five were judged to have adequate randomisation and none had a blinded outcome assessment. The quality of the review was rated as low using AMSTAR 2 as the authors were unable to control for high risk of bias in their analysis. The sample size was less than 200 for some outcomes. The HRB grades the quality of the evidence as moderate for some outcomes and low quality for other outcomes, which corresponds with the review authors’ assessment.

Comparison direct and indirect (crown) restoration material

Chisini *et al.* (2018)

Parameter	Extraction
First author and year of publication	Chisini <i>et al.</i> (2018) ⁸⁷
Objectives	Investigated the longevity of posterior restorations in primary teeth and the reasons for failure.
Participants	Primary dentition, cavitated caries, direct restorations and crowns. Population: Posterior restorations in primary teeth in children with an age range of 1–13 years. Twenty-one randomised controlled trials and 10 observational studies evaluating 12,047 posterior restorations in primary teeth in children with an age range of 1–13 years were included in this review. The studies were published between 1996

Parameter	Extraction
	and 2016, and the follow-up times varied from 1 to 4 years. Gender was not reported.
Setting/context	The studies were completed in a variety of settings comprising university-based clinics (10), private dental clinics (8), public health clinics (3), schools (2), and multi-centred settings (3). Five studies did not report their setting. The studies were completed in Australia, Brazil, Egypt, Germany, Greece, India, Ireland, Norway, the Netherlands, Sweden, Syria, Turkey, the UK, and the USA. Most studies were completed in European countries (61.3%).
Description of interventions/phenomena of interest	According to Chisini <i>et al.</i> , “the included studies evaluated the clinical performance of Class I, Class II, and crown restorations due to caries with seven different materials: amalgam (6 studies), compomers (9 studies), composite resin (6 studies), conventional glass ionomer cement (5 studies), modified resin glass ionomer cement (4 studies), resin-modified glass ionomer cement (10 studies), and steel crowns (3 studies)”. ⁸⁷ (p125–126) Comparator: Each other. Materials, techniques, and related factors associated with restoration failure were also examined.
Databases and sources searched	The authors searched four electronic databases (SciVerse Scopus, Web of Science, Cochrane Library, MEDLINE via PubMed) and the search was done in February 2017. Only studies published from 1996 to 2017 and written in the English language were considered. The syntax of the search is detailed in Appendix S1 at the end of the article. Grey literature was investigated. The authors did not report writing a protocol. Literature screening and data extraction were performed independently by two reviewers. The authors stated that “The rest of the authors declare no conflict of interests”, ⁸⁷ (p137) but do not provide clarity on who did declare a conflict of interest.
Date range (years) of included studies	The included studies were published between 1996 and 2016.
Number of primary studies included in the systematic review	Twenty-one randomised controlled trials and 10 observational studies. The sources of funding for the primary studies were not provided
Types of studies included	The inclusion criteria specified longitudinal clinical studies (prospective, retrospective, and randomised clinical trials). The authors have included prospective and retrospective clinical trials carried out in settings closer to clinical reality and including children with both low and high risk of caries. Excluded studies and reasons for exclusion are presented in an appendix in the journal article.
Country of origin of included studies	The studies were completed in Australia, Brazil, Egypt, Germany, Greece, India, Ireland, Norway, the Netherlands, Sweden, Syria, Turkey, the UK, and the USA. Most studies were completed in European countries (61.3%).
Appraisal instruments used	The Cochrane Collaboration’s risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	The risk of bias in the included studies was assessed using the Cochrane Collaboration’s risk of bias instrument, and all studies were at high risk of bias. According to Chisini <i>et al.</i> , “in general the included studies presented high risk of bias, mainly selection, performance, and detection bias”. ⁸⁷ (p126) Five of the 31 included studies were judged to have adequate randomisation, and 6 had adequate blinding for outcome ascertainment. Publication bias was not discussed.
Method of analysis	The included studies had high heterogeneity regarding study design, evaluation criteria, and longevity outcomes, contraindicating meta-analysis. Hence, a qualitative analysis was conducted on collected data. For qualitative analysis, the survival or the success rate and annual failure rate were used to compare the included studies.
Outcome assessed	Outcome: Longevity or survival Time frame: 12 months or longer The actual study follow-up times varied from 1 to 4 years. Longevity or survival: Abo-Hamar 2015; Andersson-Wenckert 1995; Andersson-Wenckert 1997; Attin2001; Buecher 2015; Croll 2001; de Amorim 2014; Duggal 2002; Dutta 2002; Espelid 1999; Folkesson 1999; Franzon 2015; Gross 2001; Holst 1996; Hubel and Mejare 2003; Kavvadia 2004; Kilpatrick 1995; Kitty andWei2 1997; Kotsanos and Arizos 2011; Kramer and Frankenberger 2001; Leith and

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	O'Connell 2011; Papagiannoulis 1999; Peters 1996; Pinto 2014; Roberts 2005; Rutar 2002; Schueler 2014; Sengul and Gurbuz 2015; Soncini 2007; Taifour 2002; Webman 2016.
Results/findings	The restoration success rates for each type of material were as follows: amalgam: 82% at 3 years; composite resin: 79% at 4 years; glass ionomer cement: 89% at 4 years; compomers: 91% at 3 years; resin-modified glass ionomer cement: 94% at 4 years; modified resin glass ionomer cement: 57% at 3 years; and steel crowns: 96% at 3 years. The highest success rate was for steel crowns, followed by resin-modified glass ionomer cement, and the highest failure rate was for modified resin glass ionomer cement. The overall annual failure rate ranges for each type of restorative material were as follows: composite resin: 2–13% over 4 years; amalgam: 1–28% over 3 years; glass ionomer cement: 0.8–17% over 4 years; compomers: 2–15% over 3 years; resin-modified glass ionomer cement: 0.9–17% over 4 years; steel crowns: 1–19% over 3 years; and modified resin glass ionomer cement: 10–29% over 3 years. Modified resin glass ionomer cement restorations had the highest annual failure rate, and composite resin had the lowest upper range for annual failure. The main reasons for failure over 3 or 4 years were secondary caries, restoration loss, marginal adaptation, and fractured teeth. The authors noted the risk of bias as a limitation but reported that it was offset by the large sample size. According to Chisini <i>et al.</i>, “there is a large variation in longevity of posterior restorations in primary teeth. Composite resin exhibited the lowest annual failure rates, whereas modified resin glass ionomer cement exhibited the highest annual failure rate. The steel crowns had the highest rate of success.”^{87 (p136)} The main finding in this review suggests that there is very low-quality regarding the best material for posterior restorations in primary teeth, due to a wide range of time points for data collection and different year end points for individual studies.
Significance/direction	Results listed by outcome.
Heterogeneity	Meta-analysis was not completed due to heterogeneity and high risk of bias in included studies.
Comments	GRADE was not used by the review authors. The review included both randomised controlled trials and observational studies. All studies were at high risk of bias. Five (16%) of the 31 included studies were judged to have adequate randomisation, and 6 (19%) had adequate blinding for outcome ascertainment. The quality of the review was rated as moderate using AMSTAR 2. Meta-analysis was not completed due to heterogeneity and high risk of bias in included studies. The HRB grades the quality of the evidence as low quality for each outcome.

Aiem *et al.* (2017)

Parameter	Extraction
First author and year of publication	Aiem <i>et al.</i> (2017) ⁸⁸
Objectives	Evaluated the clinical effectiveness (success or failure of restorations based on five criteria) of all types of aesthetic preformed crowns for restoring primary teeth, compared with conventional filling materials or other types of crowns.
Participants	Primary dentition, cavitated caries, comparison of direct restorations and crowns The authors included seven relevant articles, one covering primary incisors and six covering primary molars. Six of the seven papers included 172 children (aged 2–9 years) and seven papers included 568 teeth. Gender was not reported. All included studies compared pre-veneered stainless steel crowns with other crowns or two different pre-veneered stainless steel crowns.
Setting/context	The countries covered were Ireland, Israel, Turkey, and the United Arab Emirates. The clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: All types of aesthetic preformed crowns Comparator: Conventional filling materials (such as amalgam, composite, glass ionomer, resin-modified glass ionomer, and compomers) or other types of crowns

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	The authors described the intervention as “aesthetic preformed crowns (resin composite strip crowns, open-face stainless steel crowns, pre-veneered stainless steel crowns, and zircon crowns)”. ⁸⁸ (p274)
Databases and sources searched	Two databases were searched (MEDLINE via PubMed and the Cochrane Central Register of Controlled Trials (CENTRAL). The last search for articles was conducted in March 2016, with no restrictions on date. The researchers screened the reference lists of included studies, as well as ClinicalTrials.gov and the WHO’s International Clinical Trials Registry Platform. The authors did not report preparing or publishing a protocol. Extraction and screening were completed in duplicate. The funding source for the review was not reported. The authors declared no conflict of interest.
Date range (years) of included studies	The randomised controlled trials were published between 2003 and 2014
Number of primary studies included in the systematic review	The authors included seven relevant articles, one covering primary incisors and six covering primary molars. These seven articles corresponded to randomised controlled trials. Three split-mouth design studies and two parallel group design studies were included. The studies were published in 2003 (1), 2004 (1), and 2014 (3). The funding sources for the primary papers was not reported.
Types of studies included	Randomised controlled trials only were eligible for inclusion A list of excluded studies and reason for exclusion were not provided.
Country of origin of included studies	The studies were conducted in Ireland, Israel, Turkey, and the United Arab Emirates.
Appraisal instruments used	The Cochrane Collaboration’s risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	The overall risk of bias was high for four studies and unclear for one study. Four (80%) studies had low risk of bias and one study had a high risk of bias for randomisation. Four studies were at high risk and one (20%) study was at low risk for outcome assessment. According to the authors, “Regarding primary molars...Regarding methodology, the overall high risk of bias of the included randomised controlled trials does not permit aesthetic crowns (pre-veneered or open-face stainless steel crowns) to be recommended as replacements for SSCs [stainless steel crowns] on primary molars...Due to the different comparisons and outcomes, it was not possible to perform a meta-analysis to complete recommendations...For some outcomes, the absence of a statistically significant difference between groups when there was no calculation of sample size does not permit a conclusion because of low power.” ⁸⁸ (p279) Publication bias was not measured or discussed.
Method of analysis	According to the authors, “Due to the different comparisons and outcomes, it was not possible to perform a meta-analysis.” ⁸⁸ (p279) The authors present a narrative description of each of the studies in the results section and do not provide a synthesis of the results.
Outcome assessed	The outcomes assessed were: survival rate (number of restorative failures based on clinical criteria such as FDI and USPHS) and clinical performance, which indicates success or failure of restorations – marginal integrity/adaptation, marginal discolouration, recurrent caries, retention of composite restorations, and post-operative sensitivity. The authors stated that “We included six articles corresponding to four studies: three compared two groups and one [compared] five groups. Two of [the articles] described the same split-mouth study that compared pre-veneered stainless steel crowns with SSCs [stainless steel crowns]. One study with an unclear design compared different pre-veneered stainless steel crowns and with SSCs or open-face stainless steel crowns (NuSmile®, Pado Pearls™ and ex vivo by laboratory procedures). One study compared ex vivo pre-veneered stainless steel crowns with open-face stainless steel crowns and the last one [compared] two different brands of pre-veneered stainless steel crowns. In only one study the majority of participants received the treatment under general anaesthesia and the use of anaesthesia was not reported in two studies. In three studies, pulp treatment before placing the crowns was not reported and pulpotomies were not systematically performed in one study. The maximum follow-up time was 4 years

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	in one study; in two studies, 18 months; and in one, 1 year. The number of assessors was one, two, three, four, or not stipulated. The primary outcome, failure (or clinical effectiveness), depended on the study and was based on clinical or radiographic criteria recorded in all studies. One study used the loss of one-third or more of the aesthetic material as the primary outcome. In another study, the primary outcome was periodontal or gingival health, measured with different indices. In two studies, outcomes were crown retention, crown or buccal/occlusal facade fracture, gingival margin extension, periodontal or gingival health, occlusion, facade wear, and stain resistance. Crown adaptation and bone resorption were assessed on radiographs. Moreover, criteria definitions were not always consistent.”⁸⁸ (p275–278) According to the authors, “Only one parallel group RCT [randomised controlled trial] was carried out to compare resin composite strip crowns (3M, Filtek), pre-veneered stainless steel crowns (NuSmile), and zircon crowns. Local anaesthesia was achieved in all cases. No pulpotomy was performed before crown placement. [The assessors comprised] three trainees and one general dental practitioner...after 6 months of follow-up. The primary outcome was fracture (partial or complete) and the secondary outcomes were both gingival index and tooth wear on opposing teeth.”⁸⁸ (p278) Survival rate and clinical performance: Ram 2003; Beldüz Kara 2014; Kratunova 2014; Walia 2014; Yilmaz 2004. Follow-up of 6 months to 4 years.
Results/findings	The most succinct results are presented in the authors sections: the importance of the review to paediatric dentists and conclusions . The authors report that “This review alerts dentists to the low number of randomised clinical trials that compare aesthetic preformed crowns with SCCs [stainless steel crowns] or conventional filling materials and on the short follow-up time of these trials. They [paediatric dentists] should inform their patients on the low level of proof supporting the preformed aesthetic crowns. On temporary molars, which are less visible, aesthetic crowns cannot replace the SCCs despite the poor aesthetic of the SCCs.”⁸⁸ p280 The authors concluded that “The majority of the included RCTs [randomised controlled trials] involved primary molars. Because of the risk of bias, changing the recommendations for posterior teeth is not advised. Regarding restoration failures of the commercialised preformed paediatric crowns, zircon crowns appeared to be best [choice to restore] incisors for a follow-up of only 6 months. Zircon crowns should be evaluated over periods of at least 1 year in primary anterior and posterior teeth.”⁸⁸ (p280)
Significance/direction	The authors concluded that “The majority of the included RCTs [randomised controlled trials] involved primary molars. Because of the risk of bias, changing the recommendations for posterior teeth is not advised. Regarding restoration failures of the commercialised preformed paediatric crowns, zircon crowns appeared to be best [choice to restore] incisors for a follow-up of only 6 months. Zircon crowns should be evaluated over periods of at least 1 year in primary anterior and posterior teeth.”⁸⁸ (p280)
Heterogeneity	According to the authors, “Due to the different comparisons and outcomes, it was not possible to perform a meta-analysis.” The authors do not discuss statistical heterogeneity but do point to treatment and measurement heterogeneity across the included studies.
Comments	With regard to why this review is important to paediatric dentists, the authors noted that “This review alerts dentists to the low number of randomised clinical trials that compare aesthetic preformed crowns with SCCs [stainless steel crowns] or conventional filling materials and on the short follow-up time of these trials. They should inform their patients on the low level of proof supporting preformed aesthetic crowns. On temporary molars, which are less visible, aesthetic crowns cannot replace the SCCs despite the poor aesthetic of the SCCs.”⁸⁸ (p280)

Restoration support material

Schwendicke *et al.* (2015d)

Parameter	Extraction
First author and year of publication	Schwendicke <i>et al.</i> (2015d) ⁸⁹
Objectives	Evaluated the risk of restoration failure (proportion of teeth requiring retreatment) following restoration due to dentine caries in primary molar teeth, comparing restorations with cavity lining to restorations without cavity lining. The follow-up was 1 or more years after restoration.
Participants	Primary teeth, cavitated caries, materials to support restoration materials Population: Primary molars in children with dentine caries requiring restoration Three randomised controlled trials published between 2002 and 2010, comprising 62 participants and 130 restorations, were included in this review; the participants included children aged 4–8 years. Two of the three studies reported data on gender and 44% were male.
Setting/context	All three studies were conducted in a secondary care setting in Brazil.
Description of interventions/phenomena of interest	According to Schwendicke <i>et al.</i> , cavity lining is used to maintain pulpal vitality and liners are mainly based on calcium hydroxide. Comparator: No liner
Databases and sources searched	The authors searched four data sources: Cochrane Central Register of Controlled Trials, MEDLINE, Embase, and Biomed Central. Grey literature was screened via Open Grey. No restrictions were placed on the language or date of publication when searching the electronic databases. The search strategy was based on defined search protocol and was adapted for each database. The reference lists of relevant articles were checked, and the authors contacted known experts in the field. Screening and extraction were completed in duplicate. A protocol was not completed. The authors did not declare conflict of interest or provide source of funding for the review.
Date range (years) of included studies	Six papers from three randomised controlled trials were published between 2002 and 2010.
Number of primary studies included in the systematic review	Three randomised controlled trials were published in six papers between 2001 and 2013. The funding for two primary studies was not reported to the authors; and the third trial was funded by the Brazilian dental association.
Types of studies included	Randomised controlled clinical trials were specified in the inclusion criteria. The excluded trials and their reason for exclusion were provided.
Country of origin of included studies	The studies were completed in Brazil.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included trials.
Appraisal rating	Based on the Cochrane Collaboration's risk of bias instrument, the risk of bias was judged to be high in all three trials. All three trials were judged to have adequate randomisation and one (33%) was judged to have adequate blinding of outcome assessors. Seven of the eight included studies evaluated post-operative hypersensitivity. All studies were at unclear or high risk of bias. Four of the eight trials measured restoration longevity. Two of the studies were judged to be at high risk and two at unclear risk of bias. The authors reported that graphical evaluation via funnel plot analysis did not indicate publication bias.
Method of analysis	The authors completed random-effects intention-to-treat and per-protocol meta-analyses, and trial sequential analysis to control for random errors. Heterogeneity was assessed using both Cochran's Q and I ² -statistics.
Outcome assessed	Restoration failure measured as the proportion of teeth requiring retreatment at 1 year or longer Outcome by primary study: Restoration failure: Trial 1: Franzon 2007; Pinto 2006; Trial 2: Falster 2002; Casagrande 2009; Trial 3: Casagrande 2008; Casagrande 2010.

Parameter	Extraction
Results/findings	The authors reported that they “did not observe any significant difference between adhesively restoring the cavity without instead of with lining on risk of failure, while included studies tended to indicate potentially fewer failures in teeth without than with lining (intention-to-treat RR (95% CI) 0.71 (0.49–1.04) and per-protocol analyses 0.52 (0.24–1.10).” ⁸⁹ (p1293) Using trial sequential analysis, the authors reported that “we found that the Z curve did neither cross the conventional boundaries, the TSMB [trial sequential monitoring boundaries] for benefit or harm, nor the TSMB for futility (which was not even drawn by the program due to few data).” ⁸⁹ (p1293)
Significance/direction	No difference
Heterogeneity	Statistical heterogeneity was very low.
Comments	GRADE was used by the review authors. The quality of evidence was graded using the criteria outlined by GRADE, taking account of risk of bias within the trials, unexplained heterogeneity, inconsistency between trials, indirectness of comparisons, imprecision (few events), and risk of publication bias. The authors reported that they had “very low confidence in results, as risk of bias was high and estimates imprecise”. ⁸⁹ (p1293)

Restoration processes or techniques

Aïem *et al.* (2020)

Parameter	Extraction
First author and year of publication	Aïem <i>et al.</i> (2020) ⁹⁰
Objectives	Compared the efficacy (measured by pulp exposure and absence of pulpal or periodontal complications or restorative failures) of three caries removal techniques – complete caries removal, selective caries removal, and stepwise caries removal – for deep carious lesions in vital (absence of irreversible pulpitis or pulpal necrosis) primary teeth.
Participants	Primary dentition, cavitated caries, direct restoration technique. Children with deep carious lesions in primary teeth. There were 669 children (and 824 teeth) with an age range of 3–15 years. Gender was not reported. Dropout rates were 0–27%. The maximum follow-up time was 2 years in one study, 1 year in four studies, 4–6 months in one study, and 3–6 months in one study, and the minimum follow-up time was 4–6 weeks.
Setting/context	The study settings were not reported. The studies were completed in Brazil, Germany, Scandinavia, Thailand, and Turkey.
Description of interventions/phenomena of interest	Intervention: Complete caries removal, selective caries removal, and stepwise caries removal. Compared with each other. Randomised controlled trials considering these caries removal techniques were not included if at least one of the other compared groups was without tissue excavation (such as the Hall technique, therapeutic sealing of cavity lesions).
Databases and sources searched	The authors searched three electronic databases (MEDLINE via PubMed, the Cochrane Library, and Embase) up to 31 May 2019 using search strategies presented in the paper. There was no restriction on date, and only English- and French-language publications were included. Triplicate screening and duplicate extraction was completed. The authors also screened the reference lists of included studies. ClinicalTrials.gov and the WHO’s International Clinical Trials Registry Platform were searched to identify ongoing trials. The authors do not mention that they prepared or published a protocol. The authors declared no conflicts of interest. They did not report the source of funding for the review.
Date range (years) of included studies	The authors included eight randomised controlled trials (10 papers) published between 1977 and 2018.
Number of primary studies included in the systematic review	The authors included eight randomised controlled trials (10 papers) published between 1977 and 2018. Five trials compared selective caries removal with complete caries removal; one trial compared selective caries removal with stepwise caries removal; one trial compared stepwise caries removal with

Parameter	Extraction
	complete caries removal; and the trial reported in two papers compared the three caries removal techniques. The sources of funding for primary studies were not reported.
Types of studies included	Randomised controlled trials were eligible for inclusion. The authors listed the studies excluded at full-text screening with the reason for exclusion.
Country of origin of included studies	The studies were completed in Brazil, Germany, Scandinavia, Thailand, and Turkey.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	One of the eight studies was judged to have a high risk of bias, while four studies had an unclear risk of bias and three studies had a low risk of bias. Five of the eight studies were judged adequate for randomisation and six had adequate outcome assessment. The risk of publication bias was also considered and was dealt with through an adequate search and comparisons with other systematic reviews. The authors stratified the trials for the same outcome – pulpo-periodontal complications – according to the overall bias risk and the results were unchanged.
Method of analysis	Two authors performed conventional meta-analysis using random-effects models in Review Manager Software Version 5.3 (Nordic Cochrane Centre, Cochrane Collaboration). They calculated odds ratios (OR) and 95% CIs. They performed meta-analyses for intention-to-treat and per-protocol scenarios using RevMan 5.
Outcome assessed	Pulp exposure, pulpo-periodontal complications (clinical and radiological failures), and/or restorative failures. The restorative materials had to be the same in the different compared groups. The maximum follow-up time was 2 years in one study, 1 year in four studies, 4–6 months in one study, and 3–6 months in one study, and the minimum follow-up time was 4–6 weeks. Outcome by primary study: Pulp exposure risk during treatment: Mello 2018; Franzon 2014, 2015; Phonghanyudh 2012; Orhan 2008, 2010; Lula 2009. Pulpo-periodontal complications at the end of treatment follow-up: Mello 2018; Franzon 2014, 2015; Phonghanyudh 2012; Orhan 2008, 2010; Lula 2009; Ribeiro 1999. Subsequent restorative failures: Franzon 2014, 2015; Phonghanyudh 2012; Ribeiro 1999. Pulp exposure in stepwise caries removal and complete caries removal: Orhan 2008, 2010; Magnusson 1977. Pulp exposure in selective caries removal and stepwise caries removal: Elhennawy 2018; Orhan 2008, 2010.
Results/findings	<i>Selective caries removal and complete caries removal</i> During clinical protocol, the pulp exposure risk was lower for selective caries removal (OR: 0.11; 95% CI: 0.04–0.27; I²: 0%; 560 participants; 5 trials) compared with complete caries removal. The corresponding pooled OR was unchanged when one or both of the two types of selective caries removal groups (selective caries removal or selective caries removal only at enamel dentine junction) were included in the meta-analysis. At the end of the treatment follow-up, pulpo-periodontal complications (clinical and/or radiographic failures) were similar in the selective caries removal and complete caries removal groups as demonstrated in the intention-to-treat (OR: 0.57; 95% CI: 0.23–1.41; I²: 0%; 503 participants; 6 trials) and per-protocol meta-analyses (OR: 0.55; 95% CI: 0.22–1.37; I²: 0%; 459 participants; 6 trials). The corresponding pooled OR in intention-to-treat analysis meta-analysis was unchanged when one or both selective caries removal groups (selective caries removal, selective caries removal only at enamel dentine junction) were included in the meta-analysis. When the authors stratified the trials by risk of bias for the outcome pulpo-periodontal complications, the pooled ORs were unchanged. Subsequent restorative failures were considered in three trials using the Frencken criteria or USPHS criteria. The intention-to-treat meta-analysis based on USPHS criteria for testing composite restorations demonstrated significantly higher restorative success for complete caries removal when compared with selective caries removal (OR: 2.61; 95% CI: 1.05–6.49; 124 participants; 1 trial). The intention-to-treat meta-analysis based on the Frencken criteria found no

Parameter	Extraction
	difference between selective caries removal compared with complete caries removal (OR: 1.60; 95% CI: 0.68–3.77; 184 participants; 1 trial). <i>Stepwise caries removal and complete caries removal</i> Two trials compared pulp exposure at the time of intervention in stepwise caries removal and complete caries removal. The odds of pulp exposure in the stepwise caries removal group was significantly lower (OR: 0.20; 95% CI: 0.09–0.44; I²: 26%; 173 participants; 2 trials) compared with pulp exposure in the complete caries removal group. The pulpo-periodontal complications (clinical and/or radiographic failures) did not differ significantly between the stepwise caries removal and complete caries removal groups using intention-to-treat analysis (OR: 0.47; 95% CI: 0.04–5.44; I²: 0%; 173 participants; 2 trials) or per-protocol analysis (OR: 0.41; 95% CI: 0.03–4.82; I²: 0%; 2 trials). <i>Selective caries removal and stepwise caries removal</i> Two trials compared pulp exposure in selective caries removal and stepwise caries removal at follow-up. There was no difference in the risk of pulp exposure in the selective caries removal and stepwise caries removal groups (OR: 0.44; 95% CI: 0.09–2.06; I²: 0%; 137 teeth; 2 trials). In addition, the risk of pulpal or periodontal complications (clinical and radiographic failures) in the selective caries removal and stepwise caries removal groups was not different using intention-to-treat (OR: 1.02; 95% CI: 0.14–7.40; I²: 0%; 137 teeth; 2 trials) and per-protocol analysis (OR: 1.00; 95% CI: 0.14–7.26; I²: 0%; 130 teeth; 2 trials). The authors stated that “This review alerts dentists to the low number of randomized clinical trials that compare the efficacy of caries removal techniques for deep carious lesions in vital temporary teeth and on the short follow-up time of these trials. • They should inform their patients on the low level of proof supporting a caries removal technique. • SCR [selective caries removal] and SWR [stepwise caries removal] may result in lower frequency of pulp exposure than CCR [complete caries removal].”^{90 (p393)}
Significance/direction	Results listed by outcome.
Heterogeneity	Heterogeneity was measured but not discussed. The meta-analysis computer outputs indicated low to moderate heterogeneity.
Comments	GRADE was not used by the review authors. The sample size for some outcomes was less than the desired 200. Most studies was judged to have a high or unclear risk of bias. Five (63%) of the eight studies were judged adequate for randomisation and six (75%) had adequate outcome assessment. The quality of the review was rated as moderate using AMSTAR 2 as heterogeneity was not discussed. The meta-analysis computer outputs indicated low to moderate heterogeneity. The HRB grades the quality of the evidence as moderate for some outcomes and low for others.

Pedrotti *et al.* (2019)

Parameter	Extraction
First author and year of publication	Pedrotti <i>et al.</i> (2019) ⁹¹
Objectives	Evaluated whether selective carious tissue removal of soft dentine from deep cavitated lesions in primary teeth increases the risk of experiencing restoration failure compared with complete carious tissue removal.
Participants	Primary dentition, cavitated caries, restoration technique The review included children with at least one deep cavitated lesion in their primary teeth. Participants ranged in age from 3 to 11 years. The number of participants per trial were 38, 44, 48, and 182. According to the authors, “All studies included occlusal and occlusoproximal cavities, and a range of materials (liners and restorative materials) had been used. In 2 studies, researchers performed the restorations with rubber dam isolation.”^{91 (p585)}
Setting/context	The four included studies were undertaken in Brazil (two studies), Scotland (one study), and Thailand (one study). The clinical settings were not reported.

Parameter	Extraction
Description of interventions/phenomena of interest	Intervention: Selective carious tissue removal of soft dentine Comparator: Complete carious tissue removal of soft dentine Pedrotti <i>et al.</i> described the intervention as follows: "Carious tissue removal ensures the conditions for a long-lasting restoration, preserves remineralizable tissue, maintains pulp vitality, and achieves an adequate seal. In deep lesions, selective carious tissue removal of soft dentin has been recommended to avoid pulp exposure and allow the placement of a durable restoration."⁹¹ (p582) The comparator was described as follows: "Complete carious tissue removal in acute deep carious lesions has been proven to increase the occurrence of pulpal exposure and postoperative pulpal symptoms compared with selective carious tissue removal. Consequently, more complex interventions such as pulpotomy or pulpectomy are needed, increasing the clinical chair time and treatment costs. Furthermore, pulpotomized primary teeth tend to exfoliate earlier than those that undergo selective carious tissue removal."⁹¹ (p582–583)
Databases and sources searched	The authors searched three databases: MEDLINE via PubMed; Scopus; and the Cochrane Central Register of Controlled Trials (CENTRAL). Studies published up to 8 December 2018 were considered. The authors searched the reference lists of retrieved studies for additional relevant papers. No publication year or language limits were placed on the search results. Only English-language studies were included in the final assessment. The authors did not report preparing a protocol. Extraction and screening were completed in duplicate. This study was financed in part by CAPES. None of the authors reported any conflicts of interest.
Date range (years) of included studies	The included studies were published in 1999, 2004, 2012, and 2015.
Number of primary studies included in the systematic review	Four randomised controlled trials (three parallel group trials and one split-mouth trial), published in 1999, 2004, 2012, and 2015, were included. The sources of funding of primary studies were not reported.
Types of studies included	Randomised controlled trials only were eligible for inclusion. A list of studies excluded at the full-text stage was not provided in the review. However, the reasons for exclusion were provided in a figure.
Country of origin of included studies	The four included studies were undertaken in Brazil (two studies), Scotland (one study), and Thailand (one study).
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	All four studies were rated as having a high risk of bias. One of the four studies was rated as having a low risk of bias for randomisation and two of the four studies were rated as having a low risk of bias for outcome assessment. The authors reported that "A statement regarding the randomization method was reported in all evaluated studies; however, the authors in 1 study did not describe the method used to generate the random sequence, leading to an unclear risk of bias. Moreover, most studies had an unclear risk of bias regarding the allocation concealment. All studies were classified as having a high risk of bias regarding the blinding of operators, because blinding is not possible when performing dental restorations. Two studies had an unclear risk of bias regarding the blinding of the examiner. Thus, the risk of bias was considered high. A low quality of evidence was judged according to the guidelines of the Grading of Recommendations, Assessment, Development, and Evaluations work group."⁹¹ (p585) The authors reported that "to reduce publication bias, we checked the ClinicalTrials.gov."p583 Publication bias was not measured or discussed.
Method of analysis	According to the authors, "We performed conventional meta-analyses using random-effects models in Review Manager Software Version 5.3. We calculated odds ratios (ORs) and 95% confidence intervals (CIs). Values lower than 1.0 indicate that the selective carious tissue removal technique has a lower risk of experiencing restoration failure than the complete carious tissue removal technique, and vice versa for values greater than 1.0. We performed intention-to-treat (ITT) analysis (analysis of participants as randomized regardless of whether they received the intervention or were available for follow-up) and per-protocol (PP) analysis (analysis of participants based on the intervention they received and their availability for follow-up) to account for possible bias introduced by attrition

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	and protocol deviations. For our ITT analysis, we assumed that all missing participants experienced an event. We assessed heterogeneity using both Cochran Q and I ² statistics. Owing to the low number of trials, we performed no further subgroup or meta-regression analysis. In 1 study, researchers performed selective carious tissue removal of soft dentin followed by restoration with glass ionomer cement or by lining with black copper cement and restoration. We excluded teeth restored with black copper cement from analyses, because black copper cement is not a usual cavity lining for incomplete caries removal, and there is no solid evidence for its recommendation.” ⁹¹ (p584–585)
Outcome assessed	The outcome assessed was restoration failure. The follow-up period ranged from 12 through 24 months, with dropout rates of 0% through 28.3%. Restoration failure: Ribeiro 1999; Foley 2004; Phonghanyudh 2012; Franzon 2015.
Results/findings	According to the authors, “We observed a significant difference in the risk of experiencing failure between complete and selective carious tissue removal of soft dentin approaches, with a lower risk of experiencing failure for restorations placed after complete carious tissue removal (intention-to-treat analysis, OR 1.74 [95% CI 1.01 to 3.00]; per-protocol analysis, OR 1.79 [95% CI 1.04 to 3.09]. The heterogeneity was low, regardless of the analysis performed (4% in the intention-to-treat analysis and 0% in the per-protocol analysis).”⁹¹ (p585) The authors reported that they “performed both intention-to-treat and per-protocol analyses. per-protocol analyses served as a sensitivity analysis to intention-to-treat analyses for checking the robustness of findings and impact of attrition. Irrespective of the analysis, restorations placed after selective carious tissue removal of soft dentin had a higher risk of experiencing failure than those performed after complete carious tissue removal. The heterogeneity was low.”⁹¹ (p587) In their concluding comments on the quality of the body of evidence, the authors stated that “The effect of the underlying quality of evidence on the findings must be emphasized. We assessed few studies and few restorations. The follow-up periods of the included studies were shorter than desired (12 or 24 months), which is a major shortcoming of the dataset. Differences in restoration failure rates between approaches could be greater with longer follow-up periods. However, primary teeth have lower longevity of restorations owing to exfoliation. Allocation concealment remained unclear in most of the studies. In addition, randomization and allocation always were performed before carious tissue excavation. Thus, the operator was aware of the allocation and consequently may have removed different amounts of carious tissue. Blinding of the examiner was also unclear in some studies.”⁹¹ (p589)
Significance/direction	Pedrotti <i>et al.</i> stated that “Selective carious tissue removal of soft dentin may increase the risk of experiencing restoration failure in primary teeth. Owing to the limited evidence level, well-designed and reported randomized trials are required before definitive conclusions can be drawn.” ⁹¹ (p589)
Heterogeneity	According to the authors, “We assessed heterogeneity using both Cochran Q and I ² statistics...The heterogeneity was low, regardless of the analysis performed (4% in the intention-to-treat analysis and 0% in the per-protodcol analysis).” ⁹¹ (p585)
Comments	GRADE was used to rate the quality of evidence. Outcome 1: Selective carious tissue removal versus complete carious tissue removal —: Odds ratio: 1.79 (95% CI: 1.04–3.09; number of participants: intervention group 205 versus control group 191) Certainty of evidence: Low Outcome 2: Selective carious tissue removal versus complete carious tissue removal —Odds ratio: 1.74 (95% CI: 1.01–3.00; number of participants: intervention group 225 versus control group 209) Certainty of evidence: Low According to the authors, “To the best of our knowledge, ours is the first systematic review and meta-analysis to update the scientific literature with an answer to the question of whether selective carious tissue removal of soft dentin jeopardizes the longevity of restorations placed in primary molars. We considered only restoration failure as an outcome.”⁹¹ (p586–587) The authors explained that “The outcome in the studies in our systematic review most likely was affected by several confounders that we could not evaluate owing

Parameter	Extraction
	to the paucity of data. The authors used different criteria for determining restoration failure. The authors adopted the Modified US Public Health Service criteria in 2 studies, used Frencken and colleagues' evaluation criteria in 1 study, and performed clinical evaluation without use of validated criteria in the other study. However, in all included studies, the authors considered relevant parameters related to outcome such as marginal integrity and restoration loss (partial or total). The authors of 1 study also considered other parameters such as marginal discoloration and anatomic form, which may have overestimated the restorative failures because these aspects may not be directly related to carious tissue removal techniques. The material used (composite resin or glass ionomer cement) for cavity restoration, as well as the use or non-use of lining material, also might have affected the outcome. Nevertheless, the same restorative material was used after both complete and selective carious tissue removal techniques. The material type (composite resin, glass ionomer cement, and calcium hydroxide) does affect the risk of experiencing failure of the indirect pulp treatment in primary molars. In addition, no definitive evidence supports 1 material as being more suitable than another for restoring teeth after selective carious tissue removal. Therefore, the choice of restorative material should be based on the extent of the carious lesions, caries risk, specific patient conditions, and setting." ⁹¹ (p588)

Aparecida Silva Martins *et al.* (2018)

Parameter	Extraction
First author and year of publication	Aparecida Silva Martins <i>et al.</i> (2018) ⁹²
Objectives	Evaluated the clinical evidence of partial caries removal in the primary dentition, regardless of liner and restorer materials, measuring the longevity of the restorative treatment and clinical and radiographic success.
Participants	Primary dentition, cavitated caries, restoration techniques. Population: Children's primary teeth with cavitated caries. Six clinical studies, published between 2004 and 2015, with 423 participants were included. The reference numbers do not correlate with the references so the dates are a best guess. If the references that the Health Research Board (HRB) selected are correct, all the studies were randomised clinical trials. The age range was 3–11 years and gender was not reported. The longest follow-up periods were 12–24 months.
Setting/context	The study settings and countries were not reported.
Description of interventions/phenomena of interest	Partial caries removal. No comparator, only intervention side of trial used.
Databases and sources searched	The searched databases and grey literature were: PubMed, Embase, the Cochrane Library, Scielo, Brazilian Library in Dentistry (BBO), and Latin American and Caribbean Health Sciences Literature database (LILACS). Two keywords were provided. There was no language restriction or time limitation, and the search was conducted up to February 2016. The preparation of a protocol was not reported. Two researchers independently screened titles and abstracts for primary selection and extracted the data. Sources of funding or conflicts of interest were not reported.
Date range (years) of included studies	Six clinical studies published between 2004 and 2015 were included.
Number of primary studies included in the systematic review	Six clinical studies, published between 2004 and 2015, with 423 participants were included. The reference numbers do not correlate with the references so the dates are a best guess. If the references that the HRB selected are correct, all the studies were randomised clinical trials. The references that the HRB thinks were included are: Casagrande 2013 (36); Foley 2004 (39); Franzon 2014 (9); Franzon 2015 (38); Hesse 2014 (22); Phonghanyudh 2012 (37). The funding sources for the primary studies were not reported.
Types of studies included	Clinical studies evaluating longevity of partial caries removal. The study designs are unclear. The list of excluded studies was reported but not the reasons for exclusion.

Parameter	Extraction
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's tool for assessing risk of bias in clinical trials was used.
Appraisal rating	Four studies were classified as having an unclear risk of bias and two as having a low risk of bias. Five studies had adequate randomisation and four had adequate blinding of outcome assessment.
Method of analysis	The results were evaluated by means of percentage of the longevity of restorations and clinical and radiographic success of partial caries removal. A meta-analysis was not possible, as these studies had no comparator data, so a narrative analysis was completed.
Outcome assessed	Clinical and radiographic success rates and the longevity. The longest follow-up periods were 12–24 months. The references that the HRB thinks were included are: Casagrande 2013; Foley 2004; Franzon 2014; Franzon 2015; Hesse 2014; Phonghanyudh 2012.
Results/findings	Narrative synthesis of the six trials indicated that partial carious removal had high clinical and radiographic success rates and the longevity of the associated restorations was satisfactory. The longevity of restorations in primary molars preceded by partial caries removal compared with restorations preceded by total caries removal was not statistically significantly different. However, a reduced longevity in primary molar restorations preceded by partial caries removal was observed in one of the five trials. Clinical and radiographic evaluations showed similar results for dentine partial removal techniques (conventional restoration and atraumatic restorative treatment) when compared with partial caries removal, which was very good with success in all teeth where partial caries removal was carried out.
Significance/direction	Results listed by outcome.
Heterogeneity	A narrative analysis was completed, so heterogeneity was not measured.
Comments	GRADE was not used by the review authors. The studies are described as clinical studies. The sample size for each outcome is not provided. Four of six studies were classified as having an unclear risk of bias. Five (83%) studies had adequate randomisation and four (67%) had adequate blinding of outcome assessment. The quality of the review was rated as low using AMSTAR 2 as the authors did not measure or discuss heterogeneity. A meta-analysis was not possible, as these studies had no comparator data, so a narrative analysis was completed. The HRB grades the quality of the evidence as low quality for each outcome.

Deng *et al.* (2018)

Parameter	Extraction
First author and year of publication	Deng <i>et al.</i> (2018)⁹³
Objectives	'Compared the efficiency (operation time, bacterial count, restoration survival) and efficacy (acceptability and preference) of chemomechanical caries removal (Papacarie) in primary molar caries in children and adolescents with the conventional drilling method (controls).'
Participants	Primary dentition, cavitated caries, restoration technique In total, 438 adolescent and child patients with 1033 primary molar caries were included. The participants age ranged from 3 years to 12 years. Only human studies were included without gender restriction, although details on the proportion of males and females were not reported. Children without behavioural or psychological problems and who do not receive sedatives before treatment or any related agents for procedural sedation were included in this study.
Setting/context	The included studies were conducted in Brazil (three studies), Egypt (two studies), and India (eight studies). The clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: Patients undergoing chemomechanical caries removal (Papacarie) Comparator: Conventional caries removal method in the primary molar teeth. According to Deng <i>et al.</i> , 'Recently, in 2003, Papacarie was released as a proteolytic gel. The collagen degradation features of papain and the bactericide

Parameter	Extraction
	characteristics of chloramines were added to the new medicine. Papain makes the carious dentine softer through the interaction with exposed collagen and then dissolves the decayed tissues, which allows the removal of carious dentine without local anaesthesia and drilling...Adopting the Papacarie method in caries removal, clinicians can remove all of the carious dentine and protect the sound dentine without a special instrument. Most children are satisfied with this method, according to research on their preferred method, conventional drill or Papacarie.”⁹³ (p362) The authors described the comparator as follows: “Conventional caries removal method usually means digging and drilling by rotation handpiece to remove the decayed tissue, which is efficient in removing the bacterial dentine but is perceived as uncomfortable, uneasy, and painful by children. Because the conventional caries removal method may extend into the sound dentine, it is therefore to open more dentinal tubules. This effect is usually prone to bringing pain and tension. And the use of local anaesthesia is necessary during treatment.”⁹³ (p361)
Databases and sources searched	The authors searched seven databases – PubMed, Embase, the Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials (CENTRAL), Ovid, Google Scholar, and Web of Science – up to 20 January 2018. The language or date of publication were not limited for the search. The authors also searched the reference lists of all included studies for additional primary studies. Where additional data and figures for some literature were needed, the review authors contacted the authors of the primary studies. The authors did not report preparing or publishing a protocol. Extraction and screening were completed in duplicate. This study was funded by the Program for Innovation Team Building at Institutions of Higher Education in Chongqing in 2016. The authors declared no conflict of interest.
Date range (years) of included studies	The included trials were published from 2009 to 2016.
Number of primary studies included in the systematic review	The number of studies included varied in different sections of the paper. The authors reported that they included 15 studies in their flowchart. The reported the characteristics of 13 studies published between 2009 and 2016 in their table: 10 randomised controlled trials and 3 prospective controlled clinical trials. The assessed the risk of bias on 14 studies in the text and 13 in the table and they included 10 studies in their meta-analysis. At some stage, three studies were excluded because they did not provide mean and standard deviation data, and three studies reported the same experiment, so the HRB assume two of these three studies were excluded. The summary reports that six randomised controlled trials and four controlled clinical trials were included. However the summary table has only three prospective controlled clinical trials The authors stated that, “Among the trials included in this review, three articles reported the same experiment; therefore, they were combined...Different regimens of the Papacarie method were identified in the included articles. The type, generation, and dose of the medicine are different. Among the included studies, five trials discussed the change in bacteria in the caries lesion, and two trials were excluded in the meta-analysis for a lack of mean and SD [standard deviation] data. In addition, 10 trials assessed the outcomes of pain perception before and after different caries removal methods; nevertheless, the scales used in these trials differ considerably. Only three trials used the Wong-Baker-Face Pain Scale to evaluate pain perception and remained eligible. And seven trials with complete mean and SD data of time consumption were included in the meta-analysis.”⁹³ (p364) The sources of funding for primary studies were not provided.
Types of studies included	Randomised controlled trials and prospective controlled clinical trials were reviewed, included, and analysed accordingly. A list of excluded studies with their reasons for exclusion were not provided.
Country of origin of included studies	The primary studies were conducted in Brazil, Egypt, and India.

Parameter	Extraction
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	Eight (62%) of the 13 papers assessed were judged to be at a low risk of bias and 5 were judged to be at an unclear risk of bias. Ten (77%) of the 13 included papers were at low risk of bias for randomisation, and 11 (85%) were at low risk of bias for outcome assessment. The authors reported that unclear risk of bias affected the reliability of some outcomes and they did their utmost to exclude biased studies prior to meta-analyses. The authors reported that "Second, the power of formal tests was limited in this meta-analysis due to the lack of a long-term follow-up of the restorations, which indicates meaning that potential publication bias might have influenced our findings."⁹³ (p370)
Method of analysis	According to Deng <i>et al.</i>, The multiple studies were combined by and were assessed using "the weighted mean difference, standard deviation, and its 95% confidence intervals (CIs) of the outcome variable (the CFU [colony-forming units] of bacteria, scores of pain scale, and treatment time) were assessed. Statistical heterogeneity was explored using the chi-squared test with a 10% level of significance as the cut-off value. The I^2 statistic was used to quantify the impact of statistical heterogeneity. And a 95% confidence interval of I^2 is reported in addition to its point estimate percentage. If $I^2 > 50\%$ ($p \leq 0.10$), it will be taken to mean high heterogeneity. Then, the heterogeneity needs to be explained, and a random-effects model was used, otherwise, the fixed-effects model would be chosen. The hypothesis of homogeneity was set invalid for $p < 0.05$ (2-tailed z-tests). If the data were unable to be pooled, they were described".⁹³ (p363–364)
Outcome assessed	The outcomes assessed were: survival rate (number of restorative failures based on clinical criteria, such as FDI and USPHS), reduction of the cariogenic microbiota, pain perception, time taken for caries removal, patient preference or acceptability, and follow-up. Survival rate, reduction of the cariogenic microbiota, pain perception, time taken for caries removal, patient preference or acceptability, and follow-up: Ammari 2014; Aneundi 2012; Goyal 2015; Gulsheen 2011; Kotb 2009; Magda 2011; Mariya 2012; Maru 2014; Mastumoto 2013; Motta 2013; Motta 2014; Sanjeet 2011; Sapna 2016; Swati 2015. The data collection times included immediately after the caries removal treatment and 1, 6 and 18 months later.
Results/findings	Efficacy of Papacarie treatment in reducing the cariogenic microbiota According to the authors, "Five trials reported the outcome for reducing bacteria. Three of these have a data deficiency or differed in the bacteria measurement method. As a result, these trials are excluded from the meta-analysis. Two studies with a detailed mean and SD [standard deviation] data of log10 colony-forming units (CFUs) were adopted to be used for a meta-analysis and the forest plot was demonstrated in [a figure]. In sum, 90 patients contributed to this outcome. It was observed that the microbiota in carious dentine was significantly reduced using the Papacarie treatment (MD [mean difference]=0.57, 95% CI: 0.04 to 1.09, $p=0.03$), compared with the conventional drilling method, with low heterogeneity detected (chi-square=2.00, $p=0.37$, $I^2=0\%$, 95% CI: 0%–98%)."⁹³ (p364) Pain perception The authors stated that "Ten studies discussed the pain perception when caries in the primary teeth were treated. Means and SD [standard deviation] data of Wong-Baker-Face Pain Scale scores, however, were provided by three studies for meta-analysis. The forest plots were displayed. Although the Wong-Baker-Face Pain Scale score is a subjective measurement, it is a relatively easy and convenient way to record the feeling of child patients when they had been treated. It was observed that pain scores evaluated before and after caries removal were reduced in both the Papacarie and conventional method. Because $I^2=86\%$ (95% CI: 60%–95%) showed high degrees of heterogeneity between studies, a random-effects model was adopted. When comparing the two groups, the anxiety feeling declined more in the Papacarie group (MD=1.01, 95% CI: 1.72 to 0.30, $p<0.005$)."⁹³ (p364–365)

Parameter	Extraction
	Time taken for caries removal Deng <i>et al.</i> reported that eight studies measured “the outcomes of the treatment time. Nevertheless, only seven were eligible for the meta-analysis. The forest plot was described in [a figure]. There was a greater, that is, 200.79 (MD=200.79, 95% CI: 152.50 to 249.09, $p<0.00001$) increase in time taken for the Papacarie treatment compared with the conventional method. The results of the time taken had a high heterogeneity (chi-square=128.89, $p<0.00001$, $I^2=95\%$, 95% CI: 93%–97%) as the different studies’ may lack of consistency regarding the measurement and analysis of the time. Therefore, we chose the random-effects model to describe the outcomes.”⁹³ (p366–367) Patient acceptability According to Deng <i>et al.</i>, “The preference of the different caries removal methods was evaluated in three studies. One study recorded the preference of the conventional method and Papacarie, in which the Papacarie group had a higher proportion of 60% compared with 36.7% for the conventional method. In one study, a majority (80%) of the children in the study preferred the Papacarie method. In addition, one study compared the conventional method, Carisolv, and Papacarie for patient acceptability through a visual analogue scale. In this latter study, the patient acceptance rate was observed to be higher for the Papacarie method. These results can be explained by the fact that less pain and anxiety were experienced in patients with the Papacarie method. This finding is in accordance with the results of pain perception [measured using the] Wong-Baker-Face Pain Scale.”⁹³ (p367) Follow-up The authors reported that, “According to all of the included studies, only two studies reported the long-term follow-up of the Papacarie method. One study recorded the retention of the filling material and the incidence of secondary caries 1 month later, and the use of a different caries removal method was analysed. In addition, the restoration was predominantly present and without defects following both procedures. In the other study, the participants received regular clinical follow-up of the caries treatment. The density of the remaining dentin was assessed through radiographic examination. The recorded time includes immediately after the caries removal treatment and one (T1), six (T2), and 18 (T3) months later. In both groups, the mean radiographic density was improved after treatment in different evaluation times, and no secondary decay was observed in the two groups.”⁹³ (p367)
Significance/direction	The results listed by outcome above.
Heterogeneity	The authors discussed the substantial statistical heterogeneity for two outcomes (pain and treatment time), but were unable to do any subgroup analysis to reduce its effects.
Comments	GRADE was not used by the review authors.

Restoration material and technique combined

Tedesco *et al.* (2018)

Parameter	Extraction
First author and year of publication	Tedesco <i>et al.</i> (2018) ⁹⁴
Objectives	Undertook a review to determine the best treatment for dentine carious lesion arrestment and the success rate of different treatments of the dentine carious lesions of primary teeth. The purpose of the review was to bridge a gap in the evidence by considering whether lesions of different depths and the number of surfaces involved affect treatment outcomes. According to Tedesco <i>et al.</i> , the absence of this evidence “makes recommending the best treatment for dentine carious lesions with different levels of progression challenging”. ⁹⁴ p2
Participants	Primary dentition, cavitated caries, non-invasive, minimally invasive, and invasive treatments. Population: Children’s primary teeth. Fourteen randomised controlled trials and one non-randomised observational study published between 2002 and 2016 were included in this review. There were 3,226 participants in the 14

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	studies that reported the sample size. The number of teeth treated was not reported. Participants in the trials were aged 2–10 years. Gender was not reported.
Setting/context	The settings for the studies were divided almost equally between a school-based programme (7) and a dental clinic or group of dental clinics (8). The studies were completed in Brazil, China, Germany, Indonesia, Kuwait, South Africa, Syria, Turkey, and the UK.
Description of interventions/phenomena of interest	Two different types of restorative procedures were considered in this review. According to Tedesco <i>et al.</i> , “Atraumatic restorative treatment (ART) was considered as a restorative procedure that included caries removal using only hand instruments and restoration with high-viscous glass ionomer cement without the use of a rubber dam. Alternatively, conventional restorative technique was considered as including caries removal using rotary instruments and restoration with any restorative material, including the use of a rubber dam. Thus, studies reporting treatment procedures that differed from those definitions were not included in the present review”. ⁹⁴ (p3–4) The types of restorative materials and restorative treatments that were studied in the trials in Tedesco <i>et al.</i> ’s review included: stainless steel crown; non-restorative caries treatment; ultraconservative treatment; the Hall technique; interim restorative treatment; silver diamine fluoride; sodium fluoride; resin sealant; low-viscosity glass ionomer cement; high-viscosity glass ionomer cement; resin-modified glass ionomer cement; resin composite; and amalgam. Comparator: Rotary drill with restorative materials, compared with atraumatic restorative treatment with restorative materials; and non-invasive treatments, compared with atraumatic restorative treatment with restorative materials. The techniques and materials were also compared with each other and with no intervention.
Databases and sources searched	Three electronic databases – MEDLINE/PubMed, Web of Science, and Scopus – were searched. The grey literature (OpenSIGLE/OpenGrey) and the reference lists of identified full texts were also searched to retrieve additional relevant studies that might fulfil the inclusion criteria. No restriction was placed on the language or year of publication. The last search was performed on 14 December 2017. The authors provide keywords and search terms. A search strategy was developed for the MEDLINE/PubMed database and then adapted for the others based on the research question. A protocol was registered with PROSPERO. The titles and abstracts and, subsequently, full texts of the potentially eligible studies identified using the databases, were evaluated by two independent reviewers. One of the reviewers extracted the required information from full-text eligible studies, and a second reviewer independently verified the data extracted. Funding was provided by Fundação de Amparo à Pesquisa do Estado de São Paulo to two authors. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The authors declared that no competing interests exist.
Date range (years) of included studies	Fourteen randomised controlled trials and one non-randomised observational study published between 2002 and 2016 were included in this review.
Number of primary studies included in the systematic review	Fourteen randomised controlled trials and one non-randomised observational study published between 2002 and 2016 were included in this review. The sources of funding for primary studies were not reported.
Types of studies included	Fourteen randomised controlled trials and one non-randomised observational study published between 2002 and 2016 were included in this review. The manuscripts excluded at the full-text screening stage and their main reason for exclusion were in a supplementary table.
Country of origin of included studies	The studies were completed in Brazil, China, Germany, Indonesia, Kuwait, South Africa, Syria, Turkey, and the UK.
Appraisal instruments used	The risk of bias in the included primary studies was evaluated using the Cochrane Collaboration’s risk of bias instrument on the 14 randomised trials, and using the Risk Of Bias In Non-Randomized Studies – of Interventions (ROBINS-I) instrument on the non-randomised observational study.
Appraisal rating	Six of the randomised controlled trials were judged to have a high risk of bias and eight of the trials had an unclear risk of bias. The observational study scored low (considered positive) for four of eight parameters, unclear for three, and high for one. Many of the studies did not provide most of the information required for assessment of bias. All 14 randomised controlled trials were judged adequate for randomisation and 4 were judged adequate for blinding of outcome ascertainment. The observational study scored positively for control of confounding and negatively for loss to follow-up. Adequacy of sample size was not measured. According to Tedesco <i>et al.</i> , “The risk of bias analysis performed on the clinical trials showed that all studies received more unclear scores because of the uncertainty regarding potential bias in the

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	studies, especially those related to allocation concealment, incomplete outcome data, and baseline imbalances given that we were unable to identify this information".⁹⁴ (p16) The authors report that "publication bias was not considered because of the small number of studies included in each analysis".⁹⁴ (p11)
Method of analysis	Direct evidence was computed using a random-effects model meta-analysis in which two treatments (experimental treatment [sealing] compared with control treatment [conventional restorative treatment with resin composite]) were evaluated for the same level of carious lesion progression. Heterogeneity was evaluated using the I² inconsistency index. Otherwise, when more than two treatments were considered across different studies with regard to the same depth or surface involved, a network meta-analysis was conducted that synthesised direct and indirect comparisons in order to strengthen the evidence. Indirect comparisons were performed to simultaneously consider both direct and indirect evidence, Tedesco <i>et al.</i> performed a Bayesian mixed-treatment comparison. Because all the treatment options were performed on similar groups of patients, this network meets the transitivity assumption. First, the authors conducted mixed-treatment comparison analyses using fixed- and random-effects models. The 'goodness of fit' of the models was measured using the residual deviance and deviance information criteria. Because the deviance information criteria value of the random-effects model was lower, the authors used a mixed-treatment comparison random-effects model with homogeneous between-trial variability. A node split analysis for inconsistency was not performed because of the insufficient amount of data. The network meta-analysis and meta-analysis were conducted using the R statistical package. For each included study, the risk ratio and 95% CIs were calculated. Studies with multiple arms need specific care in order to avoid double counting; one of the possible approaches is to perform a mixed-treatment comparison, allowing each of two groups to be compared indirectly through comparisons with the third. The Becker-Balagtas method was used to calculate log relative risks to accommodate data pooling from split-mouth (cluster) and parallel group studies in a single meta-analysis and facilitate data synthesis.
Outcome assessed	Outcome: Carious lesion arrestment, and success rate Time frame: At least 12 months of treatment follow-up Outcome by primary study: Success rate of restorative treatments in outer half of dentine on occlusal surface-resin sealing compared with conventional restorative treatment with resin composite: Borges <i>et al.</i>, 2012; Hesse <i>et al.</i>, 2014. Caries arrest as a result of restorative treatments in outer half of dentine on occlusal surface-resin sealing compared with conventional restorative treatment with resin composite: Borges <i>et al.</i>, 2012; Hesse <i>et al.</i>, 2014. Success rates for restoration of occlusal surfaces: Louw <i>et al.</i>, 2002; Taifour <i>et al.</i>, 2002; Honkala <i>et al.</i> 2003; Yu <i>et al.</i>, 2004; Ersin <i>et al.</i>, 2006. Success rates for occlusoproximal surfaces: Louw <i>et al.</i>, 2002; Taifour <i>et al.</i>, 2002; Honkala <i>et al.</i> 2003; Yu <i>et al.</i>, 2004; van den Dungen <i>et al.</i>, 2004; Roberts <i>et al.</i>, 2005 (observational study); Ersin <i>et al.</i>, 2006; Mijan <i>et al.</i>, 2014; Santamaria <i>et al.</i>, 2014. Caries arrestment assessment of the occlusal and smooth surfaces: Santos <i>et al.</i>, 2012; Zhi <i>et al.</i>, 2012; Duangthip <i>et al.</i>, 2016.
Results/findings	Thirteen of the 15 studies reported data suitable for meta-analysis or network meta-analysis. Network meta-analyses and pairwise meta-analyses were conducted considering the two outcomes according to the surface involved and the depth of progression. The data were synthesised across studies that evaluated dentine carious lesions in the outer half of the dentine on the occlusal surface. A pairwise meta-analysis was performed where only two restorative treatments were considered and a network meta-analysis was done where three or more treatments were considered. Resin composite restoration had a higher success rate than resin sealant (relative risk: 1.20; 95% CI: 1.06–1.37; I²: 33%; 156 participants; 2 trials; low-quality evidence). However, when caries arrest was considered as the primary outcome, no difference was observed between the restorative treatments (relative risk: 1.02; 95% CI: 0.96–1.08; I²: 0%; 156 participants; 2 trials; low-quality evidence). Heterogeneity was not observed in the studies in the two meta-analyses. For the studies that considered only the occlusal surface without information about the depth of progression, a network meta-analysis was conducted, and six studies that considered six treatment options were included. The primary outcome was a comparison of success rates, and the results are in the table below; no mixed-treatment comparisons were statistically significantly better than their comparators. Heterogeneity was observed among the included studies. The rank probability showed that the best clinical results for occlusal surfaces are expected using conventional

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	restorative treatment with composite resin or conventional restorative treatment with compomer. After that, the ranking was: (2) atraumatic restorative treatment, (3) conventional restorative treatment with high-viscous glass ionomer cement, (4) conventional restorative treatment with amalgam, and (5) conventional restorative treatment with resin composite. These outcomes were assigned low-quality evidence due to high risk of bias in primary studies.	
	Comparison	Mixed-treatment comparison: relative risk 95% credible intervals Inconsistency (heterogeneity)
	Atraumatic restorative treatment by conventional restorative treatment with amalgam	1.0 (0.87–1.1) 74.8% (42.9–88.9%)
	Atraumatic restorative treatment by conventional restorative treatment with compomer	0.97 (0.79–1.2) No data
	Atraumatic restorative treatment by conventional restorative treatment with high-viscosity glass ionomer cement	1.0 (0.89–1.1) 0.0% (0.0–74.8%)
	Atraumatic restorative treatment by conventional restorative treatment with resin composite	0.99 (0.85–1.1) 39.2% (0.0–81.2%)
	Conventional restorative treatment with amalgam by conventional restorative treatment with high-viscosity glass ionomer cement	1.0 (0.89–1.2) 68.8% (0.0–90.9%)
	Conventional restorative treatment with compomer by conventional restorative treatment with high-viscosity glass ionomer cement	1.0 (0.84–1.3) No data
	Seven studies were considered for the analysis that considered dentine carious lesions on occlusoproximal surfaces, without information about the depth of progression, and eight possible treatments were evaluated. The primary outcome of this comparison was a comparison of success rates, and the results are presented in the table below. The Hall technique, compared with non-restorative caries treatment, had a statistically significantly higher success rate. No other mixed-treatment comparisons were statistically significantly better than their comparators in this analysis. Heterogeneity was observed among the included studies. The rank probability showed that the best result for occlusoproximal cavities is the Hall technique for applying a stainless steel crown. After that, the final ranking was: (2) non-restorative caries treatment, (3) conventional restorative treatment using compomer, (4) conventional restorative treatment using high-viscous glass ionomer cement, (5) conventional restorative treatment using resin composite, (6) atraumatic restorative treatment, (7) conventional restorative treatment using amalgam, and (8) ultraconservative treatment. These outcomes were assigned low-quality evidence due to high risk of bias in primary studies. The HRB down graded the evidence grade to low due to the inclusion of an observational study in the meta-analysis.	
	Comparison (only selected those with data)	Mixed-treatment comparison: relative risk 95% credible intervals Inconsistency (heterogeneity)
	Atraumatic restorative treatment by conventional	1.0 (0.98–1.0) 68.0% (32.9–84.8%)

Parameter	Extraction	
	restorative treatment with amalgam	
	Atraumatic restorative treatment by conventional restorative treatment with compomer	0.89 (0.77–1.0) No data
	Atraumatic restorative treatment by conventional restorative treatment with high-viscosity glass ionomer cement	0.86 (0.77–0.96) 0.0% (0.0–76.8%)
	Atraumatic restorative treatment by conventional restorative treatment with resin composite	0.99 (0.93–1.0) 0.0% (0.0–0.0%)
	Atraumatic restorative treatment by ultraconservative treatment	1.0 (0.98–1.1) 88.4% (75.6–94.5%)
	Conventional restorative treatment with amalgam by ultraconservative treatment	1.0 (0.97–1.0) 79.9% (52.7–91.5%)
	Conventional restorative treatment with compomer by conventional restorative treatment with high-viscosity glass ionomer cement	0.97 (0.82–1.1) No data
	Conventional restorative treatment with compomer by Hall technique	0.74 (0.60–0.88) No data
	Conventional restorative treatment with compomer by non-restorative caries treatment	0.96 (0.76–1.2) No data
	Hall technique by non-restorative caries treatment	1.3 (1.1–1.6) No data

Finally, three studies evaluated caries arrest on occlusal and smooth surfaces of primary teeth, considering five possible treatment options. The primary outcome of this comparison was caries arrest and the results are presented in the table below. Three mixed-treatment comparisons were statistically significantly better than their comparators: silver diamine fluoride (two applications per year) compared with silver diamine fluoride 1 (one application per year), low-viscosity glass ionomer cement compared with silver diamine fluoride 2 (two applications per year), and interim restorative treatment compared with silver diamine fluoride (one application per year). Low heterogeneity was observed among the included studies. The rank probability showed that the best performance for this type of dentine carious lesion was two annual applications of silver diamine fluoride, and this was significantly better than other silver diamine fluoride treatment frequencies. After that, the final ranking was: (2) low-viscosity glass ionomer cement, (3) one annual application of silver diamine fluoride, (4) three applications per year of silver diamine fluoride, (5) three applications per year of sodium fluoride, and (6) interim restorative treatment. This outcome was assigned a moderate level of evidence by the review authors due to high risk of bias in primary studies. The HRB graded the quality of evidence as low (see comments below).

Comparison (only selected those with data)	Mixed-treatment comparison: relative risk 95% credible intervals	Inconsistency (heterogeneity) No ranges provided

Parameter	Extraction		
	Silver diamine fluoride 1 by silver diamine fluoride 2	0.39 (0.22–0.71)	13%
	Silver diamine fluoride 1 by silver diamine fluoride 3	1.22 (0.92–1.60)	13%
	Silver diamine fluoride 2 by silver diamine fluoride 3 (3 applications per year)	1.69 (0.96–1.80)	No data
	Sodium fluoride 3 by silver diamine fluoride 1	1.77 (1.35–2.32)	13%
	Sodium fluoride 3 by silver diamine fluoride 3	1.46 (1.10–1.92)	No data
	Low-viscosity glass ionomer cement by silver diamine fluoride 1	0.86 (0.52–1.42)	13%
	Low-viscosity glass ionomer cement by silver diamine fluoride 2	2.20 (1.23–3.92)	No data
	Interim restorative treatment by silver diamine fluoride 1	3.22 (2.04–5.08)	13%
	Tedesco <i>et al.</i> (2018) state that “the treatment of dentine carious lesions in primary teeth depends on the progression depth and surface involved. However, few studies exist, and most have a high risk of bias to provide enough evidence to strongly recommend the best treatment option”. ⁹⁴ (p16)		
Significance/direction	Results listed by outcome.		
Heterogeneity	Inconsistency or heterogeneity varied across outcome analyses from low to substantial.		
Comments	GRADE was used by the review authors. The review included both randomised trials and observational cohort studies, and both types of trials were included in one meta-analysis. The sample sizes for some outcomes were less than 200. All 14 trials were judged to have a high or unclear risk of bias. The observational study scored low (considered positive) for four of eight parameters, unclear for three, and high for one. All 14 randomised controlled trials were judged adequate for randomisation and 4 (29%) were judged adequate for blinding of outcome ascertainment. The observational study scored positively for control of confounding and negatively for loss to follow-up. The quality of the review was rated as critically low using AMSTAR 2 as the authors included randomised and observational studies in one meta-analysis and were unable to control for high or unclear risk of bias in any meta-analyses. The HRB grades the quality of the evidence as very low for the different outcomes.		

Appendix H: Data extraction for studies on permanent dentition

Non-cavitated caries

Non-invasive treatment

Oliveira *et al.* (2018)

Parameter	Extraction
First author and year of publication	Oliveira <i>et al.</i> (2018) ⁸⁷
Objectives	Assessed the effect of professionally applied silver diamine fluoride (SDF) compared with no, placebo, or other active intervention in preventing and arresting caries in exposed root surfaces of adults.
Participants	Permanent dentition, non-cavitated caries, non-invasive treatment Adults of any age with exposed root surfaces were included in the review. Included four articles from three trials in which the investigators randomly assigned 895 older adults and analysed data for 544, 712, and 460 participants at 12, 24, and 30 or more months of follow-up, respectively. These participants had similar mean age (72.1-78.8 years) and low caries experience (that is, mean number of decayed and filled root surfaces at baseline ranging from 1.1-2.1) and consumed fluoridated water (0.5 parts per million).
Setting/context	The three trials were completed in China. The clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: Topical silver diamine fluoride solution (any concentration or frequency) applied by any health care worker in any setting Comparisons: No intervention, placebo, or any cariostatic agent or dental restorative material Oliveira <i>et al.</i> described the intervention as: “Silver diamine fluoride (SDF) is an alkaline topical solution containing fluoride and silver that clinicians mainly have used for caries treatment in young children. Besides reducing the growth of cariogenic bacteria and promoting the remineralization of the inorganic content of enamel and dentin, SDF prevents collagen degradation in dentin by inhibiting the activity of collagenases and cysteine cathepsins. SDF is also known for its ability to desensitize hypersensitive teeth” ⁹⁵ (p671-72) Investigators conducted all included trials in Hong Kong, used 38% silver diamine fluoride solution, and compared it with a placebo
Databases and sources searched	Cochrane Central Register of Controlled Trials, Embase, MEDLINE via PubMed, Scopus, Web of Science, Latin American and Caribbean Health Sciences Literature, Biblioteca Brasileira de Odontologia, Scielo were searched without language or date of publication restrictions to identify relevant literature. Electronic searches undertaken in April 2016 and all searches were updated in July 2017. In addition, the authors searched five registries of ongoing trials; ClinicalTrials.gov, Brazilian Clinical Trials Registry, European Union Clinical Trials Register, International Standard Randomised Controlled Trial Number Registry and Current Controlled Trials, and Australian New Zealand Clinical Trials Registry and the CAPES database. Used cross-referencing from narrative reviews about SDF for caries prevention or arrest to identify additional articles. The authors prepared and registered a protocol with PROSPERO. Extraction and screening were completed in duplicate. The review was partially funded by the National Institute On Minority Health and Health Disparities of the National Institutes of Health, and partially funded through a Patient-Centered Outcomes Research Institute (PCORI) Award. None of the authors reported any disclosures.
Date range (years) of included studies	The studies were published in 2010, 2013, and 2017.
Number of primary studies included in the systematic review	Three randomised controlled trials were published in four papers. The sources of funding for primary studies were not reported.
Types of studies included	Randomised controlled trials were the only study design eligible for inclusion.
Country of origin of included studies	The three trials were completed in China. A list of full-text excluded studies was not provided although reasons for exclusion were provided.

Parameter	Extraction
Appraisal instruments used	The Cochrane risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	Number of studies by high risk of bias, medium and low Oliveira <i>et al.</i> reported "One trial had all domains, except for allocation concealment, with low risk of bias. The other 2 trials had 6 domains with low risk of bias and 2 domains with unclear risk of bias".^{95 (p673)} All three trials were at unclear risk of bias All three trials was at low risk of bias for randomisation. All three trials were at low risk of bias for blinding of outcome assessment The risk of bias limited the evidence. Publication bias was not measured or discussed.
Method of analysis	The primary effect measures were the weighted mean differences in decayed or filled root surfaces and the mean differences in arrested carious lesions between silver diamine fluoride and control group. The authors reported "Because the estimate of between-study variance under the random-effects model has poor precision when the number of studies is small, we used the fixed-effects model to obtain pooled estimates of caries increment as weighted mean differences (WMDs) or PFs [prevented fractions] when combining the studies. We assessed study heterogeneity by using the chi-squared test for heterogeneity and the Higgins index (I^2). We grouped the studies in our meta-analyses according to the duration of their follow-up: 12, 24, or 30 months or more. We could not pool the difference in caries increments regarding the comparisons between SDF [silver diamine fluoride] and other active treatments (that is, CHX [chlorhexidine] varnish and FV [fluoride varnish]) because there was only 1 study for each comparison. When there was more than 1 SDF intervention group per study, we combined them into a single group. We performed all analyses by using software (Stata 14) and followed the procedures described in the Cochrane Handbook for Systematic Reviews of Interventions."^{95 (p673)}
Outcome assessed	Survival rate (number of restorative failures based on clinical criteria such as FDI and USPHS). The primary outcomes were the development of new carious lesions and the arrest of existing carious lesions in exposed root surfaces of permanent teeth 12 months following product application (for example, 12, 24, or 30 months or more of follow-up). The secondary outcome measures were any self-reported, caregiver-reported, or professionally diagnosed adverse events. Preventing and arresting caries: Tan 2010; Zhang 2013; Li 2017. Duration of their follow-up: 12, 24, or 30 months or more.
Results/findings	Caries prevention Oliveira <i>et al.</i> described the findings on caries prevention as follows "Results of the meta-analysis of the 3 studies with 24 months of follow-up and comparison of SDF with placebo showed that SDF [silver diamine fluoride] applications significantly decreased the number of new root carious lesions (weighted mean differences (WMDs) in decayed or filled root surfaces (DFRS): 0.56; 95% CI, -0.77 to -0.36;)"^{95 (p673)} Oliveira <i>et al.</i> reported that "The prevented fractions (PF) for root caries prevention ranged from 50.3% to 68.4%, depending on follow-up duration. When investigators compared SDF with SDF followed by KI [Potassium iodide], they observed no significant difference in caries increment after 30 months of follow-up. In one study only the test group that received a co-intervention (OHE [oral hygiene education]) had a significantly lower new caries increment in comparison with the placebo group, we performed a sensitivity analysis excluding this group from the comparison between SDF and placebo. The pooled WMD and PF changed from -0.56 to -0.54 (95% CI, -0.75 to -0.33) and from 50.3% to 52.1% (95% CI, 38.6 to 65.6), respectively. We based the comparisons between SDF and FV [fluoride varnish] or CHX [chlorhexidine] varnish on 1 study. CHX had a significantly higher preventive effect than did SDF at 12 months of follow-up, but there were no significant differences between SDF and FV at any of the follow-up periods analyzed (that is, 12, 24, or 36 months) or between SDF and CHX varnish at 24 months of follow-up or more"^{95 (p673-74)} The authors also reported "In our meta-analyses for caries prevention, we combined 2 SDF test groups into 1 SDF group in 2 of the included trials.

Parameter	Extraction
	Investigators in 1 trial tested whether the benefits of SDF applications would be increased by participation in a biannual OHE program that trained dental hygienists conducted and that emphasized the prevention of snacking habits, correct toothbrushing practices, and adoption of additional tooth cleaning aids. This program was costly and time consuming, but only the SDF plus OHE group had a significantly lower new caries increment in comparison with the placebo group. Considering that toothbrushing behavior improvement did not differ significantly between the SDF only and SDFplus OHE groups and that sugar snacking plays a major role in caries development, it is likely that an unmeasured modification of the participants' dietary habits might have contributed to the lower caries incidence in the SDF plus OHE group. However, results of a sensitivity analysis excluding the SDF plus OHE group from the comparison between SDF and placebo showed that the effect of this co-intervention on the pooled effect was negligible. The investigators in the other trial compared the use of SDF alone with the use of SDF plus KI solution. The KI application immediately after the SDF application did not interfere with the SDF's effectiveness in preventing root caries"⁹⁵ (p676-77) Caries arrest Oliveira <i>et al.</i> reported on caries arrest and "observed significantly higher mean numbers of arrested lesions in the test groups than in the placebo group after 24 months of follow-up in 1 study. In the other study, the investigators provided the results as a percentage of caries arrest, and the test groups had significantly higher percentages of carious lesions arrested than did the placebo group at 12, 24, and 30 months of follow-up. In this [second] study, the investigators randomly assigned 323 participants to the test and control groups, but only 83 subjects were included and 67 were analyzed in the authors' reporting on caries arrest."⁹⁵ (p674-75) Oliveira <i>et al.</i> stated that "Investigators in 2 studies, reported that the interventions were well accepted by the older adult participants. In 1 trial, 3.5% of all participants complained about the black staining of their treated root surfaces. In another [study], only 2 older adult participants, both in the SDF group, raised the same complaint (additional information provided by 1 of the authors)"⁹⁵ (p674-75) According to the authors "Our findings show that annual applications of 38% SDF in older adults decreased the incidence of new carious lesions in exposed root surfaces by at least 50%; the longer the duration of the intervention, the greater the effect. Limited evidence with low risk of bias indicated that SDF was significantly more effective in preventing the development of new carious lesions compared with placebo and was similar to or better than FV [fluoride varnish] and CHX [chlorhexidine] varnish"⁹⁵ (p675) Summary of results Silver diamine fluoride application had a significantly better preventive effect when compared with placebo (weighted mean difference in decayed or filled root surfaces at 24 months was -0.56 (95% CI: -.77 to -0.36) and but not at 30 months or more -0.80 (95% CI: 1.19 to -0.42). Silver diamine fluoride application was as effective as either 1% chlorhexidine or 5% sodium fluoride varnish in preventing new root carious lesions. Silver diamine fluoride was reported to provide a significantly higher caries arrest effect than did placebo (pooled results not calculated).
Significance/direction	Oliveira <i>et al.</i> stated that "Yearly 38% SDF [silver diamine fluoride] applications to exposed root surfaces of older adults are effective against caries initiation and progression. The preventive effect of SDF for root caries is similar to that of 5% FV [sodium fluoride varnish] and 1% CHX [chlorhexidine] varnish"⁹⁵ (p678)
Heterogeneity	Oliveira <i>et al.</i> reported that "we encountered moderate to considerable statistical heterogeneity when we pooled the WMDs [weighted mean differences]. This finding is difficult to explain because relevant clinical and methodological variations among the studies are not apparent, and there are not enough studies to allow a reliable statistical investigation of the reasons for heterogeneity. Some have suggested the change of the effect measure as an alternative to deal with heterogeneity. When we estimated the pooled PF [prevented fractions], we observed no heterogeneity, and results were consistent with those obtained

Parameter	Extraction
	through meta-analyses of WMDs, confirming the effectiveness of SDF [silver diamine fluoride] for preventing root caries ⁹⁵ (p678).
Comments	Oliveira <i>et al.</i> concluded “The assessment of the effect size of SDF [silver diamine fluoride] on the arrest of root caries was hindered by the difference in outcome measures used in the studies, and we could not pool the results. However, there is good quality evidence accrued from 1 trial that annual 38% SDF applications effectively arrest root caries. Moreover, KI [potassium iodide] application immediately after SDF or participation in a biannual OHE [oral hygiene education] program together with yearly SDF applications does not seem to interfere with SDF’s caries-arresting effect⁹⁵ (p678). Oliveira <i>et al.</i> warned “all of the included trials were from the same group of investigators and enrolled Chinese older adult participants with a low risk of developing caries. The extent to which the findings can be generalized to other populations (for example, older adults with higher caries risk, not exposed to fluoridated water, not receiving individualized oral hygiene instruction regularly, or having different dietary habits) and reproduced by other investigators needs to be investigated further⁹⁵ (p678)

Tao *et al.* (2018)

Parameter	Extraction
First author and year of publication	Tao <i>et al.</i> (2018) ⁹⁶
Objectives	Evaluated the efficacy of combining casein phosphopeptide-amorphous calcium phosphate and fluorides compared to fluorides monotherapy on patients with early carious lesions in permanent teeth.
Participants	Permanent dentition, non-cavitated carious lesionlesions, non-invasive treatment Permanent teeth with early carious lesions Ten randomised controlled trials published between 2007 and 2016 involving 559 patients were included in this review. The age of study participants in the trials is unclear and may be erroneous, but young adults appear to have been included. Where gender was reported, the patients were predominantly female.
Setting/context	The treatment setting or study countries were not reported.
Description of interventions/phenomena of interest	The intervention was a combination of casein phosphopeptide-amorphous calcium phosphate and fluoride treatment. According to Tao <i>et al.</i>, “casein phosphopeptide-amorphous calcium phosphate is a nanocomplex derived from milk. It can stabilise higher concentrations of calcium and phosphate in an amorphous state to enhance remineralisation...Fluoride can facilitate calcium and phosphate diffusion into the demineralised lesions to remineralise the crystalline structures. The rebuilt crystalline structures, composed of fluoridated hydroxyapatite and fluorapatite, are much more resistant to acid attack than the original ones. Furthermore, fluoride can also affect cariogenic bacterial metabolism through several complex mechanisms.”⁹⁶ (p2) The comparator was fluoride monotherapy.
Databases and sources searched	Three databases (MEDLINE, Embase, and the Cochrane Library) were searched from January 1990 to August 2017. There was no language restriction during the literature search process; however, only papers in English or Chinese were included during the selection process. The search syntax is presented in an appendix. The reference lists of all included studies were searched manually. A study protocol was prepared. Screening and extraction of papers was completed by two authors. This work was supported by the National Natural Science Foundation of China and the Specialized Research Fund for the Doctoral Program of Higher Education of China. The authors report no conflicts of interest.
Date range (years) of included studies	Ten randomised controlled trials published between 2007 and 2016 involving 559 patients were included in this review.

Parameter	Extraction
Number of primary studies included in the systematic review	Ten randomised controlled trials published between 2007 and 2016 involving 559 patients were included in this review. The sources of funding for primary studies are not provided.
Types of studies included	The inclusion criteria specified randomised controlled trials. For excluded studies, the reason for exclusion is provided but not a list of excluded studies.
Country of origin of included studies	The study countries were not provided.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess the quality of the included trials. The funding source of primary studies is not presented.
Appraisal rating	One trial was scored as having a high risk of bias, six as having an unclear risk of bias, and three as having a low risk of bias. Seven of the 10 trials were judged to have adequate random sequence generation and nine were considered to have adequate blinding of outcome assessors. Publication bias is not discussed.
Method of analysis	Mean difference for continuous data was calculated with a 95% CI for generalising effectiveness of treatment in every single report. The authors used the random-effects models to combine the studies due to the clinical and methodological heterogeneity in the primary studies. Heterogeneity of studies was evaluated using the I^2 statistical index. $I^2 > 50\%$ indicated high heterogeneity. RevMan statistical software version 5.3 was used to compare treatment with fluoride and casein phosphopeptide-amorphous calcium phosphate against fluoride monotherapy on early carious lesions and to conduct the pairwise meta-analysis. $p < 0.05$ was considered statistically significant, but when performing the test of heterogeneity, $p < 0.1$ was considered statistically significant. To evaluate the robustness of the meta-analysis results, two sensitivity analyses were planned: (1) high-quality studies compared with low-quality studies, and (2) studies with small sample size compared with studies with large sample size.
Outcome assessed	Outcome: Size of carious lesion. The follow-up period was 3–24 weeks (not predetermined). The authors measured efficacy outcomes instrumentally and/or visually. The outcomes included: (1) degree of early carious lesions measured by laser fluorescence; (2) degree of early carious lesions compared to the surrounding healthy tooth structure using quantitative light-induced fluorescence; (3) value of total lesion area divided by total surface area; and (4) visual improvement after treatment, evaluated using visual inspection scores. Measurements (1) and (2) were evaluated instrumentally while measurements (3) and (4) was evaluated visually. Measurement (4) was not able to be included in the quantitative synthesis because the lesions were scored according to different criteria and values of standard deviation were not reported and are described narratively. Outcome by primary study: Degree of early carious lesions measured by laser fluorescence: Llena 2015; Aykut 2014; Fredrick 2013; Andersson 2007; Altenburger 2010; Guclu 2016. Degree of early carious lesions measured by laser fluorescence: Brochner 2011; Beerens 2010. Visual improvement after treatment, evaluated using visual inspection scores: Huang 2013; Akin 2012. Visual inspection scores: Brochner 2011; Andersson 2007.
Results/findings	The random-effects pairwise meta-analysis showed that the combination of casein phosphopeptide-amorphous calcium phosphate and fluoride treatment was better than fluoride monotherapy for occlusal early carious lesions in this analysis using laser fluorescence results (laser fluorescence results: mean difference: -21.02; 95% CI: -27.94 to -14.10; I^2 : 0%; 3 trials; 102 participants). However, fluoride combined with casein phosphopeptide-amorphous calcium phosphate achieved the same results as fluoride monotherapy for early carious lesions on smooth surfaces (laser fluorescence results: mean difference: -13.90; 95% CI: -39.25 to 11.46; I^2 : 55%; 4 trials; 133 participants). The combined meta-analysis for both occlusal and smooth surface lesions using the laser fluorescence results indicated a significant difference with very high statistical heterogeneity (laser fluorescence results: mean difference: 95% CI: -15.64; -28.90 to -2.38; I^2 : 80%; 7 trials; 235 participants).

Parameter	Extraction
	Two studies assessed efficacy of casein phosphopeptide-amorphous calcium phosphate and fluoride when compared with fluoride monotherapy on smooth surfaces using quantitative light-induced fluorescence, and meta-analysis demonstrated no significant difference (quantitative light-induced fluorescence results: mean difference: 0.26; 95% CI: -0.50 to 1.01; I²: 0%; 2 trials; 105 participants). Heterogeneity was not detected between the two studies. Two studies calculated the total lesion area divided by total surface area of teeth tested, and meta-analysis demonstrated no significant difference between the intervention and comparator (mean difference: 4.37; 95% CI: -0.51 to 9.26; I²: 6%; 2 trials; 114 participants). The two studies measuring visual inspection scores to evaluate visual improvement after treatment were not able to be included in a quantitative synthesis because the lesions were scored according to different criteria and values of standard deviation were not reported; the two studies reported conflicting findings, with one reporting a benefit and the other reporting no difference. However, the main finding from this review suggests that there is insufficient, incomplete, and inadequate evidence upon which to judge the effectiveness of the combination of casein phosphopeptide-amorphous calcium phosphate and fluoride when compared with fluoride monotherapy. The authors state that “the limited number of studies resulted in tiny subgroups, which suggests that the evidence is incomplete and is not generalisable”.^{96 (p8)} Further well-designed studies are still needed.
Significance/direction	Depends on outcome; see above.
Heterogeneity	The authors conducted subgroup analysis for the laser fluorescence results according to different locations of lesions, reducing I ² from 80% to 0% and 55%, for the subgroup analysis. Sensitivity analysis was not completed by risk of bias or sample size, as per the authors’ plan. Studies with unclear risk of bias were included in the analysis.
Comments	GRADE was not used by the review authors. Most trials scored a high risk of bias. Seven (70%) of the 10 trials were judged to have adequate random sequence generation and nine (90%) were considered to have adequate blinding of outcome assessors. The authors identified considerable statistical heterogeneity in the main analysis that was controlled for in subgroup analysis. The sample sizes were less than 200 in all analyses with low heterogeneity. The quality of the review was rated as low using AMSTAR 2 as the authors were unable to control for the risk of bias in the meta-analysis. The HRB grades the quality of the evidence as low for the different outcomes.

Hendre *et al.* (2017)

Parameter	Extraction
First author and year of publication	Hendre <i>et al.</i> (2017) ⁹⁷
Objectives	Evaluated the effectiveness (preventing, arresting, or remineralising) of silver diamine fluoride in the management of root caries in older adults.
Participants	Permanent dentition, non-cavitated and cavitated caries, non-invasive management Population: Root caries in the permanent teeth of older adults living in their own home or an institution, although adults aged 18 years and older were included. The review comprised three randomised controlled trials, published between 2010 and 2016, with 655 participants aged over 60 years. The exact number of teeth and the gender of participants were not reported.
Setting/context	The participants were living in nursing homes or attending community-based day centres. All three studies were completed in Hong Kong, China. The funding sources of primary studies were not reported.
Description of interventions/phenomena of interest	Silver diamine fluoride (SDF) (dose or frequency not predetermined) SDF is an emerging caries preventive treatment option that is inexpensive, safe, and easily accessible. Treatment with silver diamine fluoride requires minimal instrumentation and application at less frequent intervals than other caries

Parameter	Extraction
	preventive materials. Current evidence supports silver diamine fluoride use in children. However, older adults, especially those with high caries risk and/or with limited to no access to dental services due to economic, social, or functional challenges, may benefit from this treatment as well. Silver diamine fluoride affects the tooth structure and the caries process. The effect on enamel is primarily due to fluoride, while the effect on dentine is predominantly due to silver. Formation of silver phosphate turns silver diamine fluoride-treated carious lesions black. Silver diamine fluoride does not affect the bond strength of composite resin to non-carious dentine, but may reduce bond strength to caries-affected dentine. Silver diamine fluoride is compatible with glass ionomer cements and may increase resistance of glass ionomer cements and composite resin restorations to secondary caries. Comparator: Other preventive agents (fluoride, chlorhexidine) or placebo (not predefined) All intervention groups received oral hygiene instructions.
Databases and sources searched	PubMed, PubMed Clinical Queries, Embase, the American Dental Association's Center for Evidence-Based Dentistry website, the Cochrane Library, Web of Science, the repository of the Journal of the American Dental Association, and Google Scholar were searched for articles published from 1946 to November 2015, with monthly reruns of search terms in PubMed through August 2016. The search was restricted to English-language articles only. The search strategy is presented in table and text. The bibliographies of the selected manuscripts were subsequently screened for additional articles. The preparation of a protocol was not mentioned. It was not stated whether screening or extraction were completed in duplicate. This review was funded through an unrestricted honorarium from the American Dental Association's National Elder Care Advisory Committee of the Council on Access, Prevention and Interprofessional Relations. Conflicts of interest were not published in the paper.
Date range (years) of included studies	Three randomised controlled trials published between 2010 and 2016 were included in the review.
Number of primary studies included in the systematic review	The review comprised three randomised controlled trials, published between 2010 and 2016, with 655 participants aged over 60 years. The funding sources of primary studies were not reported.
Types of studies included	Randomised controlled trials and cohort studies were eligible for inclusion. The reasons for exclusion at full-text screening were provided but not referenced to articles.
Country of origin of included studies	All three studies were completed in Hong Kong, China.
Appraisal instruments used	The critical appraisal worksheet for randomised controlled trials from the Oxford Centre for Evidence-Based Medicine was used to assess the quality and risk of bias of the selected studies.
Appraisal rating	One of the three studies met all quality criteria, and the remaining two studies met eight of the nine criteria. All three studies were judged to have adequate randomisation and assessor blinding.
Method of analysis	The effectiveness of SDF was measured using the following parameters: • Number needed to treat: The number of patients required to treat in the intervention group(s), relative to the control group, in order to prevent a root surface carious lesion from occurring or to prevent a carious root surface from progressing. • Prevented fraction: Reduction in the rate of incident caries surfaces or the increase in the rate of preventing root surface caries from progressing in the intervention group(s) relative to the control group. • Mean number of new carious surfaces and mean number of arrested root surfaces. • Relative risk: How much more likely new root surface caries are to occur, or existing root surface caries are to be prevented from progressing, in the intervention group(s) relative to the control group. • Arrest rate: Percentage of active carious lesions at baseline that subsequently became arrested per time period at 12, 24, and 30 months.

Parameter	Extraction
	The authors did not explain why they did not complete meta-analysis.
Outcome assessed	Preventing, arresting, or remineralising root caries Tan 2010 (prevention only); Zhang 2013; Li 2016. The follow-up periods ranged from 30 to 36 months.
Results/findings	Root caries prevented fraction and arrest rate for silver diamine fluoride were significantly higher than placebo. The prevented fraction for caries prevention for silver diamine fluoride compared with placebo was 71% in a 3-year study and 25% in a 2-year study. The prevented fraction for caries arrest for silver diamine fluoride was 725% greater than placebo in a 24-month study and 100% greater than placebo in a 30-month study. Silver diamine fluoride effectively arrested root caries in the studies assessing root caries arrest. The arrest rate for silver diamine fluoride and silver diamine fluoride -potassium iodide groups in the Li <i>et al.</i> study was two times (200%) greater than placebo, while Zhang <i>et al.</i> reported the arrest rate being six times (600%) greater for the silver diamine fluoride group and 7.25 times (725%) greater for the silver diamine fluoride and oral hygiene education group than for the placebo group. No severe adverse effects were observed.
Significance/direction	Favours silver diamine fluoride to arrest root caries in older adults.
Heterogeneity	No meta-analysis was conducted. The authors did not explain why they did not complete meta-analysis.
Comments	GRADE was not used by the review authors. One of the three studies met all quality criteria, and the remaining two studies met eight of the nine criteria. All three studies were judged to have adequate randomisation and assessor blinding. Heterogeneity was not discussed. The quality of the review was rated as low using AMSTAR 2 as the authors did not measure or discuss heterogeneity. The HRB grades the quality of the evidence as moderate for the different outcomes.

Wierichs and Meyer-Lueckel (2015)

Parameter	Extraction
First author and year of publication	Wierichs and Meyer-Lueckel (2015)⁹⁸
Objectives	Evaluated results of clinical studies investigating chemical agents to reduce initiation of root carious lesions or inactivate existing ones (arrest carious lesions).
Participants	Permanent dentition, non-cavitated caries, non-invasive treatment Population: Permanent teeth in adults (mainly older adults) with root carious lesions or at risk of root carious lesions Thirty-four articles, reporting 30 studies with 1 or more active interventions were included; they analysed 28 chemical agents (alone or in combination). The 30 studies (29 studies were randomised controlled trials and 1 study was a non-randomised controlled trial) were published between 1988 and 2013, and included 10,136 patients who were aged 20 to 101 years. Gender was not reported. The median (25th/75th percentiles) follow-up time was 15 (12/24) months.
Setting/context	The study countries were Brazil, Canada, China, Denmark, Germany, Hungary, Israel, Spain, Sweden, Switzerland, the Netherlands, the UK, and the USA. The studies' clinical settings were extracted but not presented.
Description of interventions/phenomena of interest	Intervention: Preventive dental regimes (e.g. oral health instruction) and/or one or more chemical agents applied on one or more occasion by a dental professional or self-applied by the patient The chemical agents were fluoride compounds, chlorhexidine, ozone treatment, etc. in different delivery systems (dentifrice, mouth rinse, and varnish) and the reviewers compared their effectiveness to each other (positive interventions) and to negative intervention (placebo treatment) or standard therapy. Eleven studies investigated dentifrices, 10 investigated rinses, 8 investigated varnishes, 3 investigated solutions, 3 investigated gels, and 2 investigated ozone applications.
Databases and sources searched	Three databases were searched (PubMed, Embase, and Cochrane Central Register of Controlled Trials [CENTRAL]) for articles published between January 1947 and May 2014. Minimal keywords and a search strategy were provided. Language was

Parameter	Extraction
	restricted to English and German. Grey literature was not evaluated. Cross-referencing was performed to identify further articles to be assessed. The preparation of a protocol was not mentioned. Two authors independently reviewed the title and abstract of articles retrieved. It is not clear who extracted the data and if it was extracted in duplicate. This study was funded by the authors and their institution. The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article.
Date range (years) of included studies	The 30 studies (29 studies were randomised controlled trials and 1 study was a non-randomised controlled trial) were published between 1988 and 2013.
Number of primary studies included in the systematic review	Thirty-four articles, reporting 30 studies with 1 or more active interventions, were included; they analysed 28 chemical agents (alone or in combination). The authors reported that 11 studies were not sponsored by the manufacturers of the tested products, indicating that 19 were industry funded.
Types of studies included	The authors included non-blinded and blinded (double-blinded), randomised and non-randomised, controlled, and prospective studies. The reasons for selecting these inclusion criteria were not explained. The articles excluded and the reasons for exclusion were provided in an appendix.
Country of origin of included studies	The study countries were Brazil, Canada, China, Denmark, Germany, Hungary, Israel, Spain, Sweden, Switzerland, the Netherlands, the UK, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included studies.
Appraisal rating	Of the 30 studies selected for inclusion, 14 were included in meta-analyses. Of these 14 studies, 10 were judged to have a high risk of bias and 4 to have an unclear risk of bias. Five of the 14 studies were judged adequate for randomisation and 11 had adequate blinding of outcome assessor. Sixteen studies were excluded from meta-analysis. Of these 16 studies, 10 were judged to have a high risk of bias and 6 to have an unclear risk of bias. Nine of the 16 studies were judged adequate for randomisation and 14 had adequate blinding of outcome assessor. Publication bias was assessed by funnel plots, but the findings and their implications were not presented.
Method of analysis	Data were tested for normal distribution and descriptively analysed accordingly. The primary measures of effect between treatment and control groups were the mean differences for studies based on the same units and standardised mean differences for studies based on the same construct but different scales. Changes were calculated for the following outcomes: decayed, missing, and filled root surfaces, surface texture (soft or hard), and root caries index. Dichotomous outcome data (e.g. surface texture) were analysed by calculating risk ratios and 95% CIs. A random-effects model was used to calculate a pooled estimate of effect. Heterogeneity was assessed via I^2.
Outcome assessed	Assessed root carious lesions initiation and/or their inactivation (arrest) through clinical or radiographic visible changes of active or inactive root caries. There was no predetermined time frame. Outcomes by primary study: 5000 ppm fluoride compared with 1100–14500 ppm fluoride dentifrice: surface texture (hard or soft) at 6–8 months follow-up: Baysan 2001; Ekstrand 2013. 1.5% arginine plus 1450 ppm fluoride compared with 14500 ppm fluoride dentifrice: surface texture at 6 months follow-up: Hu 2013; Souza 2013. Amine fluoride/stannous fluoride-containing dentifrice (1400 ppm fluoride) plus amine fluoride/stannous fluoride rinse (250 ppm fluoride) compared with sodium fluoride-containing dentifrice (1400 ppm fluoride) plus sodium fluoride rinse (250 ppm fluoride) for change in root caries index/decayed, missing, filled root surfaces at 5–24 months follow-up: Banoczy and Nemes 1991; Paraskevas 2004. 225–900 ppm fluoride compared with placebo mouth rinses for change in decayed, missing, filled root surfaces (only new root carious lesions) at 24–48 months follow-up: Fure 1998; Ripa 1987; Wallace 1993; Wyatt and MacEntee 2004. Silver diamine fluoride compared with placebo varnish for change in root caries index/decayed, missing, filled root surfaces (only new root carious lesions) at 24–36 months follow-up: Tan 2010; Zhang 2013.

Parameter	Extraction
	Chlorhexadine compared with placebo varnish for change in root caries index/decayed, missing, filled root surfaces (only new root carious lesions) at 12–36 months follow-up: Baca 2009; Banting 2000; Tan 2010.
Results/findings	Only 14 trials or 17 papers were included in pairwise fixed-effects meta-analyses. Meta-analyses revealed that dentifrices or toothpastes containing 5000 ppm fluoride (relative risk: 0.49; 95% CI: 0.42–0.57; I²: 89%; 636 teeth; 2 trials; downgraded from moderate to low-quality evidence by the HRB) or 1.5% arginine plus 1450 ppm fluoride (relative risk: 0.79; 95% CI: 0.64–0.98; I²: 0%; 528 teeth; 2 trials; low-quality evidence) were more effective in inactivating root carious lesions than dentifrices containing 1100–1450 ppm fluoride. Self-applied amine fluoride or stannous fluoride-containing dentifrice and rinse decreased the initiation of root carious lesions when compared with sodium fluoride products (standardised mean difference: 0.15; 95% CI: –0.22 to 0.52; I²: 0%; 115 teeth; 2 trials; low-quality evidence), but the decrease was not statistically significant. Patients rinsing with a mouth rinse containing 225–900 ppm fluoride revealed a significantly reduced decayed, missing, or filled root surfaces or lesions (mean difference: –0.18; 95% CI: –0.35 to –0.01; I²: 77%; 1,206 teeth; 4 trials; low-quality evidence) when compared with a placebo rinse. Significantly reduced root caries index was found for chlorhexidine use (mean difference: –0.67; 95% CI: –1.01 to –0.32; I²: 8%; 305 teeth; 2 trials; low-quality evidence) as well as silver diamine fluoride (mean difference: –0.33; 95% CI: –0.39 to –0.28; I²: 87%; 264 teeth; 2 trials; low-quality evidence) when compared with placebo varnish. Regular use of dentifrices containing 5000 ppm fluoride and quarterly professionally applied chlorhexidine or silver diamine fluoride varnishes seem to be efficacious in decreasing the progression and initiation of root caries, respectively (low-quality evidence). Heterogeneity was measured but not addressed or discussed by the authors. The authors concluded, “Based on meta-analysis, dentifrice containing 5,000 ppm F⁻ [fluoride] and professionally applied CHX [chlorhexidine] or SDF varnish may inactivate existing and/or reduce the initiation of RCLs [root carious lesions]. However, results should be interpreted with caution, due to the low numbers of clinical trials for each agent, the high risk of bias within studies, and the limiting grade of evidence.”⁹⁸ (p269)
Significance/direction	Results listed by outcome.
Heterogeneity	Heterogeneity was not addressed by the authors.
Comments	GRADE was used by the review authors. The non-randomised study was not included in the meta-analyses. Of the 14 randomised trials included in the meta-analysis, all were judged to have a high or unclear risk of bias. Five (36%) of the 14 studies were judged adequate for randomisation and 11 (79%) had adequate blinding of outcome assessor. The sample sizes was less than 200 for some outcomes. The quality of the review was rated as critically low using AMSTAR 2 as the authors did not control for the risk of bias in the meta-analysis or discuss the heterogeneity in the results. The HRB grades the quality of the evidence as low or very low for the different outcomes which corresponds with review authors rating for the secondary outcomes but is lower the review authors’ moderate rating for the main outcome.

Non-cavitated caries and cavitated

Comparison of non-invasive, microinvasive, and minimally invasive treatment

Schwendicke *et al.* (2015a)

Parameter	Extraction
First author and year of publication	Schwendicke <i>et al.</i> (2015a) ³²
Objectives	Compared non-invasive, microinvasive, and minimally invasive treatments with each other, with no active treatment or a placebo treatment, or with standard oral home care for treating pit-and-fissure lesions in permanent posterior teeth in

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	adults. Various treatment options are available for pit-and-fissure lesions in permanent posterior teeth: (1) non-invasive treatments (like fluoride) to avoid any dental hard tissue removal; (2) microinvasive treatments (sealants), which remove only a few micrometers of hard tissues by etching; and (3) minimally invasive methods (sealants and restoration), which remove carious dentine but avoid sacrificing sound tissues.
Participants	Permanent dentition, non-cavitated caries and cavitated, non-invasive, microinvasive, and minimally invasive management Population: Pit-and-fissure lesions in permanent posterior teeth. The overall age range was 5–68 years. However, 8 of the 14 included studies included children and adolescents only. For two studies, age was not recorded. Gender was not reported.
Setting/context	The treatment settings were not reported. The study countries were Albania, Brazil, Canada, China, Denmark, the USA, and Zimbabwe.
Description of interventions/phenomena of interest	According to Schwendicke <i>et al.</i> , “non-invasive strategies e.g. fluoride avoid any removal of hard tissues and focus, for example, on influencing the equilibrium of demineralization and remineralization or removing/controlling the biofilm activity. Microinvasive strategies, e.g. sealants, involve conditioning of dental hard tissues and are thus not completely non-invasive; however, only a few micrometers of enamel or dentine are removed. These strategies aim at establishing a diffusion barrier for acids, minerals, or carbohydrates via sealing the lesion...minimally invasive treatments include preventive resin restorations, sealant restorations, or enameloplasty and do not follow the principle of ‘extension for prevention’ but are guided by the extension of the carious lesion and aim at preserving hard tissues. Occlusally, they can be performed without greatly sacrificing sound tooth tissue (which is a difference to treatment of proximal lesions), while the effectiveness of the resulting restoration is largely independent from patients’ compliance, with potentially long retention times of such minimally invasive restorations.” (p522–523) Comparator: Each other, or no active or placebo treatment, or standard oral home care
Databases and sources searched	Three electronic databases (Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE via PubMed, and Embase) were systematically searched up to September 2013. The search was not restricted by language. Two additional databases were searched – ClinicalTrials.gov for unpublished trials and OpenGrey for grey literature – and cross-referencing of included primary studies was completed. The search strategy was provided in an appendix. The authors do not mention preparing a protocol. Title and abstract of identified studies were screened by two reviewers and extraction was completed in duplicate. This study was funded by the authors and their institutions through grants from the German Research Foundation and from the Ministry of Science and Technology in Taiwan. The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article.
Date range (years) of included studies	Ten randomised and four non-randomised controlled trials published between 1976 and 2012 were included.
Number of primary studies included in the systematic review	Ten randomised and four non-randomised controlled trials published between 1976 and 2012, involving 1,440 patients with 3,551 treated lesions in permanent posterior teeth, were included in this review. The funding sources of primary studies were not reported.
Types of studies included	The inclusion criteria specified randomised or non-randomised clinical trials. Non-randomised trials were included only if the lesions treated in different groups were comparable. Non-randomised studies were included in order to increase the comprehensiveness of the review, and this has been shown to not generally introduce systematic bias. The reasons for excluding full-text studies were provided, but not a list of references.
Country of origin of included studies	The study countries were Albania, Brazil, Canada, China, Denmark, the USA, and Zimbabwe.

Parameter	Extraction
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess the risk of bias.
Appraisal rating	Based on the Cochrane Collaboration's risk of bias instrument, all 14 studies were judged to have a high risk of bias. Six of the 14 studies were judged to have adequate random sequence generation, but none were considered to have had adequate blinding of outcome assessors. The authors did not detect publication bias using statistical or graphical means.
Method of analysis	Traditional pairwise random-effects meta-analysis allows direct comparisons for each pair of treatments using the odds ratio (OR), while network meta-analysis permits both direct and indirect evidence for multiple treatment comparisons. The differences in the results were used to detect potential inconsistency between direct and indirect evidence. Whenever appropriate, the authors used Cochran's Q test and I^2 to evaluate the heterogeneity in the pairwise comparisons within the network. The unit of analysis for meta-analysis was the patient. When patients contributed more than one tooth/lesion, adjustments were made by converting the number of teeth to the number of patients by assuming that teeth were evenly distributed among patients. Funnel plot analysis and the Egger test were performed to assess small study effects or publication bias. Evidence for each pairwise estimate was graded using GRADEpro 3.6 according to GRADE guidelines. Network meta-analysis was performed using Bayesian random-effects hierarchical models and a Markov chain Monte Carlo simulation. To fit the model, the authors used a non-informative uniform prior distribution and assessed convergence and inspection of history plots. Simulations were performed with 50,000 tuning iterations and a further 50,000 simulations per chain at a thinning interval of 50 with 3 chains of initial values. The authors calculated posterior medians and 95% credibility intervals. The consistency between direct and indirect results was evaluated using the statistical software Stata. Subgroup analyses were performed to evaluate the effects of participants' age (aged under 18 years compared with over 18 years), lesion depths (enamel compared with dentinal lesions), surface integrity (non-cavitated compared with cavitated), and sealant materials (resin based compared with glass ionomer cement sealant) on effect estimates. Similarly, the authors explored the effects of study design (randomised compared with non-randomised controlled trials) and case definition (questionable compared with certain presence of carious lesions). Last, effect estimates were based on calculations using the intention-to-treat-principle, counting all lost cases as failure, thereby accounting for imbalanced attrition.
Outcome assessed	Outcome: Avoidance of retreatment (progression of the lesion, sealant loss, secondary caries or fracture of restorations, pulpal complications) Time frame: 6 months or over Risk of subsequent invasive treatment: Going 1976; Gibson and Richardson 1980; Mertz-Fairhurst 1986; Heller 1995; Frencken 1996, 1998; Mertz-Fairhurst 1998; Florio 2001; Hamilton 2002; Maltz 2003; Xhemnica 2008; Bakhshandeh 2012; Borges 2010; Borges and de Souza Borges, 2012; Liu 2012. Risk of retreatment: Going 1976; Gibson and Richardson 1980; Mertz-Fairhurst 1986; Heller 1995; Frencken 1996, 1998; Mertz-Fairhurst 1998; Florio 2001; Hamilton 2002; Maltz 2003; Xhemnica 2008; Bakhshandeh 2012; Borges 2010; Borges and de Souza Borges, 2012; Liu 2012.
Results/findings	Pairwise and network meta-analyses were planned and robust, although they include non-randomised trials. The authors completed an analysis comparing the outcomes in randomised compared with non-randomised trials; however, the results are not reported in the paper. Comparing microinvasive or minimally invasive treatments with controls, microinvasive or minimally invasive treatments significantly reduced the risk of invasive retreatment being required (OR: 0.13; 95% CI: 0.07–0.26; I^2 : 73%; 8 trials) or (OR: 0.13; 95% CI: 0.0–0.50; 1 trial), respectively, while no significant effect could be shown for non-invasive treatment compared with controls (OR: 0.64; 95% CI: 0.39–1.026; I^2 : 55%; 3 trials). Microinvasive and non-invasive treatments (OR: 0.99; 95% CI: 0.50–1.96; I^2 : 0%; 2 trials) or microinvasive and minimally invasive treatments (OR: 0.32; 95% CI: 0.06–1.73; I^2 : 27%; 2 trials) did not

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	significantly differ from one another with regard to the risk of requiring invasive retreatments. No pairwise estimate could be calculated to compare non-invasive with minimally invasive treatments. Microinvasively treated lesions required retreatments significantly more often (OR: 17.8; 95% CI: 5.94–53.5; I²: 0%; 2 trials) than non-invasively treated lesions. Similarly, lesions in control groups required retreatment more frequently than minimally invasively treated lesions (OR: 0.24; 95% CI: 0.09–0.72; 1 trial). The effect estimate comparing non-invasive treatment with controls did not reach statistical significance (OR: 0.64; 95% CI: 0.39–1.06; I²: 55%; 3 trials). No significant differences were found between microinvasive and minimally invasive treatments (OR: 0.60; 95% CI: 0.07–5.00; I²: 36%; 2 trials) or microinvasive treatments and controls (OR: 0.59; 95% CI: 0.13–2.76; I²: 94%; 7 trials). No effect estimate was calculated for the comparison between minimally invasive and non-invasive treatments. The analysis showed that microinvasive and minimally invasive treatments were potentially effective in avoiding invasive retreatments after treating pit-and-fissure lesions in permanent posterior teeth. In addition, there was some evidence that non-invasive treatments might also be effective in avoiding invasive retreatments after treating pit-and-fissure lesions in permanent posterior teeth. The need for any retreatment was significantly higher in microinvasively sealed lesions than in those that received non-invasive or minimally invasive treatments. However, the main finding of this review suggests that the evidence is low or very low quality (due to the high risk of bias in all included studies and heterogeneity between studies), and there is very low-quality evidence upon which to judge the effectiveness of the interventions under evaluation. These findings were reflected in the strategy ranking stemming from network meta-analysis (first, minimally invasive; second, microinvasive; third, non-invasive). However, microinvasive treatment required significantly more total retreatments (including resealing) than minimally invasive or non-invasive treatments. According to Schwendicke <i>et al.</i>, “the studies supporting these findings were mostly of limited quality; thus, the overall certainty of our findings [based on GRADE] is thus low or very low.”³² (p531)
Significance/direction	Varies by comaprison.
Heterogeneity	Varies by comaprison, but moderate to substantial in most analyses.
Comments	GRADE was used by the review authors. The authors use a mix of randomised and non-randomised trials. All 14 studies were judged to have a high risk of bias. Six (43%) of the 14 studies were judged to have adequate random sequence generation, but none were considered to have had adequate blinding of outcome assessors. The confidence intervals for two outcomes were very wide indicating a small sample size. High or substantial heterogeneity was present in some analysis. The quality of the review was rated as low using AMSTAR 2 as the authors could not control for the risk of bias in the meta-analysis. The HRB concurs with the review authors and grades the quality of the evidence as very low for the different outcomes, which corresponds with review authors’ rating.

Cavitated caries

Direct restoration material

Medeiros Maran *et al.* (2020)

Parameter	Extraction
First author and year of publication	Medeiros Maran <i>et al.</i> (2020) ⁹⁹
Objectives	Evaluated survival or clinical performance (two primary outcomes: colour match and surface texture and six secondary outcomes) of nanofilled/nanohybrid

Parameter	Extraction
Participants	restorations compared with hybrid composite restorations in patients with direct posterior restorations. Permanent dentition, cavitated caries, direct restoration material The age of the patients, with the direct posterior restorations of interest, ranged from 13 years to 82 years; the mean age was 32.7 years. Except for one study, more females were included than males. Four studies did not report on the sex of the patients. Seven studies included Class I and Class II restorations, seven studies only included Class I restorations, and five only included Class II restorations. The mean cavity width was one-third of the intercuspal distance in nine studies and one-quarter of the intercuspal distance in one study. The rest of the studies did not report on cavity width. Nine studies used rubber dam isolation and 10 studies used cotton rolls and saliva ejectors. In 12 studies, restorations were made due to primary carious lesions or unsatisfactory restorations, and 7 studies did not report on this item. Twelve studies reported that bevelling of the enamel margins was not performed, while two studies did report bevelling of the enamel margins. Etch-and-rinse adhesive systems were used in 14 studies, self-etch adhesive systems were used in three studies, and two studies used both types of adhesive systems. For the protection of the dentine-pulp complex, three studies applied a glass ionomer cement, two studies applied a calcium hydroxide cement, and five studies applied both materials. The other studies either did not use such materials or did not report on whether or not these materials had been used. In the majority of the studies, the incremental technique had been applied. In nine studies, finishing and polishing of the restoration was performed immediately after composite placement, while in two studies the restorations were finished and polished in the next clinical appointment or 1 week after the initial restoration. In four studies, the restorations were finished immediately after placement but the restorations were polished only 1 week after the initial restoration. Four studies did not report on this procedure.
Setting/context	The vast majority of the included trials were undertaken in a university setting. The study countries were not reported.
Description of interventions/phenomena of interest	Intervention: Nanofilled/nanohybrid composites. Comparator: Hybrid composite. The authors described the intervention as follows: "Nanofilled composites consist of nanometer-sized particles in the composite matrix, which are mostly clustered into larger secondary particles, and nanohybrid composites take the approach of combining nanometer and micrometer-sized fillers."⁹⁹ (p2)
Databases and sources searched	The authors developed a search strategy for MEDLINE, which they then adapted for use with other electronic databases. The authors searched four databases (MEDLINE, the Cochrane Library, BBO, and LILACS) and two citation databases (Scopus and Web of Science). The search was conducted initially on 8 April 2018, and was updated on 24 April 2020. No year or language restrictions were applied. The authors searched the grey literature by examining the abstracts of the annual conference of the International Association for Dental Research and its regional divisions (2001–2019), OpenSIGLE, and dissertations and theses using the ProQuest Dissertations & Theses Global full-text database, as well as the CAPES database. Ongoing studies were searched in the following clinical trial registries: the ISRCTN registry, the WHO's International Clinical Trials Registry Platform, ClinicalTrials.gov, ReBEC (the Brazilian Registry of Clinical Trials), and EU Clinical Trials Register. Additionally, they hand-searched the reference lists of all primary sources and eligible studies included in the systematic review for additional relevant publications. This systematic review was registered in PROSPERO. Extraction and screening were completed in duplicate. Funding: No funding sources were reported.

Parameter	Extraction
	The authors stated that there was no conflict of interest present during the undertaking of this study. The study did not receive any internal or external funding.
Date range (years) of included studies	The studies were published between 2006 and 2016.
Number of primary studies included in the systematic review	Nineteen trials were reported in 28 articles that were included in this review as there were multiple reports of the same study with different follow-ups. Data from studies with different follow-ups were collected in a single form, resulting in a total of 19 studies being included: 18 split-mouth trials and 1 parallel trial. The studies were published between 2006 and 2016. The funding sources for primary studies were not reported.
Types of studies included	Parallel and split-mouth randomised clinical trials were eligible for inclusion. The excluded studies and their reason for exclusion were reported in the text.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	None of the included trials was considered to be at low risk of bias; 4 were considered to be at high risk of bias and the remaining 15 were judged to be at unclear risk of bias. Only eight (42%) of the 19 included studies was found to be at low risk of bias for randomisation, while 17 of the 19 (89%) studies were at low risk of bias for outcome assessment. According to the authors, "For the majority of studies, bias was judged as unclear, as allocation concealment was not reported or the patient and/or operator were not blinded during assessment. On the other hand, the majority of studies reported blinding of the evaluator, with the exception of two studies that did not report on this item. At study level, of the 19 studies, none was considered to be at low risk of bias; four were considered to be at high risk of bias and the remaining were judged to be at unclear risk of bias." ⁹⁹ (p8) The authors explained that "The unclear risk of bias of most studies, as well as the imprecision observed in all meta-analyses, make our confidence in the estimates and conclusion of this systematic review moderate to low." ⁹⁹ (p14) The authors reported that to minimize publication bias, no year or language restrictions were applied to the search and publication bias was also considered in the authors GRADE assessment.
Method of analysis	According to Medeiros Maran <i>et al.</i> , "Data have been analyzed using RevMan 5.3. Meta-analyses were performed in studies classified as at low or at unclear risk of bias in the key domains; studies judged to be at high risk of bias in the key domains were not included in the meta-analysis. Data of eligible studies have been summarized by calculating the risk difference and the 95% confidence interval. As studies reported outcomes from different follow-ups, the meta-analysis was performed in range periods of 12–18 months, 24–31 months, 36–60 months, and 72 months or more. When one study reported data twice within the same range period, data of the longest follow-up period have been taken into account. For all meta-analyses, we used the random-effects model, as this is the most appropriate model for studies from different populations. Heterogeneity was evaluated using the Cochran's Q test and I ² statistics, but as this is a measure of dispersion, it was only presented in the discussion section when more than five studies were included in the meta-analysis. The 95% prediction interval was calculated in all meta-analyses with at least five studies. Sensitivity analyses have been conducted to investigate the reasons for high heterogeneity, whenever detected." ⁹⁹ (p4)
Outcome assessed	The primary outcome variables were surface texture and colour match, which were clinically evaluated according to the USPHS criteria. Anatomic form/fracture, marginal discolouration, marginal adaptation, post-operative sensitivity, loss of restoration, and secondary caries were secondary variables. In 18 studies, the USPHS criteria were used for clinical evaluation. Only one study used the FDI criteria. Survival or clinical performance (two primary outcomes: colour match and surface texture and 6 secondary outcomes): Andrade 2010; Öztürk-Bozkurt 2016; Yazici 2014; Andrade 2012; De Andrade 2011; Çelik 2014; Arhun 2010; Beck 2014;

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	Dresch 2006; Efes 2006a; Efes 2006b; Efes 2013; Frankenberger 2014; Krämer 2011; Krämer 2015; Krämer 2009a; Krämer 2009b; Mahmoud 2014; Mahmoud 2008; Palaniappan 2009; Palaniappan 2010; van Dijken 2014; van Dijken 2013; Schirrmeister 2006; Schirrmeister 2009; Sadeghi 2010; Ernst 2006; Walter 2014.
Results/findings	Surface texture The authors reported that “Risk differences for the comparison between nanofilled and hybrid composite varied from –1% (95% CI: –4% to 1%) at the 12–18 months follow-up to –2% (95% CI: –8% to 3%) at the 36–60 months recall. Risk ratios for the comparison between nanohybrid and hybrid composite varied from –3% (95% CI: –10% to 3%) at the 12- to 18-month follow-up to 0% (95% CI: –3% to 3%) at the 72 months or more recall. None of the comparisons yielded statistically significant differences ($p>0.05$). Surface texture showed... heterogeneity, varying from 27% to 81%.”⁹⁹ (p8) Assessment of the quality of evidence (GRADE) Surface texture According to the review authors, “The body of evidence for surface texture was classified as moderate or low... We observed that some meta-analyses were classified as moderate, due to the unclear risk of bias for most included studies. However, other meta-analyses were classified as low, due to two aspects: unclear risk of bias associated with inaccurate data and low number of included studies.”⁹⁹ (p9) Colour match Medeiros Maran <i>et al.</i> stated that “Risk differences for the comparison between nanofilled and hybrid composite varied from –2% (95% CI: –6% to 2%) at the 12–18 months recall to –4% (95% CI: –9% to 2%) at the 36 months or more follow-up. Risk ratios for the comparison between nanohybrid and hybrid composite varied from –7% (95% CI: –21% to 7%) at the 12- to 18-months recall to –1% (95% CI: –5% to 4%) at the 72 months or more follow-up. None of the comparisons yielded statistically significant differences ($p>0.05$). Color match showed a trivial heterogeneity in the nanofilled versus hybrid composite comparison and a substantial heterogeneity in the nanohybrid versus hybrid composite comparisons. Heterogeneity not due to chance varied from 0% to 100% between studies.”⁹⁹ (p8) Assessment of the quality of evidence (GRADE) Colour match The authors said, “Similarly, the body of evidence for color match was classified as moderate or low for the same reasons that were elucidated for surface texture.”⁹⁹ (p9) Secondary outcome variables “Other secondary outcomes variables, such as anatomic form/fracture, marginal discoloration, marginal adaptation, post-operative sensitivity, loss of restoration, and secondary caries had also been evaluated... There were no statistically significant differences for the above mentioned secondary outcomes variables.”⁹⁹ (p8–9) Sensitivity analysis The authors found that “There is some heterogeneity in all meta-analyses. A non-significant p-value for heterogeneity does not mean an absence of heterogeneity, but that the variation may be trivial. In cases of significant heterogeneity, we found specific characteristics in some studies that differ from the other studies. In a sensitivity analysis, we attempted to identify the studies that were responsible for the heterogeneity in the meta-analysis. This fact was not pre-specified in the protocol registered in PROSPERO and these findings should only be considered as speculative.”⁹⁹ (p9) They explained, “In spite of the heterogeneity of the clinical studies and the bias of many of them, it seems no less reasonable to assume that there is no clinical effect of different filler concepts of materials (nano/nanohybrid/microhybrid/hybrid) on color match, gloss stability, fracture incidence and overall longevity. The results might be different if the same operator applies the same materials in the same patients; this would rule out or at least diminish patient- and operator-related effects. Also, the results might be different if the analysis focuses on different brands which, however, would only

Parameter	Extraction
	be feasible if an adequate number of clinical studies with the same brands would be available for analysis. One can speculate about confounding factors, such as patient factors (diet, oral hygiene, caries activity, chewing forces), operator factors (skill of operator general dental practitioner versus academic setting, shade selection) and tooth factors (type of tooth, extension of restoration)."⁹⁹ (p13) The authors noted that "Although sensitivity analysis tried to identify the causes of heterogeneity, as described in the results section of this paper, its results are observational, not causal. It is possible that some of the different features of the studies causing heterogeneity (reported in the results section) may be responsible for the observed variation in the effect sizes. However, it is also possible that the difference is due to some other unknown variable. This is the reason why these analyses should not be seen as definitive, but rather exploratory."⁹⁹ (p13)
Significance/direction	Medeiros Maran <i>et al.</i> stated that "The present meta-analysis revealed no significant differences between nanofilled/nanohybrid and hybrid composite in any of the investigated parameters (color match, surface texture, surface staining, fracture incidence, overall longevity). However, most of the included studies showed some degree of bias which emphasized the need for well-conducted randomized controlled clinical trials."⁹⁹ (p14)
Heterogeneity	Heterogeneity was assessed with the Cochran Q test and I² statistics. According to the authors, "The heterogeneity in some of the meta-analyses presented in this study needs further comments. Heterogeneity is not inherently good or bad in meta-analysis, but it casts doubt on the reasonability to believe in an overall estimate that applies to all the encompassed studies. In the absence of between-study heterogeneity or the presence of trivial heterogeneity, we can consider that the mean effect size applies to all comparable populations. However, in the presence of heterogeneity, there is no common effect size that applies to all populations. As expected in the meta-analyses of this study, substantial heterogeneity (significant <i>p</i>-value and moderate and high I² value) was observed, meaning that there are other factors, apart from the ones investigated, that affect the magnitude of the intervention effect size. It would not be justifiable to measure an average intervention effect if heterogeneity was observed in the direction of the effects, with some studies showing beneficial effects and others showing the opposite. As we did not observe heterogeneity in the direction of the effect sizes, it seems reasonable and useful to estimate an average intervention effect among studies. The treatment effect varies substantially among treatments, and future studies should therefore focus on the identification of factors that can explain this variability, to inform clinicians on the type of population that may benefit best from a specific treatment."⁹⁹ (p12)
Comments	GRADE was used by the review authors.

Raiane Mamede Veloso *et al.* (2019)

Parameter	Extraction
First author and year of publication	Raiane Mamede Veloso <i>et al.</i> (2019)¹⁰⁰
Objectives	Evaluated whether the clinical performance (failure measured by eight criteria) of bulk-fill resin composites is comparable to that of conventional composites in restored permanent posterior (molars and premolars) teeth.
Participants	Permanent dentition, cavitated caries, direct restoration material Patients with direct resin restorations in permanent posterior teeth were included in the review. The authors described the participants as follows: "A total of 1,076 restorations were performed in 459 patients, and 941 restorations were evaluated. Rubber dam isolation was only reported in four studies; the remaining six studies used only cotton rolls and saliva ejectors. In one of these four studies rubber dam isolation was only employed when cotton rolls/saliva ejector were insufficient. Most studies did not report the use of a lining material. In two studies calcium hydroxide cement was used as a liner in deep cavities, and in one study calcium hydroxide cement and/or glass ionomer cement was used in deeper cavities. Regarding the bonding agent used, self-etch systems were used in both the intervention and control groups of six studies, three studies used etch-and-

Parameter	Extraction
	rinse systems, and one study used an etch-and-rinse system in the control group and a self-etch system in the intervention group. All base/flowable bulk-fill resin composites were used with a 2 mm capping of a conventional resin composite.”¹⁰⁰ (p226) The studies included in this review evaluated Class I and II direct restorations in posterior teeth. Five studies evaluated only Class II restorations. The study countries or clinical settings were not reported.
Setting/context	
Description of interventions/phenomena of interest	Intervention: The intervention was posterior teeth restored with a bulk-fill resin composite. Comparator: A comparison was performed with posterior teeth restored with a conventional resin composite. The intervention was described in the review as follows: “Bulk-fill resin composites have been designed to simplify the restorative technique because they can be placed into posterior teeth cavities in a single increment of 4–5 mm. These materials offer greater translucency, allowing greater light dissipation through the material; incorporation of more reactive photoinitiators, which enable a greater depth of cure; and include monomers that act as modulators of the polymerization reaction, achieving low polymerization shrinkage. Two types of these materials are commercially available: base and full-body bulk-fill resin composites. Base bulk-fill materials are low-viscosity resin composites and therefore are also known as flowable bulk-fill resin composites. These materials involve lower filler loading than conventional/standard microhybrid or nanohybrid resin composites, which require incremental filling. Therefore, they are used as a liner/base, followed by capping with the conventional resin composites. Full-body bulk-fill resin composites can be applied in one increment without the need for coverage or capping. Because of their viscosity, they are also referred to as sculptable or paste-like bulk-fill resin composites, allowing the reconstruction of the lost tooth structures. In addition, these materials have high inorganic filler loading and are therefore used in areas of high masticatory load.”¹⁰⁰ (p222) According to the review authors, “One [primary] study evaluated four groups: two full body/sculptable bulk-fill composites, a base/flowable bulk-fill composite covered with a conventional resin composite, and a conventional resin composite by itself. The remaining studies compared full-body/sculptable bulk-fill resin composites with conventional composites (incremental technique).”¹⁰⁰ (p226)
Databases and sources searched	The authors searched four databases up to January 2018 and without any language restrictions: MEDLINE via PubMed, Embase, the Cochrane Library, and Web of Science. The electronic search was complemented by manual searches of the following journals: <i>Journal of Orofacial Sciences</i>, <i>Operative Dentistry</i>, <i>Dental Materials</i>, and <i>Journal of Dentistry</i>. Additionally, the reference lists of the included studies were checked to identify possible relevant studies. The study protocol was registered with PROSPERO. Extraction and screening were completed in duplicate. The work was funded by CAPES. Conflicts of interest: The authors declared that they had no conflicts of interest.
Date range (years) of included studies	The included studies were published in 2010 (two studies), 2016 (two studies), and 2017 (six studies).
Number of primary studies included in the systematic review	Ten randomised controlled trials – published in 2010 (two studies), 2016 (two studies), and 2017 (six studies) – were included, nine of which were split-mouth randomised clinical trials and one of which was a parallel group randomised clinical trial. The mean follow-up time was 33.6 months (12–72 months). Five studies did not report sample size calculation. The sources of funding for primary studies were not reported.
Types of studies included	The following three criteria were used to determine study inclusion: (1) only randomised clinical trials, (2) studies with a follow-up period of at least one year, and (3) studies evaluating Class I and II direct restorations in permanent posterior teeth restored with bulk-fill and conventional resin composites. The list of excluded studies with their reasons for exclusion were provided in the text.
Country of origin of included studies	The study countries were not reported.

Parameter	Extraction
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	The authors provided the following information regarding risk of bias: "Six of the [9] included studies did not describe the randomization process. Three studies used coin tossing for randomization and one study used a random number table of the groups. None of the studies mentioned the method used for allocation concealment. Four studies were unclear about the blinding of participants and personnel, and the other studies reported that patients were blinded. Only one study [of the 9] was unclear about the blinding of outcome assessment. The incomplete outcome data domain was unclear in four studies because of unexplained reasons for participant loss. All studies had a low risk of bias regarding selective reporting. Even when the study protocol was unavailable, it was clear that the published reports clearly included all expected outcomes, including those that were prespecified."¹⁰⁰ (p228) None of the studies were at low risk of bias for randomisation, whereas nine of the ten included studies were at low risk of bias for outcome assessment. The authors reported that "the randomization procedure and allocation concealment are fundamental to the design of randomized clinical trials to avoid selection bias. Most of the included studies did not provide a full description of these steps."¹⁰⁰ (p231) The authors reported dealing with publication bias as follows: "A funnel plot was used for assessing the publication bias. The funnel plot of the studies included in this review exhibited symmetry, indicating low heterogeneity and the possible absence of publication bias."¹⁰⁰ (p228)
Method of analysis	The authors described their justification for narrative or meta-analysis as follows: "The relative risk and 95% confidence interval (CI) were calculated for each study. The data of the eligible studies were ordinal, referring to the scores for the characteristics of the restorations evaluated using the modified versions of the U.S. Public Health Service (USPHS) [criteria]. For further analysis, these data were dichotomized as either acceptable or unacceptable. The acceptable restorations were those that received the Alpha and Bravo scores. The unacceptable restorations were those that received the Charlie and Delta scores in at least one of the characteristics. Therefore, failed restorations were those that were classified as unacceptable. The I² index was used to measure the percentage of variation across studies that was due to heterogeneity, where 25% corresponded to low heterogeneity, 50% to moderate heterogeneity, and 75% to high heterogeneity. A fixed-effects model was used because no statistically significant heterogeneity was found among the studies ($p>0.10$)."¹⁰⁰ p225
Outcome assessed	The outcome assessed was survival rate (number of restorative failures based on clinical criteria such as FDI and USPHS). The studies included in this review evaluated Class I and II direct restorations in posterior teeth (molars and premolars). Five studies evaluated only Class II restorations. Evaluated outcomes were failures due to anatomical shape, marginal adaptation and discolouration, surface roughness, colour, secondary caries, loss of retention, fracture, and post-operative sensitivity. Clinical performance (failure measured by eight criteria): Atabek 2017; Alkurdi and Abboud 2016; Arhun 2010; Bayraktar 2017; Çolak 2017; Karaman 2017; Manhart 2010; van Dijken and Pallesen 2017; van Dijken and Pallesen 2016; Yazici 2017. Studies with a follow-up period of at least one year were included.
Results/findings	According to the authors, "The meta-analysis included the 10 studies selected in the systematic review. The failure rates of bulk-fill and conventional resin composite restorations were evaluated using subgroups for the classification of the bulk-fill resin composites (base/flowable and full-body/sculptable). No significant differences were observed between conventional resin composites and base/flowable (relative risk: 1.49; 95% CI: 0.69–3.25; $p=0.31$) and ($I^2=56\%$; $p=0.10$;) or full-body/sculptable bulk-fill resin composites (relative risk:: 1.89; 95% CI: 0.84–4.24; $p=0.12$) and ($I^2=0\%$; $p=0.51$)."¹⁰⁰ (p228) According to Raiane Mamede Veloso <i>et al.</i>, "The clinical performance of bulk-fill resin composites is comparable to conventional resins in direct posterior restorations. The studies included in this review reported similar results with the

Parameter	Extraction
	use of bulk-fill resin composites, regardless of type (base/flowable and full-body/sculptable)...All studies included in this review used the modified USPHS criteria, but observed variations resulted in a lack of standardization among the studies. Thus, the different analyzed aspects and various instruments and assessment criteria used hampered the comparison of the results...Similarly, the randomization procedure and allocation concealment are fundamental to the design of randomized clinical trials to avoid selection bias. Most of the included studies did not provide a full description of these steps...Sample size calculation was also not clearly described in five of the included studies...Additionally, most studies described sample size calculation inadequately. Although the absence of sample size calculation does not affect the risk of bias of clinical trials, it may result in underpowered studies that are unethical and wastes considerable resources. Small samples are unable to highlight small differences in the results...The results of the present review should be interpreted with caution because of the small number of clinical studies evaluated. Further randomized clinical trials with longer observation periods are still needed before a full recommendation of clinical protocol change [can be made] regarding direct restorations of posterior teeth with resin composites" ¹⁰⁰ (p228–231)
Significance/direction	The authors noted that "This systematic review and meta-analysis revealed that the clinical performance of bulk-fill and conventional resin composites in direct restorations of posterior teeth was similar, within a follow-up period of 12 to 72 months." ¹⁰⁰ (p231)
Heterogeneity	Regarding heterogeneity, the authors made the following statement: "The I ² index was used to measure the percentage of variation across studies that was due to heterogeneity, where 25% corresponded to low heterogeneity, 50% to moderate heterogeneity, and 75% to high heterogeneity. A fixed-effects model was used because no statistically significant heterogeneity was found among the studies ($p>0.10$)." ¹⁰⁰ (p225)
Comments	GRADE was not used by the review authors.

CADTH (2018)

Parameter	Extraction
First author and year of publication	CADTH (2018) ¹⁰³
Objectives	Evaluated the comparative efficacy of direct dental restorations made of composite resin compared with amalgam for the treatment of dental caries in posterior permanent teeth. The HRB prepared separate extraction forms for effectiveness and safety. The HRB included the Clinical Review chapter of this document. The HRB excluded the economic evaluation and patient experiences chapters, as they are not based on randomised controlled trials or cohort studies. The remaining chapters were not relevant to our brief. CADTH updated the Cochrane Review by Rasines Alcaraz <i>et al.</i> and identified one additional study that assessed efficacy from Turkey with 25 participants.
Participants	Population: Children and adults with posterior permanent teeth requiring fillings. Rasines Alcaraz <i>et al.</i> identified seven trials. Two included trials were parallel group studies involving 1,645 composite restorations and 1,365 amalgam restorations (921 participants) in the analysis. The other five included trials were split-mouth studies involving 1,645 composite restorations and 595 amalgam restorations among an unknown number of participants. Due to major problems with the reporting of the data for the six split-mouth studies, the primary analysis is based on the two parallel group trials. The exact age of participants was unclear in some studies; however, both children and adults with posterior permanent teeth requiring fillings were included. CADTH identified one additional randomised controlled trial by Kemaloglu <i>et al.</i> (2016). In this trial, 50 teeth were randomly assigned to either amalgam or composite resin restorations in 25 adult patients aged between 18 and 60 years, increasing the number to six split-mouth studies involving 1,645 composite restorations and 595 amalgam restorations in an unknown number of children

Parameter	Extraction
	and 25 adults. In Kemaloglu <i>et al.</i> , each patient had at least two carious lesions at baseline, allowing for a split-mouth design that featured each patient having at least one tooth randomised to amalgam and one tooth randomised to composite resin. Data on gender were not reported.
Setting/context	Four of the seven original trials reported their setting. Two trials were based in a university-based facility, one trial was in a community-based clinic, and another trial was in both a university- and community-based setting. The additional trial by Kemaloglu <i>et al.</i> was conducted at one dental clinic site in Turkey. The study countries were a cross-country trial in Europe, and individual country trials in Portugal, Turkey (Kemaloglu <i>et al.</i>), the UK, and the USA.
Description of interventions/phenomena of interest	Composite resin was compared with amalgam for the treatment of cavitated dental caries. Resin composites have become an aesthetic alternative to amalgam restorations and there has been a remarkable improvement in their mechanical properties to restore posterior teeth. Amalgam has been the traditional material for filling cavities in posterior teeth since the 1870s and, due to its effectiveness and cost, amalgam is still the restorative material of choice in certain parts of the world. There have been concerns over the use of amalgam restorations (fillings) relating to the mercury release in the body and the environmental impact following its disposal.
Databases and sources searched	The authors searched five databases from 1 January 2012 to 26 June 2017: the Cochrane Oral Health Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE via Ovid, Embase via Ovid, and Latin American and Caribbean Health Sciences Literature database (LILACS) via BIREME Virtual Health Library. CADTH did not apply language or date restrictions when searching the electronic databases. CADTH made small changes to the search syntax such as adding additional keywords and exploding three MeSH terms. The full electronic search strategy is provided in one appendix in the report. Grey literature (literature that is not commercially published) was identified by searching the Grey Matters checklist. Two review authors screened the abstracts; one extracted the data from each paper and a second reviewer validated the extraction, whereas Rasines Alcaraz <i>et al.</i> completed these procedures in duplicate.¹¹ One author received funding/honorariums for writing a chapter concerning human exposure to mercury for the WHO. CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.
Date range (years) of included studies	The additional trial was published in 2016. The other seven randomised controlled trials, published between 1986 and 2007.
Number of primary studies included in the systematic review	Rasines Alcaraz <i>et al.</i> identified seven trials. Two included trials were parallel group studies involving 1,645 composite restorations and 1,365 amalgam restorations (921 participants) in the analysis. The other six included trials were split-mouth studies involving 1,645 composite restorations and 595 amalgam restorations among an unknown number of participants. Due to major problems with the reporting of the data for the six split-mouth studies, the primary analysis is based on the two parallel group trials. Kemaloglu <i>et al.</i> reported that no funding or support was provided.
Types of studies included	The inclusion criteria required randomised controlled trials. A list of the studies excluded from this review and the reasons for their exclusion were reported.
Country of origin of included studies	The study countries were a cross-country trial in Europe, and individual country trials in Portugal, Turkey (additional trial), the UK, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	Based on the Cochrane Collaboration's risk of bias instrument, the seven trials were judged by Rasines Alcaraz <i>et al.</i> to be at high risk of bias. Rasines Alcaraz <i>et al.</i> judged three of the seven trials to have adequate randomisation, and no trial had blinded the outcome assessor. Publication bias was dealt with as part of the comprehensive search and considered in the GRADE assessment. CADTH judged the additional trial to be overall at high risk of bias, adequate for randomisation, and at high risk of bias for ascertainment of outcomes. CADTH did not use GRADE.

Parameter	Extraction
Method of analysis	CADTH updated the Cochrane Review by Rasines Alcaraz <i>et al.</i> (2014) to evaluate the comparative efficacy of direct dental restorations made of composite resin compared with amalgam for the treatment of dental caries in permanent posterior teeth. CADTH made some small changes to the Cochrane protocol: their population was people rather than restorations, some additional fields were added to the search, and three MeSH terms were exploded. In addition, full-text screening and extraction was completed by single reviewers, but checked by a second reviewer. GRADE was not used. CADTH completed narrative syntheses to describe the direction and size of observed effects across outcomes and studies. Following an assessment of clinical and methodological heterogeneity between studies, meta-analysis was not feasible.
Outcome assessed	Outcome: Failure rate at three years or over, fracture, secondary caries rate, adverse events Outcome by primary study: Failure rate: Two of the seven studies were parallel group trials (The Casa Pia Study of Health Effects of Dental Amalgam in Children started in 1996 and was followed up for seven years [Casa Pia 2007], and The New England Children's Amalgam Trial [NECAT 2007]), while the other five were split-mouth studies (Cunningham 1990; Hendriks 1986; Letzel 1989; Norman 1990). The data from Robinson 1988; and Kemaloglu 2016) were not used in the final analysis of failure. Reason for failure at three years or over: Fracture (Casa Pia 2007; NECAT 2007) and secondary caries (Casa Pia 2007; NECAT 2007), and separately (Cunningham 1990; Hendriks 1986; Norman 1990; Robinson 1988). Adverse events: Casa Pia 2007. Costs: No evidence.
Results/findings	Fixed-effect meta-analyses were completed as there were small numbers of trials per analysis; however, there was substantial or considerable heterogeneity. According to Rasines Alcaraz <i>et al.</i>, "There is low-quality evidence to suggest that resin composites lead to higher failure rates based on pairwise fixed-effects meta-analysis at 5–7 years (fixed-effects model; relative risk 1.89; 95% CI 1.52 to 2.35; I^2 87%; 2910 participants; 2 trials; low-quality evidence), and risk of secondary caries was higher in resin composites than in amalgam restorations at 5–7 years (relative risk 2.14; 95% CI 1.67 to 2.74; I^2 92%; 2910 participants; 2 trials; low-quality evidence)."^{11 (p18)} However, there is adequate evidence that restoration fracture is the same for both amalgam and resin composite fillings (relative risk: 0.87; 95% CI: 0.46–1.64; I^2: 0%; 2,910 participants; 2 trials; moderate-quality evidence; downgraded to low-quality evidence by the HRB). The parallel group trials indicated that resin restorations had a significantly higher risk of failure than amalgam restorations (low-quality evidence) and increased risk of secondary caries (low-quality evidence), but there was no evidence of an increased risk of restoration fracture (moderate-quality evidence downgraded to low-quality evidence by the HRB). The results from the split-mouth trials (which included adults) were consistent with those of the parallel group trials. CADTH reported that the additional study, Kemaloglu <i>et al.</i> (2016), reported zero events of restoration failure and secondary caries in either treatment arm at three years follow-up, or 100% survival in both arms. CADTH stated that "Because of methodological and clinical heterogeneity, incorporation of the data from the 2016 split-mouth RCT [randomised controlled trial] identified in the update was not possible with data from the 2014 Cochrane systematic review. The findings from the 2016 split-mouth RCT appear to contrast with those of the 2014 Cochrane systematic review; although, there are several cautions against overinterpreting the findings of the individual study, most notably the small sample size and relatively short follow-up duration (i.e. the minimum sufficient follow-up was deemed to be three years) in the newer study."^{103 (p36)} GRADE was not applied to the study, but given the study limitations, the evidence added is of very low quality.
Significance/direction	The evidence from the Cochrane Review stands.
Heterogeneity	"Because of methodological and clinical heterogeneity, incorporation of the data from the 2016 split-mouth RCT [randomised controlled trial] identified in the

Parameter	Extraction
	update was not possible with data from the 2014 Cochrane systematic review." ¹⁰³ p36
Comments	GRADE was not used by the review authors. All eight trials were judged to be at high risk of bias. Four (57%) of the seven trials had adequate randomisation, and no trial had blinded the outcome assessor. Methodological and clinical heterogeneity prevented pooled analysis of all eight trials. The quality of the review was rated as moderate using AMSTAR 2. The HRB grades the quality of the evidence as low for the different outcomes.

Parameter	Study 2 extraction
First author and year of publication	CADTH (2018)¹⁰³
Objectives	Evaluated the comparative safety of dental restorations made of composite resin compared with amalgam in children and adults (separate extraction forms for effectiveness and safety).
Participants	Permanent teeth, cavitated caries, safety of restoration materials. Population: Children and adults with posterior permanent teeth requiring fillings. The safety studies included 1,081 patients whose ages ranged from six to 60 years. Males comprised approximately 50% of the study participants.
Setting/context	The study countries were Portugal, Turkey, and the USA.
Description of interventions/phenomena of interest	Composite resin was compared with amalgam for the treatment of cavitated dental caries. Resin composites have become an aesthetic alternative to amalgam restorations and there has been a remarkable improvement in their mechanical properties to restore posterior teeth. Amalgam has been the traditional material for filling cavities in posterior teeth since the 1870s and, due to its effectiveness and cost, amalgam is still the restorative material of choice in certain parts of the world. There have been concerns over the use of amalgam restorations (fillings) relating to the mercury release in the body and the environmental impact following its disposal.
Databases and sources searched	CADTH searched five databases from 1 January 2012 to 26 June 2017: the Cochrane Oral Health GroupsTrials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE via Ovid, Embase via Ovid, and Latin American and Caribbean Health Sciences Literature database (LILACS) via BIREME Virtual Health Library. CADTH did not apply language or date restrictions when searching the electronic databases. The full electronic search strategy is provided in an appendix of the report. Grey literature was identified by searching the Grey Matters checklist. Two review authors screened the abstracts; one extracted the data from each paper and a second reviewer validated the extraction. One author received funding/honorariums for writing a chapter concerning human exposure to mercury for the WHO. CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.
Date range (years) of included studies	The systematic review assessing the safety of amalgam compared with resin composite included three randomised controlled trials (NECAT 2007–2012, Casa Pia 2007–2009, and Kemaloglu <i>et al.</i> 2016) published in ten papers.
Number of primary studies included in the systematic review	The systematic review assessing the safety of amalgam compared with resin composite included three randomised controlled trials (NECAT 2007–2012, Casa Pia 2007–2009, and Kemaloglu <i>et al.</i> 2016) published in 10 papers.
Types of studies included	The inclusion criteria allowed randomised controlled trials, controlled trials, and prospective cohort studies to ensure that all safety concerns were collated. A list of the studies excluded from this review and the reasons for their exclusion were reported.
Country of origin of included studies	The study countries were Portugal, Turkey, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	The three trials were judged to have an overall high risk of bias. An overall pattern was that reports of the New England Children's Amalgam Trial (NECAT, one trial group) generally had lower risk of bias scores compared with those from the Casa Pia (the second trial group) or Kemaloglu <i>et al.</i> trials. Overall, two of the three trials had adequate randomisation and one trial had adequate blinding for

Parameter	Study 2 extraction
	outcome assessment. Assessments identified a high risk of performance bias in all of the studies, in addition to high risks of bias in other domains that varied across trials.
Method of analysis	Narrative syntheses were undertaken to describe the direction and size of observed effects across outcomes and studies.
Outcome assessed	Outcome by primary study: Toxicity or sensitivity outcomes (no predetermined time frame): NECAT 2007–2012; Casa Pia 2007–2009; Kemaloglu <i>et al.</i> 2016.
Results/findings	Safety: Toxicity Statistically significant differences in urinary mercury excretion between patients receiving amalgam and those receiving composite resin at follow-up time points of up to 5–6 years were reported in two large trials. Unadjusted urinary mercury levels were no longer significantly different between treatment groups at 7 years follow-up in one of the large trials, suggesting, according to CADTH, that mercury exposure from dental amalgam restorations may diminish over time. These two large trials found no differences between patients receiving amalgam and those receiving composite resin in three of four measures of renal function examined, but in one large trial, the prevalence of microalbuminuria was found to be statistically significantly higher in the amalgam-treated group at three and five years follow-up; however, the other large trial did not report this finding. Four of five measures of physical development in one of the large trials indicated no differences between patients receiving amalgam and those receiving composite resin. However, a subgroup analysis of females at one study site had a statistically significantly greater probability of menarche initiation in the amalgam group compared with the composite resin group. Ten of 12 measures of neuropsychological function in one large trial identified no differences between patients receiving amalgam and those receiving composite resin; one subscale from each of the remaining two measures suggested a statistically significant difference – one favouring the amalgam (Wide Range Assessment of Memory and Learning) and the other (Trail Making Test – Part B: time to complete) favouring composite resin. In an evaluation of psychosocial outcomes from one of the two large trials, two (competence and externalising behaviour composite scales) of four sub-scores from a child behaviour checklist for both the primary and secondary measures indicated no statistically significant difference between patients receiving amalgam and those receiving composite resin, whereas the other two sub-scores (internalising behaviour and problem behaviour) for both measures did indicate statistically significant differences – all of which positively favoured the amalgam group over the composite resin group. The psychosocial outcomes indicated no statistically significant difference between groups in two of the four global scores (i.e. school and clinical maladjustment). However, the remaining two global scores (personal adjustment and emotional symptoms indices) indicated a statistically significant difference between the two groups, once again favouring the amalgam group. No statistically significant differences between treatment groups were observed in evaluations of neurological symptoms, immune function, and urinary porphyrin excretion. Safety: sensitivity Post-operative sensitivity did not differ between amalgam and composite resin restorations at follow-ups between 2 and 52 weeks, although a statistically significant difference was reported at 36 months follow-up in two trials, favouring the composite resin group. The NECAT authors did not comment on the clinical significance of this latter finding but discussed the variability in the bonding materials used as these may play a role in post-operative sensitivity.
Significance/direction	The evidence from the Cochrane Review stands.
Heterogeneity	There was no meta-analysis completed so the authors did not examine heterogeneity.
Comments	GRADE was not used by the review authors. The three trials were judged to have an overall high risk of bias. Two (66%) of the three trials had adequate randomisation and one (33%) trial had adequate

Parameter	Study 2 extraction
	blinding for outcome assessment. Heterogeneity was not discussed. The quality of the review was rated as low using AMSTAR 2 as heterogeneity was not measured or discussed. The HRB grades the quality of the evidence as low for the different outcomes.

de Castro Kruly *et al.* (2018)

Parameter	Extraction
First author and year of publication	de Castro Kruly <i>et al.</i> (2018) ¹⁰¹
Objectives	Compared the clinical behaviour (marginal integrity/adaptation, marginal discolouration, recurrent caries, retention of composite restorations, and post-operative sensitivity) of restorations performed with low polymerisation shrinkage resin composite (bulk fill) resins in comparison with methacrylates-based (conventional) resin composite (in humans with Class I or II restorations in the permanent dentition).
Participants	Permanent dentition, cavitated caries, dental restoration (direct) Population: Humans with Class I or II restorations in the permanent dentition The 21 randomised controlled clinical trials, published between 2006 and 2016, included 1,724 restorations. The age, gender, and number of participants were not reported. The follow-up was 12 months.
Setting/context	The studies were completed in Austria, Belgium, Brazil, Canada, Denmark, Egypt, Spain, Sweden, Turkey, and the USA. The study settings were not reported.
Description of interventions/phenomena of interest	The intervention was low polymerisation shrinkage resin composite (bulk fill) resins. Resin materials with new monomeric compositions and modifications do not contain as a main monomer the BisGMA or traditional di- or methacrylates, and new monomers and modified monomers containing composites allow dentists to increase the depth of cure, modify the incremental restorative technique, and reduce the volumetric shrinkage and/or polymerisation stress. In order to minimise the polymerisation shrinkage stress problem, recent changes in resin composites have focused on the polymer matrix. As a result, new resin composites with modified monomers, such as the ormocer and silorane resins, have been developed in an attempt to reduce long-term clinical problems caused by polymerisation shrinkage stress. Single-increment composites (bulk fill resins) have also been developed to facilitate clinicians' work, reduce working time, and simplify the restorative procedure. Laboratory studies show that resin composites with modified monomers present less volumetric polymerisation shrinkage than the methacrylate resins. Comparator: Methacrylate resin composites (conventional)
Databases and sources searched	The authors searched five electronic databases (PubMed, Web of Science, Scopus, Latin American and Caribbean Health Sciences Literature database (LILACS) and Embase) using a predefined search strategy up to 2016 (not stated, so we have used the date of most recent trial as a proxy). No filter was used for specific languages. The reference lists of selected articles were screened for additional studies, and authors were contacted for additional studies or information when necessary. This systematic review was registered with PROSPERO. Two independent reviewers screened the articles to identify studies for inclusion and extracted the data. This study was supported by the Brazilian Coordination of Higher Education National Council for Scientific and Technological Development in Brazil. The authors declared no competing interests exist.
Date range (years) of included studies	The 21 randomised controlled clinical trials included were published between 2006 and 2016.
Number of primary studies included in the systematic review	The 21 randomised controlled clinical trials included, published between 2006 and 2016, included 1,724 restorations. The funding sources for primary studies were not reported.
Types of studies included	Randomised controlled clinical trials with follow-up after at least six months were eligible for inclusion. The authors provide the reasons for excluding studies but not a listing of excluded studies.
Country of origin of included studies	The studies were completed in Austria, Belgium, Brazil, Canada, Denmark, Egypt, Spain, Sweden, Turkey, and the USA.

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Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	Ten of the 21 studies were judged to be at high risk of bias, and 11 had an unclear risk of bias. None had a low risk of bias. Thirteen studies were judged to have adequate randomisation and 14 had adequate blinding of outcome assessment. The authors comment that the figure presenting the results of the risk of bias assessment "indicate an overall low risk of bias"^{101 (p4)} for the review. "Because of the nature of the included studies, the quality of the evidence was considered good, and the risk of bias was low. Blinding of participants and personnel involved in the study (performance bias) was the most common problem in the selected studies, resulting in the largest number of unclear and high risk of bias."^{101 (p12)} The authors comments contradict their assessment of bias. Using the Cochrane Collaboration criteria, the HRB judges these trials to be at high or unclear risk of bias. Publication bias was not measured.
Method of analysis	Data on the clinical performance of restorations conducted with composites containing new modified monomers and methacrylate resin composites evaluated were: marginal integrity/adaptation, marginal discolouration, recurrent caries, retention of resin restorations, and post-operative sensitivity. RevMan software was used to perform the fixed-effects pairwise meta-analysis and create the comparative tables for each clinical criterion by follow-up assessment periods. Statistical heterogeneity is measured in the meta-analysis printouts but not discussed.
Outcome assessed	Outcome by primary study: Clinical performance which indicates success or failure of restorations: Marginal integrity/adaptation, marginal discolouration, recurrent caries, retention of composite restorations, and post-operative sensitivity At least six months follow-up (predetermined) 12 and 24 months actual time frame Bayraktar 2016; Gasparello 2016; Karaman 2016; Schmidt 2015; Attia 2014; Beck 2014; El-Eraky 2014; Mahmoud 2014; Santos 2014; van Dijken 2014; Walter 2014; Yazici 2014; Baracco 2013; Efes 2013; Goncalves 2013; Baracco 2012; Schmidt 2011; Bottenberg 2009; van Dijken 2009; Bottenberg 2007; Efes 2006.
Results/findings	The authors reported that marginal adaptation at twelve months was better in the conventional resin composite group than in the bulk fill resin composite group . (OR: 1.77; 95% CI: 1.25–2.50; I²: 0%; 2,280 restorations; 18 trials; high-quality evidence assigned by review authoes but low-quality evidence assigned by HRB). However marginal adaptation at 24 months was similar in both the conventional resin composite group and the bulk fill resin composite group (OR: 1.46; 95% CI: 0.92–2.33; I²: 0%; 9,557 restorations; 8 trials) There was no level of evidence assigned although this seems to the HRB to indicate low-quality evidence of no difference between bulk fill and conventional resin composite. There was no difference in marginal discolouration at 12 or 24 months (OR at 12 months: 1.53; 95% CI: 0.98–2.41; I²: 0%; 2,082 restorations; 16 trials; low-quality evidence assigned by HRB of no difference between bulk fill and conventional resin composite and OR at 24 months: 1.08; 95% CI: 0.64–1.84; I²: 0%; 482 restorations; 7 trials; low-quality evidence assigned by HRB of no difference between bulk fill and conventional resin composite). There was no difference in the incidence of secondary caries following bulk fill and conventional resin composite at 12 months (OR at 12 months: 1.51; 95% CI: 0.64–3.57; I²: 0%; 2,087 restorations; 16 trials; low-quality evidence assigned by HRB of no difference between bulk fill and conventional resin composite). There was no difference in retention rates of bulk fill and conventional resin composite at 12 months: (OR: 0.83; 95% CI: 0.33–2.09; I²: 0%; 1,834 restorations; 13 trials; low-quality evidence assigned by HRB of no difference between bulk fill and conventional resin composite). There experience of post-operative sensitivity was similar in bulk fill and conventional resin composite at 12 months (OR: 1.65; 95% CI: 0.71–3.81; I²: 0%; 970 restorations; 13 trials; low-quality evidence of no difference).

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	The authors concluded that “The scientific evidence that emerged from this review of randomized controlled clinical trials indicates that restorations conducted with low polymerization shrinkage composites, such as silorane, ormocer and bulk-fill type showed clinical performance similar to restorations with conventional resin composites.” ¹⁰¹ (p15)
Significance/direction	Results listed by outcome.
Heterogeneity	Statistical heterogeneity is measured in the meta-analysis printouts but not discussed. However, it is low and does not affect the findings.
Comments	GRADE was used by the review authors. All 21 studies were judged to be at high or unclear risk of bias. Thirteen studies (62%) were judged to have adequate randomisation and 14 (67%) had adequate blinding of outcome assessment. The quality of the review was rated as low using AMSTAR 2 as the authors could not control for risk of bias in the meta-analysis. The review authors reported the grade of evidence as high, however, the HRB grades the quality of the evidence as low for the different outcomes after taking account of bias in the primary trials and the quality of the systematic review.

Monsarrat *et al.* (2017)

Parameter	Extraction
First author and year of publication	Monsarrat <i>et al.</i> (2017) ¹⁰²
Objectives	Evaluated the clinical performance (such as survival rates or quality of restorations) of the first generation of ormocer-based fillings against those of conventional composite restorations and glass ionomer restorations; and (2) explored the influence of different clinical factors and the impact of the quality of studies on published results.
Participants	Permanent dentition, cavitated caries, direct restoration material Patients or teeth allocated to ormocer-based or conventional materials. The mean age of participants ranged from 20 to 53 years. Females were the majority of participants in seven of the eight included studies. The rubber dam formed the method of isolation in four studies and the cotton roll formed the method of isolation in four studies. Seventy-five per cent of the eight included trials concerned Class I/II restorations.
Setting/context	The study countries were Belgium, Denmark, Egypt, Germany, Italy, Sweden, and Turkey (two studies). The studies clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: Ormocer-based material. Comparator: Control materials could be conventional composite (CC), polyacid-modified resin composite (CP), silorane (SI), or glass ionomer (GI). The authors provided the following definition of the intervention: “Ormocer is the acronym for ORganically MODified CERamic. These materials were developed by the Fraunhofer Institute for Silicate Research (ISC) and have been commercialized in dentistry since 1998. They are composed of inorganic-organic co-polymers with inorganic silanated filler particles. The solution and gelation process (sol-gel process) induces polymerization of multi-functional urethane and thioether oligo (meth)acrylate alkoxysilanes, producing a silica glass by hydrolysis of the alkoxy groups followed by water and alcohol polycondensation. This results in a matrix of long inorganic silica chain backbones with organic lateral chains, able to react during curing using conventional photoinitiators. The larger size of the monomer molecules may reduce polymerization shrinkage, wear, and leaching of monomers, and the materials are expected to combine the advantages of both organic polymers (e.g. flexibility and impact resistance) and inorganic materials (e.g. thermal stability, mechanical strength and chemical resistance)...A higher toxicity of this first generation of ormocers is suspected...the ormocer matrix seemed to be sensitive to degradation processes, with greater degradation of optical properties, particularly in acidic media.”¹⁰² (p213)
Databases and sources searched	The authors searched seven databases: the Cochrane Central Register of Controlled Trials (CENTRAL), the Health Technology Assessment (HTA) database, the Database of Abstracts of Reviews of Effects (DARE), Ovid MEDLINE In-Process and Other Non-Indexed Citations (via Ovid), MEDLINE (1950 to present) (via

Parameter	Extraction
	PubMed), BIOSIS (1997 to present) (via Ovid), and LILACS (via the Virtual Health Library (VHL) search form) (1982 to present). There was no restriction on language of publication. The last search was conducted on 1 August 2017. Reference lists of query studies were inspected to identify any additional relevant published or unpublished data. For literature that is difficult to trace (grey literature), the authors sought out unpublished and ongoing trials by searching the WHO's International Clinical Trials Registry Platform, which provides access to several trial registries including ClinicalTrials.gov and the International Standard Randomised Controlled Trial Number Register. They also searched for conference proceedings from the International Association for Dental Research database and the Academy of Dental Materials. Google Scholar was also queried to identify additional references, such as theses, using the same search strategy. The authors did not report preparing or registering a protocol. Extraction and screening were completed in duplicate. Funding: This study was supported by funding from the Midi-Pyrénées Region, Paul Sabatier University, and the research platform of Toulouse Dental Faculty. Conflicts of interest: Conflicts of interest were not reported.
Date range (years) of included studies	The included studies were published from 2006 to 2015.
Number of primary studies included in the systematic review	Eight unique studies, published from 2006 to 2015, were included. The studies were clinical trials, but the overall description of the study designs is inadequate. Funding: In two studies, funding was provided by an industrial company responsible for only one composite product, and the studies were therefore classified as having a high risk of bias.
Types of studies included	Non-randomised and randomised controlled clinical trials were eligible for inclusion. A list of excluded studies with their reasons for exclusion was not reported
Country of origin of included studies	The study countries were Belgium, Denmark, Egypt, Germany, Italy, Sweden, and Turkey (two studies).
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	All eight studies had a high (n=4) or unclear risk of bias (n=4). Six of the eight studies had a low risk of bias for randomisation and five had a low risk of bias for outcome ascertainment. The authors provided the following comment on the effect that the risk of bias had on the quality of the evidence: "Quality assessment determined that 1 study did not provide details about randomization or was not randomized at all. In 2 studies, funding was provided by an industrial company responsible for only one composite product and the studies were therefore classified as having high risk of bias. A performance or detection bias was identified in only one study. For attrition bias, no studies were classified as high risk, but 2 studies were considered as having unclear risk of bias. The sensitivity analysis performed did not reveal significant difference between randomized and non-randomized studies or between studies with at least one high risk of bias and the others, and the industrial funder of studies did not significantly influence the results obtained."¹⁰² (p215) Publication bias was not reported on in the review.
Method of analysis	The authors stated that "The restoration was considered as the statistical unit. Split-mouth and parallel studies were both included. For each study, event incidence rates were calculated as the total number of events divided by the total restoration exposure time in years. For each study, the last time point was considered. The number of events was considered to follow a Poisson distribution for a given sum of exposure years. Consequently, a multivariate random-effects Poisson's regression (metafor R package) was used to obtain a summary estimate, either for global results or subgroup analyses (according to the brand of ormocer or type of restoration). Sensitivity analyses were also performed using such multivariate regression to investigate whether event rates were influenced by the factors mentioned above (age, gender, isolation method, number of restorations per patient). Survival curves were built from the data for all time points of each study to compare them between ormocers and other biomaterials."¹⁰² (p215)

Parameter	Extraction
Outcome assessed	Failure of a restoration was defined as the need to repair, remove, or replace it. Clinical performance (such as survival rates or quality of restorations): Bottenberg 2007/2009; Demirci 2015; dall'Orologio 2014; Mahmoud 2013; Schirrmeyer 2006 and 2009; Schmidt 2011 and 2015; van Dijken 2011 and 2015; Yaman 2014.
Results/findings	Ormocer compared with the other biomaterials According to the authors, "There was no difference in the quality of restorations at baseline, whatever the outcome considered, when ormocer restorations were compared to those with other composites ($p>0.05$, data not shown). No trial reported data on deciduous teeth. Although non-significant, a different downward trend was observed for ormocer compared to other composites when the cumulative survival rate curve was built: the global failures were higher for ormocers (0.22 [95% CI: -0.16 to 0.61]. Subgroup analysis was conducted to compare failure rates of the different types of ormocers with those of other composites. Ceram X and Admira did not exhibit significant differences of global success for Class I/II restorations, even if there was a trend of a better behavior of Ceram X. Subgroup analyses did not reveal significant differences per location of restorations: the log incidence rate ratio was 0.13 [95% CI: -0.88 to 1.14] and 0.24 [95% CI: -0.18 to -0.66] for Class V and Class I/II restorations, respectively. The heterogeneity could be considered as insignificant. For Class I/II restorations, a significantly higher failure rate due to sensitivity was observed for ormocer-based materials than for other composites (0.76 [95% CI: 0.15 to 1.37])." ^{102 (p215)} Sensitivity analyses: Study and restoration characteristics The authors stated that "While no factor emerged to explain global failures, an increase of age, an increase of the proportion of females and a decrease of the number of restorations per patient were associated with fewer marginal adaptation failures for ormocers in Class I/II obturations." ^{102 (p215)}
Significance/direction	Authors' overall conclusion In conclusion, the authors noted that "This systematic review and meta-analysis does not identify any clear advantages in using the first generation of ormocer-based fillings rather than conventional composites. On the contrary, their clinical behavior appeared to be worse, in particular after long-term aging." ^{102 (p218)}
Heterogeneity	According to Monsarrat <i>et al.</i> , "the I^2 statistic was used to quantify the amount of heterogeneity as probably not important (0%–40%), moderate (30%–60%), substantial (50–90%) or considerable (75%–100%). Meta-regression, subgroup and sensitivity analyses were planned to explain such statistical heterogeneity and determine whether difference in the efficacy of ormocer restorations compared to other materials was influenced by methodological factors (such as risk of bias) and/or clinical factors (variability in the participants and interventions)." ^{102 (p214)}
Comments	The authors noted that a limitation to their review was that "almost all the studies failed to report how they computed sample size, and how they took the specificity of split-mouth designs into account (with the complexity of the number of teeth to be treated in the same mouth). Both superiority and non-inferiority trials should report how sample sizes were calculated. The lack of evidence may be linked to underpowered studies and any evidence about a putative equivalence between ormocer and conventional composite should be treated with caution." ^{102 (p218)}

Hayes *et al.* (2016)

Parameter	Extraction
First author and year of publication	Hayes <i>et al.</i> (2016) ¹⁰⁵
Objectives	Compared the clinical performance of restorative materials for the treatment of root caries in the permanent teeth of adult patients.
Participants	Permanent dentition, cavitated caries, direct restorations. Population: Adult participants (aged over 18 years) with active root caries (Class V) were included. Five trials published between 1990 and 2011 including 269 adult participants (629 restorations) were included in the review. Forty-four per cent were male. Four studies involved middle-aged to older adults, including post-radiotherapy

Parameter	Extraction
	xerostomic individuals who were prescribed fluoride gel for home use. One study included elderly nursing home residents. The remaining study did not provide a detailed description of the participants' health conditions
Setting/context	The study countries were Belgium, Canada, China, and the USA. Four studies involved middle-aged to older adults, including post-radiotherapy xerostomic individuals who were prescribed fluoride gel for home use. One study included elderly nursing home residents. The remaining study did not provide a detailed description of the participants' health conditions or setting.
Description of interventions/phenomena of interest	Studies that compared different types of dental restorative materials were considered. Those that solely compared different techniques of placing the same material were not included. Glass ionomer cement, resin-modified glass ionomer cement, resin composite, and amalgam were the restoration materials examined. Three of the studies also prescribed sodium fluoride gel for participants.
Databases and sources searched	Three electronic databases – PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL) – and the grey literature database OpenSIGLE were searched. The three scholarly databases were searched for studies published up to and including 8 January 2014, with no language restriction. Basic search terms were provided. The preparation of a protocol is not mentioned. Duplicate screening and extraction were completed. The source of funding for the review was not stated and conflicts of interest were not declared.
Date range (years) of included studies	The five included trials were published between 1990 and 2011.
Number of primary studies included in the systematic review	Five trials published between 1990 and 2011 including 269 adult participants (629 restorations) were included in the review. The funding sources for primary studies were not stated.
Types of studies included	Studies that compared two or more restorative materials in the restoration of carious lesions on root surfaces were included. All randomised controlled trials and non-randomised controlled trials were eligible for inclusion. The reason for this decision was not explained. The excluded articles and reasons for exclusion were not reported.
Country of origin of included studies	The study countries were Belgium, Canada, China, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included studies.
Appraisal rating	Using Cochrane guidelines, all five studies were judged as having a high risk of bias. Using the authors' adapted guidelines, three studies were found to be at low risk of bias and two were found to be at high risk of bias. Three of the five studies were judged adequate for randomisation and for blinding of outcome assessment. Publication bias was not addressed.
Method of analysis	Clinical heterogeneity was assessed by examining the characteristics of the studies, the similarity between the types of participants, the interventions, and the outcomes as specified in the criteria for included studies. Statistical heterogeneity was assessed using a chi-square test and the I^2 statistic, where I^2 values of 30–50% indicate moderate to high statistical heterogeneity, and values of 50–90% indicate substantial heterogeneity. Following assessment of heterogeneity, where possible, it was planned to perform a meta-analysis and calculate weighted mean differences using the Review Manager 5 software programme. A preliminary evaluation of the included papers showed considerable heterogeneity in study populations and study design. Due to the clinical heterogeneity between studies, a meta-analysis was not appropriate and a descriptive analysis was used.
Outcome assessed	Studies that reported cumulative failure rates and/or point in time failure rates were eligible for inclusion. Three of the studies prescribed sodium fluoride gel for recipients in addition to the restorative material. Outcome by primary study: Both failure rate and secondary caries rate: De Moor 2011; Lo 2006; McComb 2002; Wood 1993; Levy and Jensen 1990.

Parameter	Extraction
	Time frame 12 and 24 months (not predetermined)
Results/findings	The analysis was a descriptive analysis of each individual study rather than a combined synthesis of the studies. However, the discussion provides a synthesis-like section covering failure rates and failure due to marginal caries, and the HRB reports this synthesis. Three of the studies included in this review evaluated resin composite restorations. Resin composite is more technique sensitive than glass ionomer cement, and moisture control can be challenging close to the gingival margin. Many root carious lesions also extend subgingivally. Root carious lesions often exhibit mixed cavity margins positioned in enamel as well as the dentine, and it is well-documented that the bond between resin composite and dentine is not as strong as the bond between resin composite and enamel. None of the three studies in this review applied a rubber dam when placing the restorations, and one did not acid etch the enamel prior to applying the bonding agent. Resin composite displayed lower failure rates (17% at 12 months and 73% at 24 months) than conventional glass ionomer cement (36% at 12 months and 82% at 24 months) in three of the five studies that could be combined, but higher rates of failure due to marginal caries (5% at 12 months and 22% at 24 months), than conventional glass ionomer cement (2% at 12 months and 4% at 24 months). The very high failure rates in glass ionomer cement were attributed to concurrent use of a mildly acidic (pH 5.8) gel. The review authors conclude that “there is insufficient evidence to recommend any specific material for routine use in the restoration of root carious lesions. There is a need for further research in this area as there are insufficient good quality randomised clinical trials currently available to guide practitioners. In particular, there is a need to evaluate restorative materials in a more generalised population, as many of the studies included in this systematic review were confined to post-radiation, xerostomic patients.”^{105 (p306)}
Significance/direction	Results listed by outcome.
Heterogeneity	The authors conducted a preliminary evaluation of the included papers that found considerable heterogeneity in study populations and study design. Due to the clinical heterogeneity between studies, a meta-analysis was not appropriate and a descriptive analysis was employed.
Comments	GRADE was not used by the review authors. The review included both randomised and non-randomised trials. All five studies were judged as having a high risk of bias. Three (67%) of the five studies were judged adequate for randomisation and for blinding of outcome assessment. Due to the clinical heterogeneity between studies, a meta-analysis was not appropriate and a descriptive analysis was employed. The quality of the review was rated as moderate using AMSTAR 2. The HRB grades the quality of the evidence as low for the different outcomes.

Moraschini *et al.* (2015)

Parameter	Extraction
First author and year of publication	Moraschini <i>et al.</i> (2015)¹³
Objectives	Compared the failure rates of amalgam and composite resin in occlusal and occlusoproximal restorations in posterior permanent teeth.
Participants	Permanent dentition, cavitated caries, direct restorations Population: Posterior permanent teeth The number of participants in the studies ranged from 27 to 472 and had a mean age of 21.6 years; the participants appear to be young adults. Gender was not reported.
Setting/context	The study countries and settings were not provided.
Description of interventions/phenomena of interest	Intervention: Composite resin restorations in occlusal and occlusoproximal posterior permanent teeth Comparator: Amalgam posterior restorations in the same types of permanent teeth. According to Moraschini <i>et al.</i>, “although amalgam restorations still have the highest functional durability, its use has been questioned in recent decades due to the incorporation of mercury to the metal alloy. In addition, the need for more dental

Parameter	Extraction
	preparation, necessary to promote greater restoration retention, makes amalgam questionable for conservative dentistry. For these reasons, the use of composite resins has been increasing throughout the world for direct posterior teeth restorations...The most frequent reason for failure [in composite resins] is recurrent or secondary marginal restoration caries, thus indicating possible failures in the adhesion process. On the other hand, amalgam restorations reduce the possibility of secondary caries over time by forming oxides in the margin of the cavities as a result of the natural corrosion of the material, mainly in alloys with high copper content."¹³ (p1044)
Databases and sources searched	An electronic search without restriction on the dates or languages was performed in three databases (PubMed/MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), and Web of Science) up until March 2015. A search strategy is provided in a table in the report. Authors were contacted for additional study details and updates. There is no mention of completing a protocol for the review. Literature screening was completed by two independent reviewers. The number of reviewers who extracted data was not presented. The source of funding for the review was not reported. There is no declaration of conflicts of interest.
Date range (years) of included studies	Eight studies published between 1992 and 2013 were included in this review.
Number of primary studies included in the systematic review	Eight studies published between 1992 and 2013 were included in this review. Five prospective studies, one retrospective cohort study, and two randomised controlled trials were included. The sources of funding for primary studies were not reported.
Types of studies included	Randomised controlled trials, controlled clinical trials, and prospective and retrospective cohort studies were included in this review. The eligibility criteria included clinical trials in humans with follow-up after at least 12 months comparing the failure rates between occlusal and occlusoproximal amalgam and composite resin restorations. After careful full-text reading, 13 studies were excluded because they did not fit the eligibility criteria of this review. The reasons for exclusion were provided but there is no list of excluded studies.
Country of origin of included studies	The study countries were not provided.
Appraisal instruments used	The Newcastle-Ottawa Scale was used to assess the primary studies.
Appraisal rating	Based on the Newcastle-Ottawa Scale, where the maximum score assigned to a study is nine stars/points (highest level of scientific evidence), all eight included studies had a score higher than six and were classified as high quality. None of the trials was representative of a defined population. All studies scored positively for assessment of outcome. The funnel plot showed no asymmetry when the failure of the restorations was analysed, indicating a low probability of publication bias.
Method of analysis	The binary variables (failure of restorations, secondary caries, and fractures) of the included studies were analysed using meta-analysis when at least two studies analysed the same data types. The estimate of the effects of intervention was expressed as risk ratio (relative risk) with a CI of 95%. The inverse-variance method was used as a random-effects model or fixed-effects model. The I^2 statistic was used to express the percentage of heterogeneity of the studies. Values up to 25% were classified as low heterogeneity, and values of 50% and 70% were classified as medium and high heterogeneity, respectively. When significant heterogeneity was found ($p < 0.10$), the results of the random-effects model were validated. When low heterogeneity was observed, the fixed-effects model was employed. The level of statistical significance was set at $p < 0.05$. Publication bias was graphically explored through a funnel plot. Asymmetry in a funnel plot can indicate possible publication bias. The data were analysed using the statistical software Review Manager (version 5.2.8).
Outcome assessed	Outcome: Failure rate, longevity, fracture, and secondary caries Time frame: Follow-up after at least 12 months Outcome by primary study:" Restoration failure (proxy for longevity): Johnson 1992; Mjor and Mokstad 1993; Collins 1998; Mair 1998; Wilson 2002; Bernardo 2007; Levin 2007; Kim 2013. Secondary caries: Mjor and Mokstad 1993; Collins 1998; Bernardo 2007; Levin 2007.

Parameter	Extraction
	Fracture: Johnson 1992; Mjor and Mokstad 1993; Collins 1998; Wilson 2002; Bernardo 2007; Levin 2007.
Results/findings	The approach to meta-analysis is adequate for its time. No sensitivity or subgroup analyses were planned. According to Moraschini <i>et al.</i>, “this systematic review revealed that occlusal and occlusoproximal amalgam posterior restorations have greater clinical longevity when compared to composite resin restorations...The results of this meta-analysis were expressed as RR (relative risk), a statistical analysis often used in binary results, which is defined as the probability of an event to occur. Regarding restoration failures, this random-effects meta-analysis indicated a relative risk of 0.46 (95% CI: 0.28–0.78; I² 78%; 3,486 restorations; 7 trials;) in favour of amalgam, i.e. the composite resin restorations have a 54% higher probability of failure when compared to amalgam restorations”.¹³ (p1048–1049) The authors acknowledge the considerable heterogeneity in this meta-analysis but do not state how it affects the results. “The presence of secondary caries was significantly higher in composite resin restorations”¹³ (p1048–1049) with a relative risk of 0.23 in favour of amalgam (95% CI: 0.18–0.30; I²: 1%; 2,742 restorations; 4 trials; fixed-effects model). The evidence is inconclusive in comparing amalgam with composite restorations regarding fractures as, according to Moraschini <i>et al.</i>, “with regard to fractures, there was no statistically significant difference between the two materials...indicating a lower sensitivity of the posterior restorations to fracture when compared to recurrent caries.”¹³ (p1049) The results were: relative risk: 1.24; 95% CI: 0.71–2.16; I²: 0%; 2,894 restorations; 5 trials; fixed-effects model. The authors combined randomised and non-randomised trials in their meta-analysis and had considerable statistical heterogeneity in their analysis of failure outcome. These findings question the validity of the study.
Significance/direction	Low-quality evidence in favour of amalgam.
Heterogeneity	The authors acknowledge the considerable heterogeneity but do not state how it affects the results. No sensitivity or subgroup analyses were planned.
Comments	GRADE was not used by the review authors. The review included randomised controlled trials, controlled clinical trials, and prospective and retrospective cohort studies. None of the trials was representative of a defined population although studies scored positively for assessment of outcome. The authors acknowledge the considerable heterogeneity but do not state how it affects the results. Randomised and non-randomised trials were pooled in the meta-analysis and no sensitivity or subgroup analyses were completed. The quality of the review was rated as critically low using AMSTAR 2 as the authors did not address bias or heterogeneity in the analysis or discussion. The HRB grades the quality of the evidence as very low for the different outcomes.

Rasines Alcaraz *et al.* (2014)

Parameter	Extraction
First author and year of publication	Rasines Alcaraz <i>et al.</i> (2014) ¹¹ (Cochrane Review)
Objectives	Compared the restoration failure of direct composite resin fillings with amalgam fillings for permanent posterior teeth.
Participants	Permanent teeth, cavitated caries. direct restorations Population: Children and adults with permanent teeth at the back of the mouth that required fillings. Two included trials were parallel group studies involving 1,645 composite restorations and 1,365 amalgam restorations (921 participants) in the analysis. The other five included trials were split-mouth studies involving 1,620 composite restorations and 570 amalgam restorations among an unknown number of participants. Due to major problems with the reporting of the data for the five split-mouth trials, the primary analysis is based on the two parallel group trials. The exact age of participants was unclear in some studies; however, both children and adults with permanent teeth at the back of the mouth that required fillings were included. Data on gender were not reported.

Parameter	Extraction
Setting/context	Two trials were in a university-based facility, one trial was in a community-based clinic, and another trial was in both a university- and community-based setting. The setting was not reported for three trials. The study countries were a cross-country trial in Europe, and individual country trials in Portugal, the UK, and the USA.
Description of interventions/phenomena of interest	Composite resin was compared with amalgam for the treatment of cavitated dental caries. Resin composites have become an aesthetic alternative to amalgam restorations and there has been a remarkable improvement in their mechanical properties to restore posterior teeth. Amalgam has been the traditional material for filling cavities in posterior teeth for the last 150 years [since 1870] and, due to its effectiveness and cost, amalgam is still the restorative material of choice in certain parts of the world. There have been concerns over the use of amalgam restorations (fillings) relating to the mercury release in the body and the environmental impact following its disposal. The exact age of participants was also unclear in some studies; however, both children and adults with permanent teeth at the back of the mouth that required fillings were included. According to Rasines Alcaraz <i>et al.</i>, "Dental resin composites were developed in response to people's demands for tooth-colored restorations. Dental resin composites are particle-reinforced resins. The indications of resin composites have expanded from anterior teeth to restricted posterior restorations and even to stress-bearing posterior restorations as amalgam substitutes or amalgam alternatives. Other advantages of dental resin composite restorations include their conservative design and reparability."¹¹ (p6) Comparator: Amalgam has been the traditional material for filling cavities in posterior teeth due to its effectiveness and cost
Databases and sources searched	The authors searched five databases: the Cochrane Oral Health Group Trials Register (to 22 October 2013), Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library 2013, Issue 9), MEDLINE via Ovid (1946 to 22 October 2013), Embase via Ovid (1980 to 22 October 2013), and Latin American and Caribbean Health Sciences Literature database (LILACS) via BIREME Virtual Health Library (1980 to 22 October 2013). They did not apply language or date restrictions when searching the electronic databases. The full electronic search strategy is provided in an appendix. The authors contacted manufacturers of dental materials to obtain any unpublished studies. Hand-searching for this review was done as part of Cochrane's worldwide hand-searching programme. The authors completed and published a protocol. At least two review authors screened the literature independently and in duplicate. Two authors extracted the data in duplicate but independently. The authors declared no conflicts of interest and acknowledged their source of funding for the review as the Cochrane Oral Health Group Global Alliance, UK.
Date range (years) of included studies	Seven randomised controlled trials, published between 1986 and 2007.
Number of primary studies included in the systematic review	Seven randomised controlled trials, published between 1986 and 2007, with data drawn from 10 articles on these trials, were included in this review. Two trials were parallel group studies involving 1,645 composite restorations and 1,365 amalgam restorations (921 children) in the analysis. The other five trials were split-mouth studies involving 1,620 composite restorations and 570 amalgam restorations in an unclear number of children. Due to major problems with the reporting of the data for the five split-mouth trials, the primary analysis is based on the two parallel group trials. Three studies were funded by the same dental industry, one was funded by a research grant (Casa Pia 2007), and the other three studies did not state their funding sources.
Types of studies included	The inclusion criteria required randomised controlled trials. A list of the 44 studies excluded from this review and the reasons for their exclusion were reported.
Country of origin of included studies	The study countries were a cross-country trial in Europe, and individual country trials in Portugal, the UK, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included trials.

Parameter	Extraction
Appraisal rating	Based on the Cochrane Collaboration's risk of bias instrument, the seven trials were judged to be at high risk of bias. Three of the seven trials were judged to have adequate randomisation, and no trial had blinded the outcome assessor. Publication bias was dealt with as part of the comprehensive search and considered in the GRADE assessment.
Method of analysis	The authors combined relative risks for dichotomous data from the studies that were considered appropriate to be included in the meta-analysis. They intended to combine the treatment effects from split-mouth trials with those from parallel group trials where appropriate, as outlined in the <i>Cochrane Handbook for Systematic Reviews of Interventions</i> , but it was not possible because of poor reporting. Therefore, they treated the split-mouth trials as a subgroup so that the results could be examined either in isolation or in combination with the parallel group studies. They used random-effects models where there were more than three studies in any meta-analysis; otherwise, they used fixed-effects models. The Cochrane Collaboration's test for statistical heterogeneity was used and quantified using the I^2 statistic. The authors were unable to complete the subgroup or sensitivity analyses due to lack of data.
Outcome assessed	Failure rate at 3 years or over, fracture, secondary caries rate, adverse events Outcome by primary study: Failure rate: Two of the seven studies were parallel group trials (Casa Pia 2007; NECAT 2007), while the other five were split-mouth studies (Cunningham 1990; Hendriks 1986; Letzel 1989; Norman 1990; Robinson 1988). Reason for failure at 3 years or over: Fracture (Casa Pia 2007; NECAT 2007) and secondary caries (Casa Pia 2007; NECAT 2007), and separately (Cunningham 1990; Hendriks 1986; Norman 1990; Robinson 1988). Adverse events: Casa Pia 2007. Costs: No evidence.
Results/findings	Fixed-effects meta-analyses were completed as there were small numbers of trials per analysis; however, there was substantial or considerable heterogeneity. According to Rasines Alcaraz <i>et al.</i>, "There is low-quality evidence to suggest that resin composites lead to higher failure rates based on pairwise fixed-effects meta-analysis at 5–7 years (fixed-effects model; relative risk 1.89; 95% CI 1.52 to 2.35; I^2 87%; 2910 participants; 2 trials; low-quality evidence), and higher risk of secondary caries than amalgam restorations at 5–7 years (relative risk 2.14; 95% CI 1.67 to 2.74; I^2 92%; 2910 participants; 2 trials; low-quality evidence)."^{11 (p18)} However, there is adequate evidence that restoration fracture is the same for both amalgam and resin composite fillings (relative risk: 0.87; 95% CI: 0.46–1.64; I^2: 0%; 2,910 participants; 2 trials; moderate-quality evidence downgraded by HRB to low-quality evidence). The parallel group trials indicated that resin restorations had a significantly higher risk of failure than amalgam restorations (low-quality evidence) and increased risk of secondary caries (low-quality evidence), but there was no evidence of an increased risk of restoration fracture (moderate-quality evidence downgraded by HRB to low-quality evidence). The results from the split-mouth trials (which included adults) were consistent with those of the parallel group trials. With respect to adverse events, data were reported for neurobehavioural assessment, kidney function, psychosocial function, and physical development. None of these outcomes were reported in more than one study. The authors concluded that the evidence on adverse events was insufficient.
Significance/direction	Results listed by outcome.
Heterogeneity	High statistical heterogeneity in analysis on restoration failure.
Comments	GRADE was used by the review authors. All seven trials were judged to be at high risk of bias. Three (43%) of the seven trials were judged to have adequate randomisation, and no trial blinded the outcome assessor. The authors acknowledge the substantial heterogeneity in two of the meta-analyses. The quality of the review was rated as low using AMSTAR 2 as the authors did not address heterogeneity in the discussion. The HRB grades the quality of the evidence as low for the different outcomes.

Sharif *et al.* (2014a)

Parameter	Extraction
First author and year of publication	Sharif <i>et al.</i> (2014a) ¹⁴ (Cochrane Review) Empty review (no studies identified for inclusion)
Objectives	Compared the effects of replacing resin composite with repairing it (with resin composite) in the management of defective resin composite dental restorations in permanent molar and premolar teeth.
Participants	Permanent dentition, cavitated caries, restoration materials (repair of) Population: Permanent molar and premolar teeth No trials met the inclusion criteria.
Setting/context	No trials met the inclusion criteria.
Description of interventions/phenomena of interest	Replacing (with resin composite) compared with repair (with resin composite) in the management of defective resin composite dental restorations in permanent molar and premolar teeth. Comparator: Repair (with resin composite) in the management of defective resin composite dental restorations.
Databases and sources searched	For the identification of studies relevant to this review, the authors searched six databases with peer review articles: the Cochrane Oral Health Groups Trials Register (to 24 July 2013); Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library 2013, Issue 6); MEDLINE via Ovid (1946 to 24 July 2013); Embase via Ovid (1980 to 24 July 2013); BIOSIS via Web of Knowledge (1969 to 24 July 2013); Web of Science (1945 to 24 July 2013); and OpenGrey (to 24 July 2013). No restrictions were placed on the language or date of publication when searching the electronic databases. The full electronic search strategy is provided in an appendix. Researchers, experts, and organisations known to be involved in this field were contacted in order to trace unpublished or ongoing studies. Only hand-searching done as part of Cochrane's worldwide hand-searching programme and uploaded to CENTRAL was included. The authors completed and published a protocol. At least two review authors screened the literature independently and in duplicate. The authors were National Institute for Health Research (NIHR)-funded researchers. No other conflicts of interest are declared.
Date range (years) of included studies	No trials met the inclusion criteria.
Number of primary studies included in the systematic review	No trials met the inclusion criteria.
Types of studies included	The inclusion criteria required randomised controlled trials (including split-mouth studies). A list of the two studies excluded from this review and the reasons for their exclusion are reported.
Country of origin of included studies	No trials met the inclusion criteria.
Appraisal instruments used	No trials met the inclusion criteria.
Appraisal rating	No trials met the inclusion criteria.
Method of analysis	No trials met the inclusion criteria.
Outcome assessed	Outcome: Failure of restoration Presence of clinical symptoms (pain, swelling, diagnosis of pulpitis, abscess formation). Extraction of tooth due to caries. Perioperative or post-operative pain or discomfort. Patient satisfaction as measured by aesthetic scales.
Results/findings	There are no published randomised controlled trials relevant to this review question.
Significance/direction	No trials met the inclusion criteria.
Heterogeneity	No trials met the inclusion criteria.
Comments	It was intended to use GRADE. There is no evidence upon which to judge the effectiveness of resin composite replacement compared with repair, as no trials met the inclusion criteria.

Sharif *et al.* (2014b)

Parameter	Extraction
First author and year of publication	Sharif <i>et al.</i> (2014b) ¹⁰⁴ Cochrane Review) Empty review
Objectives	Compared the effects (retention, survival) of replacing (with amalgam) compared with repair (with amalgam) in the management of defective amalgam dental restorations in permanent molar and premolar teeth.
Participants	Permanent dentition, cavitated caries, restoration materials (repair of) Adults (aged 16 years or over) with one or more defective amalgam restoration(s) in a molar or premolar tooth/teeth treated by like-for-like replacement (i.e. replacement with amalgam) or like-for-like repair (i.e. repair with amalgam) or both.
Setting/context	No trials met the inclusion criteria.
Description of interventions/phenomena of interest	Replacing (with amalgam) compared with repair (with amalgam). Replacement involves the complete removal of old amalgam together with base or lining materials and carries a risk of the inadvertent removal of sound tooth tissue. Repeated replacement is therefore associated with a progressive increase in cavity size. In addition, each time dentine is cut during cavity preparation, there is a risk of damage to the dental pulp and the development of clinical symptoms. The belief that microleakage of oral fluids into marginal or interfacial defects leads to secondary caries or pulpal pathology underpinned the traditional support for replacement over repair. However, although microleakage may be observed under laboratory conditions, it does not necessarily occur in the clinical situation. In the repair of a defective amalgam restoration, only the defective area is removed and replaced. Repair offers a pragmatic approach and has a number of potential advantages: it is more conservative, quicker, cheaper, and less traumatic to the patient and the tooth, and local anaesthesia may not be required. Comparator: Replacement of a defective amalgam restoration in a permanent molar or premolar tooth with amalgam.
Databases and sources searched	For the identification of studies relevant to this review, the authors searched six peer review journal sources: Cochrane Oral Health Groups Trials Register (to 5 August 2013); the Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library 2013, Issue 7); MEDLINE via Ovid (1946 to 5 August 2013); Embase via Ovid (1980 to 5 August 2013); BIOSIS via Web of Knowledge (1969 to 5 August 2013); Web of Science (1945 to 5 August 2013); and OpenGrey (to 5 August 2013). No restrictions were placed on the language or date of publication when searching the electronic databases. The full electronic search strategy is provided in an appendix. Researchers, experts, and organisations known to be involved in this field were contacted in order to trace unpublished or ongoing studies. Only hand-searching done as part of Cochrane's worldwide hand-searching programme and uploaded to CENTRAL was included. The authors completed and published a protocol. At least two review authors screened the literature independently and in duplicate. The authors were National Institute for Health Research funded researchers. No other conflicts of interest are declared.
Date range (years) of included studies	No trials met the inclusion criteria.
Number of primary studies included in the systematic review	No trials met the inclusion criteria.
Types of studies included	The inclusion criteria required randomised controlled trials (including split-mouth studies). A list of the two studies excluded from this review and the reasons for their exclusion are reported.
Country of origin of included studies	No trials met the inclusion criteria.
Appraisal instruments used	No trials met the inclusion criteria.
Appraisal rating	No trials met the inclusion criteria.
Method of analysis	No trials met the inclusion criteria.
Outcome assessed	The main outcome of interest was success or failure of the replacement or repair restoration and associated tooth as assessed by clinical examination. The primary outcome measures were therefore the clinical acceptability or unacceptability of each restoration, defined by the United States Public Health Service (USPHS)

Parameter	Extraction
	criteria, Ryge criteria, or modifications of these scales, and assessed by clinical examination. Success or failure of restoration. Further restoration (repair, restoration, placement of crown inlay, root filling) required (studies should have determined success or failure according to the same criteria used in the decision to replace or repair the restoration). Presence of clinical symptoms (pain, swelling, diagnosis of pulpitis, abscess formation). Extraction of tooth due to decay. Outcome data from all periods of follow-up were to be included, but where the period of follow-up differed between studies, this was to be categorised as medium term (less than 5 years) or long term (5 years or more). Time-to-event (survival data) was to be collected and analysed where available.
Results/findings	There are no published randomised controlled trials relevant to this review question. There no evidence upon which to judge the effectiveness of amalgam replacement compared with repair, as no trials met the inclusion criteria. There is therefore a need for methodologically sound randomised controlled trials that are reported according to the Consolidated Standards of Reporting Trials (CONSORT) statement. Further research also needs to qualitatively explore the views of patients on repairing compared with replacement and investigate themes around pain, distress and anxiety, time, and costs.
Significance/direction	No trials met the inclusion criteria.
Heterogeneity	No trials met the inclusion criteria.
Comments	It was intended to use GRADE. There is no evidence upon which to judge the effectiveness of resin composite replacement compared with repair, as no trials met the inclusion criteria.

Indirect restoration material

Bustamante-Hernández *et al.* (2020)

Parameter	Extraction
First author and year of publication	Bustamante-Hernández <i>et al.</i> (2020) ¹⁰⁶
Objectives	Evaluated the clinical behaviour (survival) and the possible complications of posterior region onlays in adults' permanent posterior teeth by the type of material used for the onlay restoration 1 year or more after restoration intervention.
Participants	Permanent dentition, cavitated caries, indirect restoration Patients aged over 18 years treated with onlays (partial restorations covering at least one dental cusp) in the posterior region of the tooth, involving follow-up of one year or more. Twenty-nine articles (17 clinical trials and 12 cohort studies) published between 2000 and 2019 met the inclusion criteria and were included in the qualitative analysis, and 27 were included in the quantitative synthesis as all the required data were available in these articles. A total of 29 articles were entered in the qualitative analysis. The sample sizes ranged from 14 to 231 restorations, and the duration of follow-up varied between 2 and 15 years. The age, gender, clinical settings, and study countries were not reported.
Setting/context	The clinical settings and study countries were not reported.
Description of interventions/phenomena of interest	The intervention refers to onlay restoration in the teeth in the posterior region of the mouth made from a variety of materials and compared with each other. The onlay materials were likely to be fabricated from ceramics, zirconia, or resin composite. The materials analysed were feldspathic ceramic reinforced with lithium disilicate, conventional feldspathic ceramic or feldspathic ceramic reinforced with leucite, hybrid materials, and resin composite.
Databases and sources searched	Four electronic databases were searched without restrictions up to April 2020: PubMed, Scopus, Embase, and Cochrane databases. The keywords for the search strategy were provided in the text. No additional searches were reported. The authors published a protocol on PROSPERO. Three authors screened and extracted the data. The authors declared no conflict of interest and reported that they received no external funding.
Date range (years) of included studies	Twenty-nine articles (17 clinical trials and 12 cohort studies) published between 2000 and 2019 met the inclusion criteria.
Number of primary studies included in the systematic review	Twenty-nine articles (17 clinical trials and 12 cohort studies) published between 2000 and 2019 met the inclusion criteria and were included in the qualitative analysis, and 27 were included in the quantitative synthesis as all the required data were available in these articles. A total of 29 articles were entered in the qualitative analysis. The funding sources for primary studies were not reported.
Types of studies included	Randomised controlled trials and retrospective and prospective studies were eligible for inclusion. The excluded studies were not listed, but reasons for exclusion were reported.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The methodological quality of the studies was assessed using two specific scales: the Newcastle-Ottawa Scale for the evaluation of cohort studies, and the PEDro scale for the evaluation of clinical trials.
Appraisal rating	Seven of the 12 cohort studies were of high quality according to the Newcastle-Ottawa Scale, with a score of seven or higher. The remaining five studies had a score of seven or lower, indicating that they were low quality. The representativeness of all 12 studies was categorised as 'somewhat' (scored one star out of a possible two), and all scored positively for outcome ascertainment. Control of confounding is a very important issue to ensure valid analysis from cohort studies, and seven scored one star out of a possible two while five scored zero stars. This indicates that the studies were not representative and key differences were not controlled for. Six of the clinical trials were judged as having high methodological quality with scores of six or higher (denoting low risk of bias) using the PEDro scale, and the other 11 clinical trials yielded scores of five or lower, indicating low quality (or

Parameter	Extraction
	high risk of bias). Only five of the clinical trials were judged to have adequate randomisation, and four had adequate blinding for outcome ascertainment. The HRB notes that using the Cochrane risk of bias and scoring system, all of the clinical trials were at high risk of bias. The authors reported that "Quality was most often adversely affected because of failure to fulfil items related to subject or measurement blinding."^{106 (p6)} There was no further mention of bias. The analysis indicated a low probability of publication bias.
Method of analysis	For the meta-analysis, the included studies were combined by means of a random-effects pairwise model. The effect size was the events rate, with calculation of the corresponding 95% CI. The statistical heterogeneity between studies was assessed based on Cochran's Q test and I² statistic. The presence of differences between subgroups was evaluated using the between-group Q test. Meta-regression analysis was performed based on a mixed effects model, determining the existence of significant co-variables with the moderators' test. Publication bias in turn was assessed using the trim and fill method. A graphic representation of the meta-analysis was provided in the form of forest plots, with meta-regression being depicted in the form of scatter plots and publication bias as funnel plots. Statistical significance was considered as $p < 0.05$. The data were analysed using the R statistical package. Both trials and prospective studies were combined in the meta-analyses. Sensitivity analyses by study design or risk of bias were not completed.
Outcome assessed	Clinical behaviour (survival) and possible complications over time 1 year or more after restoration intervention The duration of follow-up ranged from 2 to 15 years. Clinical behaviour (survival) and possible complications over time: Felden 2000; Barghi 2002; Smales 2004; Stoll 2007; Naeselius 2008; Federlin 2010; Van Dijken 2010; Barnes 2010; Atali 2011; Roggendorf 2012; Ozyoney 2013; Fennis 2014; Real Dias 2016; Spitznagel 2017; Cosçkun 2019; Fasbinder 2019; Edelho 2019.
Results/findings	A random-effects model estimated a percentage survival for onlays of 94.2% (95% CI: 92.3–96.1), with a prediction interval of between 84.0% and 100.0%. The observed heterogeneity between studies (Q test=220.8; $p < 0.001$) was substantial (I²: 84.1%). The survival varied by type of onlay material and, according to the authors, this explained the high heterogeneity: Hybrids (resin nanoceramic and hybrid ceramic): Proportion: 0.99; 95% CI: 0.96–1.00; $p < 0.01$; 3 studies Feldspathic ceramic reinforced with lithium disilicate: Proportion: 0.98; 95% CI: 0.96–1.00; $p < 0.01$; 8 studies Conventional feldspathic ceramic reinforced with leucite: Proportion: 0.93; 95% CI: 0.90–0.96; $p < 0.01$; 18 studies Resin composites: Proportion: 0.90; 95% CI: 0.83–0.98; $p < 0.01$; 5 studies Based on survival experience to date, the authors estimated that percentage survival would be 88% for ceramic or hybrid materials compared with 80% for resin composite at 12.5 years follow-up. Fracture was the most important reason for restoration failure (4%) in the eight studies that reported reason for failure, followed by discolouration (1%). On analysing restoration complications using the modified USPHS criteria, 89.8% (95% CI: 87.5–92.1) of the restorations corresponded to category Alpha, while 9.8% (95% CI: 7.7–1.9) corresponded to category Bravo. The proportion of restorations classified as pertaining to categories Charlie or Delta combined was 0.1% ($p = 0.855$; $p = 1$). The authors reported that, "Based on the results obtained, it can be considered that all the restorations were regarded as acceptable."^{106 (p18)} The most common complications referred to were changes in surface texture or colour. On analysing restoration complications using the Canadian Dental Association criteria, 77.6% (95% CI: 73.6–81.8) of the restorations were categorised as successful. In addition, 19.4% (95% CI: 16.5–22.4) of the restorations were classified as surviving with minor deterioration. Only 0.79% (95% CI: 0.28–1.30) of the restorations corresponded to failure and required replacement. The complications were linked to structure of the restoration (anatomy, surface texture, and marginal integrity).

Parameter	Extraction
	The influence of the cementing technique has not been analysed due to the clinical heterogeneity of the different adhesion protocols used.
Significance/direction	Results listed by outcome.
Heterogeneity	The authors noted high heterogeneity and analysed survival by restoration material.
Comments	GRADE was not used by the review authors. The review included 17 randomised controlled trials, and 12 prospective and retrospective cohort studies. The prospective and retrospective studies were not representative of defined populations and key differences among the populations were not controlled for. Using the Cochrane risk of bias and scoring system, all of the clinical trials were at high risk of bias. Only five (29%) of the 17 clinical trials were judged to have adequate randomisation, and four (24%) had adequate blinding for outcome ascertainment. Randomised trials and cohort studies were pooled in the meta-analysis and no sensitivity or subgroup analyses were completed. The quality of the review was rated as critically low using AMSTAR 2 as the authors did not address bias in the analysis or discussion. The HRB grades the quality of the evidence as very low for the different outcomes.

Becker Rodrigues *et al.* (2019)

Parameter	Extraction
First author and year of publication	Becker Rodrigues <i>et al.</i> (2019) ¹⁰⁷
Objectives	Evaluated the difference in longevity of tooth-supported ceramic prostheses designed by a computer-aided design/computer-aided manufacturing system compared with a conventional manufacturing (milling) system.
Participants	Permanent dentition (not stated but deduced from age), cavitated lesions (not stated but deduced from intervention), crown, or inlay/onlay. Patients with an anterior and/or posterior tooth-supported single crown or multiple-unit or partial crowns.
Setting/context	Most (nine) studies were conducted in universities, while three were conducted in private practices and two were conducted jointly between a university and private practice. The study countries were not reported.
Description of interventions/phenomena of interest	Tooth-supported ceramic prostheses designed by computer-aided design/computer-aided manufacturing system compared with conventional manufacturing system. Three types of tooth-supported restorations were searched in the included studies: single crown, multiple-unit, and partial ceramic crown. The intervention group was patients with at least one ceramic restoration made with the computer-aided design/computer-aided manufacturing system. The control group was patients with at least one ceramic restoration made with the conventional manufacturing system.
Databases and sources searched	Four databases were searched, with no limits, between 1966 and October 2017: Web of Science, PubMed, Scopus, and Latin American and Caribbean Health Sciences Literature database (LILACS). Appropriate MeSH terms and their combinations were used in the database searches. In addition, the references of all of the identified articles were manually searched for further relevant studies. The authors prepared but did not publish their protocol. Screening and extraction were completed by two independent reviewers. The review was funded by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (public funding).
Date range (years) of included studies	Eleven randomised controlled trials and three prospective cohort studies published between 1999 and 2017, with 1,209 restorations placed in 957 patients, were included.
Number of primary studies included in the systematic review	Eleven randomised controlled trials and three prospective cohort studies published between 1999 and 2017, with 1,209 restorations placed in 957 patients, were included. Seven of the 14 studies obtained financial support or material donations from industry.
Types of studies included	Clinical studies that compared the survival rate of conventional and computer-aided design/computer-aided manufacturing techniques were included.

Parameter	Extraction
	The studies excluded at full-text screening were not listed, although reasons for exclusion were provided.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included randomised controlled trials, while the Newcastle-Ottawa Scale was used to assess the prospective cohort studies.
Appraisal rating	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the eleven randomised controlled trials, and the authors judged that three trials had a high risk of bias, five had an unclear risk of bias, and three had a low risk of bias. Ten of the 11 randomised controlled trials were judged to have adequate randomisation and all 11 had adequate blinding. For the three prospective cohort studies, the quality score for each study was assessed out of a possible total of 11 stars: two studies scored 6 stars and one study scored 7 stars. The authors reported that the major bias in these studies was a risk of bias in the selection of samples because the participants were mostly from university and private dental offices. Furthermore, blinding was not possible in these studies. Control for confounding factors was not addressed in two of the studies. Overall, the quality scores indicate low-quality or high risk of bias studies. Egger's and Begg's tests indicated no evidence of publication bias either without dropouts counted as failures or with dropouts counted as failures. The authors acknowledge that they used all studies, regardless of risk of bias, in the meta-analysis in order to increase the power of the meta-analysis. However, they did not do a sensitivity analysis to determine the effect of risk of bias.
Method of analysis	The risk of failure for each group of included studies was calculated based on the number of baseline restorations (number of initial restorations) and the number of failures at the end of the follow-up period. The relative risks from all studies were pooled in a fixed-effects meta-analysis using the default Mantel-Haenszel method for binary variables. Publication bias was assessed using a funnel plot, and heterogeneity was assessed using the I^2 inconsistency index. The risk difference was also calculated. The authors included dropouts either as failures or as successes in a sensitivity analyses. Therefore, all analyses were duplicated to check for possible selection bias and robustness. The effects of missing data, but not other biases, were assessed as part of outcome analyses. All analyses were carried out with Stata version 13.
Outcome assessed	Longevity of manufactured restorations measured as failure Follow-up: At least 2 years. The follow-up of patients in the studies ranged from 24 to 84 months Longevity of manufactured restorations measured as failure: Randomised controlled trials: Molin 2000; Sailer 2009; Christensen 2010; Pelaez 2012; Passia 2013; Guess 2013; Akin 2015 Zenthöfer 2015; Nicolaisen 2016; Rinke 2016; Monaco 2017; Prospective cohort studies: Walter 1999; Vigolo 2012; Federlin 2010..
Results/findings	There were 72 restoration failures in the final analysis. Failures were analysed by type and material restoration. Using per-protocol analysis, which is not best practice, the computer-aided design/computer-aided manufacturing techniques system resulted in a 1.84 times higher relative risk (fixed-effects pairwise meta-analysis: 95% CI: 1.28–2.63; I^2: 0%; 14 trials, 2 of which had more than one arm) than conventional manufacturing of ceramic restoration. When dropouts were included as a failure risk (intention-to-treat analysis, which is best practice), the computer-aided design/computer-aided manufacturing techniques system resulted in a 1.32 times higher relative risk (fixed-effects pairwise meta-analysis: 95% CI: 1.10–1.58; I^2: 37%; 14 trials, 2 of which had more than one arm). Considering dropouts as failures, the authors reported failure rates of 4.23 and 5.88 per 100 restoration years for the control and computer-aided design/computer-aided manufacturing technique groups, respectively. The meta-analysis results suggest very low-quality evidence that the longevity of tooth-supported ceramic prostheses made by the computer-aided design/computer-aided manufacturing system is lower than that of crowns made by the conventional milling technique.

Parameter	Extraction
Significance/direction	Results listed by outcome.
Heterogeneity	The authors regarded statistical heterogeneity as acceptable and point to the existence of clinical heterogeneity.
Comments	GRADE was not used by the review authors. The review included 11 randomised controlled trials, and three prospective cohort studies. The prospective and retrospective studies were not representative of defined populations and key differences among the populations were not controlled for. Most of the trials were at high risk of bias. Ten (91%) of the 11 randomised controlled trials were judged to have adequate randomisation and all 11 had adequate blinding. The key quality scores (representativeness, blinding and confounding) for prospective cohort studies indicate low-quality or high risk of bias studies. Randomised trials and cohort studies were pooled in the meta-analysis and sensitivity or subgroup analyses were not completed for risk of bias or study design. There was moderate statistical heterogeneity in the intention-to-treat analysis. The quality of the review was rated as critically low using AMSTAR 2 as the authors did not address bias in the analysis or discussion. The HRB grades the quality of the evidence as very low for the different outcomes.

Sampaio *et al.* (2019)

Parameter	Extraction
First author and year of publication	Sampaio <i>et al.</i> (2019)¹⁰⁸
Objectives	Evaluate the survival rate of indirect composite and ceramic inlays, onlays, and overlays following different manufacturing methods in children and adults teeth.
Participants	Permanent dentition [age], cavitated caries, indirect restoration material Patients who received indirect composite or ceramic inlays, onlays, and overlays were included in this review. The age of the study participants ranged from 12 to 79 years.
Setting/context	The study settings were private clinics and university/academic clinics. The 13 included studies were undertaken in Australia, Germany (five studies), Iran, Italy, Japan, Portugal, Sweden (two studies), and Switzerland.
Description of interventions/phenomena of interest	Intervention: Indirect restorations including inlays, onlays, and overlays made of ceramic or resin composite Comparator: Each other Commenting on the interventions, the authors stated that "Ceramics and composites have characteristics with regard to structure and manufacturing methods that, associated with the luting agents and intraoral conditions, are important factors attributed to longevity of inlay, onlay, and overlay restorations. However, this choice [of material] is conducted based on criteria such as strength, translucency/opacity degree, preference of the dental laboratory technician, and advertising claims. On the other hand, manufacturing methods directly influence several of these criteria, with strength being the most important factor for the survival rate. Fractures were the most frequent cause of failure... Indirect composite restorations can be obtained from a temperature-, humidity-, time-, and light-controlled environment, resulting in a well-cured restoration with improved mechanical properties. Prefabricated blocks, with a relatively pore-free structure, have high-quality polymers, and better properties of polishability, reduced pigmentation, and increased strength...The influence of different manufacturing methods on the aesthetic inlays, onlays, and overlays is very important clinical information for clinicians to support their decisions, since manufacturing methods are still an unknown variable for restoration success."¹⁰⁸ (p561–562)
Databases and sources searched	Three databases – MEDLINE via PubMed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) – covering the period 1983 to 2017 were searched up to 9 January 2019, with no language restrictions. References in all included articles were checked manually. The authors did not report preparing a protocol. Extraction and screening were completed in duplicate.

Parameter	Extraction
	The authors reported no conflicts of interest and no financial support for this study, and they did not have any financial interest in the companies whose materials were included in these articles.
Date range (years) of included studies	The publication years of the included studies ranged from 1998 to 2016.
Number of primary studies included in the systematic review	Thirteen studies – 8 retrospective cohort studies, 4 prospective cohort studies, and 1 randomised controlled trial – published from 1998 to 2016 were included in this review. Twelve articles focused on ceramic restorations and 1 article focused on indirect composite restorations. The sources of funding of primary studies were not reported.
Types of studies included	Randomised controlled clinical trials and clinical follow-up studies were eligible for inclusion. A list of excluded studies was not reported. However, the reasons for exclusion were provided.
Country of origin of included studies	The 13 included studies were undertaken in Australia, Germany (five studies), Iran, Italy, Japan, Portugal, Sweden (two studies), and Switzerland.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included trials. The Newcastle-Ottawa Scale was used to evaluate the 12 observational studies.
Appraisal rating	The randomised controlled trial was judged to have an unclear risk of bias. The randomised controlled trial was at low risk of bias for randomisation and unclear risk of bias for outcome assessment. The data for each domain of the 12 observational studies cannot be interpreted and so we cannot assess representativeness, control for confounding, or observer blinding. The authors stated that, "Considering the overall assessment, the quality of primary studies was scored as moderate, because this systematic review included only one RCT [randomised controlled trial] with slight limitations and 12 well-delineated observational studies with consistent findings. Despite the high quality of evidence in four items, the indirect evidence obtained moderate quality, being the main reason for downgrading the confidence of the analysis. When studies did not directly compare the interventions (head-to-head), effect estimates are presented based on indirect comparisons, providing compelling reasons why the indirect estimate is likely to be biased." ¹⁰⁸ (p564) Publication bias was not measured or discussed.
Method of analysis	According to Sampaio <i>et al.</i> , "Descriptive statistics and meta-analysis were performed for estimated survival rates analyses. A Cochran Q test was performed ($p < 0.1$ with 95% CI) to evaluate the presence of heterogeneity among studies and the presence and extent of heterogeneity was measured using an inconsistency test ($I^2 > 50\%$); since there is a small number of included studies, both tests present low statistical power, and thus results should be interpreted with caution. The inverse-variance method was used, with the estimator of DerSimonian-Laird for the I^2 . Data were transformed and the individual CI of studies was calculated by the Clopper-Pearson method (software program R 3.1.0, R Core Team, 2014) with the aid of the Meta package. Meta-analysis with survival rates was performed including studies evaluating survival rates for each manufacturing method individually (computer-aided design/computer-aided manufacture [CAD/CAM]; pressable and stratified). When studies did not present variance (or standard deviation), it was calculated, analyzing the number of failures and censorship during the follow-up time. Data were collected from texts or calculated using the Kaplan-Meier graphs or life tables for those articles where estimate of survival in the specific periods (5 and 10 years) was not explicit. The Greenwood formula was used to calculate variance, assuming that censorships occurred uniformly over time, together with failures." ¹⁰⁸ (p563)
Outcome assessed	The outcomes assessed were survival rate (number of restorative failures based on clinical criteria such as FDI and USPHS) and clinical performance, which indicates success or failure of restorations – marginal integrity/adaptation, marginal discolouration, recurrent caries, retention of composite restorations, and post-operative sensitivity. Survival rate: Dias 2016; Nejatidan 2015; Frankenberger 2008; Krämer 2008; Otto and Schneider 2008; Reiss 2006; Schulte 2005; Smales and Etemadi 2004; Sjögren 2004; Schulz 2003; Posselt and Kerschbaum 2003; Hayashi 2000; Fuzzi and Rappelli 1998.

Parameter	Extraction
Results/findings	At least 5 years follow-up (predetermined) Indirect composite The authors reported that “One study of indirect composite inlays, onlays, and overlays could be identified in the data collection process; hence, meta-analysis could not be performed for this material. The authors concluded that in a 5-year period, resin cuspal coverage of endodontic-treated teeth had a success rate of 96% and the tooth survival rate was 100%. One study evaluated the survival rate of ceramics and composites, fulfilling various inclusion criteria, but they did not present the number of patients per material.”^{108 (p565)} Ceramics Subgroup analysis and meta-analysis for inlays, onlays, and overlays According to Sampaio <i>et al.</i>, “Meta-analysis was performed by separating CAD/CAM [computer-aided design/computer-aided manufacturing], pressable, and stratified manufacturing methods, including studies that evaluated survival rates for each technique, respectively. Twelve studies were retained for quantitative analysis: five with CAD/CAM, three with pressable, and four with the stratified method. In the CAD/CAM group, glass ceramics and feldspathic porcelains were included; in the pressable group, only glass ceramics; and in the stratified group, only feldspathic porcelains. Analyses of survival in the subgroups were then performed for each manufacture method. For the CAD/CAM group, with a clinical follow-up time of 5 years (N=3,746), the cumulative survival rate was 97% (95% CI: 97%–98%; $I^2=0\%$; $p=0.41$). For the clinical follow-up time of 10 years (N=1,259), the survival rate was 89% (95% CI: 87%–91%; $I^2=0\%$; $p=0.99$). For the pressable group, with a clinical follow-up time of 5 years (N=909), the cumulative survival rate was 95% (95% CI: 93%–96%; $I^2=0\%$; $p=0.97$). Only one study presented a clinical follow-up time of 10 years. For the stratified group, with a clinical follow-up time of 5 years (N=413), the cumulative survival rate was 88% (95% CI: 71%–96%, $I^2=91\%$; $p<0.01$). For the clinical follow-up time of 10 years (N=290), the survival rate was 93% (95% CI: 67%–99%; $I^2=92.4\%$; $p=0.0003$).”^{108 (p565)} The authors stated, “In the present study, pooled estimated survival rates at the follow-up times of 5 and 10 years were 97% and 89%, respectively, for the CAD/CAM method. After 5 years, the survival rate for pressable glass ceramics was 95%. For the stratified group, survival rates at the follow-up times of 5 and 10 years were 88% and 93%, respectively. Only the stratified group presented a lower survival rate at the 5-year follow-up than after 10 years. This was due to the inclusion of one study that presented lower survival rates than those found in other studies. The authors concluded that including bruxist patients led to a higher number of fractures, but this statement should be interpreted with caution as currently there is no consistent evidence to support an association between bruxist patients and increased number of fractures in regards to ceramic restorations.”^{108 (p568)} Authors’ overall conclusions Sampaio <i>et al.</i> concluded that “Regardless of the manufacturing methods, vitreous ceramic inlays, onlays, and overlays showed high survival, providing evidence that these restorations are a safe treatment, but no conclusive evidence is available about indirect composite or crystalline ceramic inlays, onlays, and overlays. Based on risk of bias and quality of evidence, the current evidence level for this clinical approach is low and high-moderate, respectively.”^{108 (p570)}
Significance/direction	According to the authors, “The estimated cumulative survival rate for CAD/CAM [computer-aided design/computer-aided manufacturing] was 97% after 5 years and 89% after 10 years; for pressable it was 95% after 5 years, and for stratified it was 88% after 5 years and 93% after 10 years. Regardless of the manufacturing method, vitreous ceramic inlays, onlays, and overlays showed high survival, providing evidence that these restorations are a safe treatment.”^{108 (p561)}
Heterogeneity	The review authors provided the following comment on heterogeneity: “A Cochran Q test was performed ($p<0.001/95\%$ CI) to evaluate the presence of heterogeneity among studies and the presence and extent of heterogeneity was measured using an inconsistency test ($I^2>50\%$); since there is a small number of included studies, both tests present low statistical power, and thus results should

Parameter	Extraction
	be interpreted with caution. The inverse-variance method was used, with the estimator of DerSimonian-Laird for the I^2.”¹⁰⁸ (p563) Sampaio <i>et al.</i> stated, “In order to assist the evaluation of possible sources of heterogeneity, visual inspection was performed on each analyzed subgroup. Only the stratified group presented a high heterogeneity and for all the other subgroups it was 0%. In reality, a high level of heterogeneity was expected, because clinical articles generally present many methodological and clinical variations. The random-effects model was used for the analyses when I^2 was higher than 50%.”¹⁰⁸ (p568) The authors noted that “Well-defined success and survival criteria are of great importance to ensure that authors are not too strict or too flexible when classifying failures... Differences between authors in relation to what was considered as failures may have changed the mean failure of a given outcome; for example, chipping and fracture concepts were often merged, and sometimes not even considered as failures if a burnish or composite repair was agreed with the patient. Survival and success concepts must be very evident... Survival of teeth or restoration is also an important difference. This lack of concept standardization seems to be a strong possibility for [the cause of] heterogeneity.”¹⁰⁸ (p568)
Comments	GRADE was used by the review authors. The authors reported that the “quality of the evidence (GRADE) was considered moderate, since the survival rate was considered a critical outcome for decision-making, and this one [survival rate] remained high, regardless of time, can be inferred in a more pragmatic evaluation of the balance between risks and benefits points to a safe clinical recommendation.”¹⁰⁸ (p570) They also stated that “Based on the present review and on several previous systematic ones about inlay, onlay, and overlay restorations, there is a gap in clinical evidence concerning the best fabrication technique for indirect composite or crystalline ceramic restorations, pressable ceramics after 5 years, and ceramics (milled, stratified, or pressable) after 10 years.”¹⁰⁸ (p569) Sampaio <i>et al.</i> noted that “a limitation is that a small number of included studies, Cochran Q and I-squared tests present low statistical power, and thus results should be interpreted with caution.”¹⁰⁸ (p569)

Vagropoulou *et al.* (2018)

Parameter	Extraction
First author and year of publication	Vagropoulou <i>et al.</i> (2018) ¹⁰⁹
Objectives	Investigated whether different types of indirect restorations (inlay, onlay, both inlay and onlay, and crown) used for single permanent anterior, premolar, or molar teeth had different biological or technical complications, or different survival rates. At least one year follow-up.
Participants	Permanent teeth, cavitated caries, indirect restorations, and crowns Single permanent anterior, premolar, or molar teeth. There were 775 participants in seven of nine studies, and the age of the participants in six of the included studies was between 18 and 91 years. Details on gender were reported for five primary studies; more females than males participated in four of these five studies. Vagropoulou <i>et al.</i> point out that “the restorative treatments examined in the studies included in this systematic review were performed in both males and females and in a very wide range of ages, covering the whole spectrum of adulthood”.¹⁰⁹(p915)
Setting/context	The study settings were university clinics in three studies, private clinics in four studies, and combinations of private and university clinics in two studies. The study countries were not reported.
Description of interventions/phenomena of interest	Different types of indirect restorations (inlay, onlay, both inlay and onlay, and crown) were examined in this review. According to Vagropoulou <i>et al.</i>, “complete coverage restorations are used extensively in everyday clinical practice, especially when tooth structure loss is more than 50%. gold, metal ceramic, all ceramic, and zirconia crowns have been

Parameter	Extraction
	used successfully and they all represent different restorative material options...Ceramic inlays and onlays present very high survival rates too...Failures in both complete and partial coverage restorations are related to fractures/chipping, endodontic complications, recurrent decay, retention loss and in cases of all-ceramic restorations severe marginal staining may result as well".¹⁰⁹ (p904) Not a comparative intervention study.
Databases and sources searched	An electronic search was performed in three electronic databases (MEDLINE, Scopus, and Embase) to identify articles published between 1980 and 2017. The search terms were categorised into four groups: inlay, onlay, inlay/onlay, and crown. The time frame was selected in an effort to include restorative materials that are currently in use. The search is presented in the text of the paper. The electronic search was supplemented by a manual search of seven relevant journals over the same time period. Additionally, all references included in the selected full-text articles were screened. Primary study authors were contacted. Two reviewers did a portion of the abstracts and then agreed refined criteria and split the work for the remainder of the screening. Three reviewers agreed the selection of the full texts. Data from all included studies were extracted independently by three authors using a standardised sheet and agreed rules. The study protocol was established (but not registered) by first conducting a pilot PubMed search followed by a systematic assessment of five potentially eligible studies, which were randomly selected. This preliminary search revealed that randomised controlled studies on survival and complications of indirect restorations would be very limited or even non-existent. Therefore, an eligibility assessment of non-randomised clinical studies, after a detailed quality evaluation protocol, was adopted. No funding was obtained from any institution or agency. This work was supported solely by its authors. The authors have stated explicitly that there were no conflicts of interest in connection with this article.
Date range (years) of included studies	Nine studies (cohort studies) published between 2003 and 2015 were selected for inclusion: three prospective and six retrospective cohort studies. The authors state that no randomised controlled trials were identified from their search.
Number of primary studies included in the systematic review	Nine studies (cohort studies) published between 2003 and 2015 were selected for inclusion: three prospective and six retrospective cohort studies. The authors state that no randomised controlled trials were identified from their search. The studies involved mainly adults (permanent anterior, premolar, or molar teeth). Funding sources of primary studies were not reported.
Types of studies included	The preliminary search revealed that randomised controlled studies on survival and complications of indirect restorations would be very limited or even non-existent. Therefore, an eligibility assessment of non-randomised clinical studies, after a detailed quality evaluation protocol, was adopted. Randomised and non-randomised clinical studies could be included. The full-text studies excluded from the study were listed with reasons for exclusion.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	A modified version of the Cochrane Collaboration's risk of bias instrument was used to assess the risk of bias in the primary studies.
Appraisal rating	Based on a modified version of the Cochrane Collaboration's risk of bias instrument, seven of the studies were assessed as having a high risk of bias, and two as having an unclear risk of bias. The overall quality of evidence for the nine included studies was low. None of the nine studies was judged to have adequate random sequence generation as they were cohort studies, and three were considered to have adequate blinding of outcome assessors. Vagropoulou <i>et al.</i> stated that, "Generally, publication bias of various forms is almost assured, but fail-safe analyses cannot be trustworthily statistically tested and evaluated mainly due to the limited number of studies."¹⁰⁹ (p911)
Method of analysis	The restorations' survival rate was the primary outcome of the present study. The failure rate of the various types of specific failures was the secondary outcome. Within the methodological frame of meta-analysis, survival rate and failure rate were considered as indices of effect size. In both cases, the contribution (weight)

Parameter	Extraction
	of each study in the analysis was based on the number of restorations and it was determined according to the following scheme: arms within studies were weighted according to the quantity $W=1/SE$, with $SE=r/\sqrt{rN}$, where r is the survival rate or failure rate, as appropriate, of the arm (computed as ratios) and N is the total number of restorations used in the arm (for survival rate) or the total number of failures (for failure rate). All statistical comparisons were carried out within the methodological frame of the random-effects model of meta-analysis in order to overcome probable bias resulting from methodological or other differences among the selected studies. Differences among groups of studies were tested by the comparison of the estimated mean survival rate (or failure rate) according to the degree of overlap of the corresponding bias-corrected bootstrap 95% CIs. Groups were considered statistically significantly different if the corresponding 95% CIs for mean survival rate (or failure rate) did not overlap. Analysis of variance results are reported in the manuscript; however, these results were not assessed because of the limited number of studies and the fact that there was no evidence relative to the normality of the distribution of the effect size indices (survival rate or failure rate) used in the current analyses. The heterogeneity of studies was assessed with Cochran's Q test at significance level $p \leq 0.10$ in order to increase the power of the test. A scatter plot was produced for the graphical representation of the association between survival rate and follow-up time (in months). Spearman's Rho correlation coefficient was computed for evaluating the strength of association. Using SPSS version 15.0, a weighted smoothing curve was plotted on the corresponding scatter plot to verify the examined relationship. MetaWin v.2.1 software was used for performing the analysis
Outcome assessed	Survival rates or failure rates of indirect restorations At least one year follow-up Outcome by primary study: Survival rates: Barnes 2010; Beier 2012; Donovan 2004; Fabbri 2014; Heckland 2003; Kelly 2004; Reich 2004; Sulaiman 2015; van Dijken 2010. Type of complications: Barnes 2010; Beier 2012; Fabbri 2014; Reich 2004.
Results/findings	Based on the narrative and descriptive analysis of the included studies, the mean survival rate of inlays was 90.9% at five years, while for onlays and crowns it was 93.5% and 95.4%, respectively. For the fourth study group, consisting of both inlays and onlays, the survival rate was found to be 99.4%. This means that indirect restorations show survival rates over 90%, which is judged to be very high by the authors. In addition, the analysis demonstrated caries to be the main biological complication for all types of restorations, followed by root and/or tooth fracture incidence and endodontic incidence. Ceramic fractures represented the most common technical complication, followed by loss of retention and porcelain chipping. An association between the kind of complications and different types of restorations could not be established. Nevertheless, a relatively high failure rate due to caries and ceramic fractures was noted. However, the evidence is derived from non-randomised studies with high or unclear risk of bias, and therefore the HRB designated it to be low-quality evidence upon which to assess the survival of indirect restoration techniques. There was no evidence for comparisons between direct and indirect restoration materials. According to Vagropoulou <i>et al.</i>, "The overall quality of evidence of the 9 studies was low. Due to the heterogeneity of the included studies no meaningful comparison could be made between types or restoration of materials".^{109 (p917)}
Significance/direction	This means that indirect restorations show survival rates over 90%, which is judged to be very high by the authors. The analysis demonstrated caries to be the main biological complication for all types of restorations, followed by root and/or tooth fracture incidence and endodontic incidence.
Heterogeneity	According to Vagropoulou <i>et al.</i>, "Due to the heterogeneity of the included studies no meaningful comparison could be made between types or restoration of materials".^{109 (p917)} The risk of bias was unclear and the authors did not assess confounding, but did discuss it as a limitation in their discussion.

Parameter	Extraction
Comments	GRADE was used by the review authors. All nine of the cohort studies were assessed as having a high or unclear risk of bias. None of the nine studies was judged to have adequate random sequence generation as they were cohort studies, and three (33%) were considered to have adequate blinding of outcome assessors. The review authors report clinical and methodological heterogeneity. The quality of the review was rated as moderate using AMSTAR 2. The HRB grades the quality of the evidence as low for the different outcomes which corresponds with the review authors rating.

Morimoto *et al.* (2016)

Parameter	Extraction
First author and year of publication	Morimoto <i>et al.</i> (2016)²⁹
Objectives	Evaluated the survival rate of resin and ceramic inlays, onlays, and overlays at five years and ten years in permanent teeth (deduced from reported age range and intervention), and identified the types of complications associated with the main negative clinical outcomes. ²⁹ (p986)
Participants	Permanent teeth (based on age and length of follow-up), cavitated caries, indirect restorations Population: The age of the 2,080 participants involved in the studies ranged from 12 to 79 years, but the type of teeth is not stated. Gender was not reported. There were 7,427 posterior teeth restored.
Setting/context	The 14 studies were published between 1997 and 2012. The studies were completed in Austria, Germany, Italy, Japan, Sweden, and Switzerland.
Description of interventions/phenomena of interest	Intervention: Resin and ceramic inlays, onlays, and overlays to most likely permanent teeth (this was not specifically stated) According to Morimoto <i>et al.</i>, "partial indirect restorations classified as inlays (without covering the cusps), onlays (covering at least 1 cusp), and overlays (covering all cusps), enable conservation of the remaining dental structure, promoting reinforcement of a tooth compromised by caries or fractures. Numerous resin or ceramic materials are currently available for fabricating indirect partial restorations and mechanical strength is important for their durability in posterior applications...Differences in the mechanical properties of resin-based and ceramic materials raise the question as to which material can survive longer, especially in loadbearing posterior regions of the mouth."²⁹ (p985–986) Comparator: None
Databases and sources searched	Two reviewers searched three databases (PubMed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL)) for articles published between 1983 and April 2015. The authors selected 1983 as the starting point because adhesive procedures for ceramics with the use of hydrofluoric acid and silanization were first introduced in that year. References of the included articles were checked manually. There was no mention of a study protocol in the article. It was not clear who or how many authors screened the abstracts and full texts. Duplicate extraction was completed. This study was funded by Ibirapuera University in São Paulo, Brazil. The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article.
Date range (years) of included studies	The 14 included studies were published between 1997 and 2012.
Number of primary studies included in the systematic review	Eleven retrospective studies, two prospective cohort studies, and one randomised controlled trial were included in this review. The funding source for primary studies was not provided.
Types of studies included	The study design was clinical studies (prospective studies, retrospective studies, or randomised controlled trials in humans) with a follow-up period to measure survival. The reasons for exclusion were reported but the study references were not provided.
Country of origin of included studies	The studies were completed in Austria, Germany, Italy, Japan, Sweden, and Switzerland.

Parameter	Extraction
Appraisal instruments used	The authors used a bespoke quality assessment instrument that was previously used by Hayashi <i>et al.</i> 2003 and Morimoto <i>et al.</i> 2016
Appraisal rating	The authors reported that the percentage likelihood of bias in the individual studies ranged from 46.1% to 76.9%. The table of quality scores was examined, and 3 of the 14 included studies had adequate randomisation, 2 had adequate blinding of outcome assessors, 2 justified their sample size, 11 measured variance, and 12 had adequate retention of participants at follow-up. The cohort studies were not examined for the influence of confounding. Publications bias is not mentioned.
Method of analysis	Descriptive statistical analysis, meta-regression, and meta-analysis were performed, based on the estimated survival rates for intervals of 5 and 10 years. The Cochran Q test was performed to evaluate heterogeneity among the studies. The presence of statistical heterogeneity was analysed using the inconsistency test ($I^2 \geq 50\%$). Data were transformed and the individual CIs of the studies were calculated by the Clopper-Pearson method. A meta-regression was performed considering the type of material used, the highest survival rate, the study design (retrospective compared with prospective), and the study settings (university compared with private clinic). Analyses of survival in the subgroups were then performed for each ceramic type (feldspathic porcelain compared with glass ceramic). When the study did not present variance or a standard deviation, the survival rate was calculated based on the analysis of the number of failures and censorship during the follow-up duration. Data collected from the full-text articles were calculated using the Kaplan-Meier method for 12 articles (Roulet 1997; Felden <i>et al.</i> 1998; Fuzzi and Rappelli 1998; Hayashi <i>et al.</i> 2000; Posselt and Kerschbaum 2003; Sjögren <i>et al.</i> 2004; Schulte <i>et al.</i> 2005; Reiss 2006; Frankenberger <i>et al.</i> 2008; Kramer <i>et al.</i> 2008; Otto and Schneider 2008; Beier <i>et al.</i> 2012) and life tables for 2 articles (Schulz <i>et al.</i> 2003; Smales and Etemadi 2004). The Greenwood formula was used to calculate the variance, assuming that the censorship occurred uniformly together with the failures over time. Failure rates were collected for the subgroups focusing on fracture/chipping, endodontic problems, secondary caries, debonding, and severe marginal staining. Although different evaluation criteria were used, such as the modified USPHS or California Dental Association/Ryge criteria, the worst criterion (Charlie, or score 3) was selected for the analysis of marginal staining. Odds ratios were calculated considering tooth vitality (vital compared with endodontically treated), type of tooth (premolar compared with molar), extension of cusp coverage (inlay, onlay, and overlay compared with each other), and location (maxilla compared with mandible).
Outcome assessed	Outcome: Survival rate at five years and ten years, and of complications associated with the main negative clinical outcomes. Time frame: The meta-analysis of survival rates was performed by ceramic types at five years and ten years after the intervention. Outcome by primary study: Survival rates: Glass ceramic: Beier (2012); Frankenberger (2008); Kramer (2008); Schulte (2005); Roulet (1997); Reiss (2006); Felden (1998). Feldspathic porcelain: Otto and Schneider (2008); Smales and Etemadi (2004); Sjögren (2004); Schulz (2003); Hayashi (2000); Fuzzi and Rappelli (1998); Reiss (2006); Felden (1998). Ceramic (not specified): Posselt and Kerschbaum (2003).
Results/findings	No studies of resin inlays, onlays, and overlays were identified due to non-compliance with inclusion criteria or incomplete data. In the ceramics group, six studies had participants with feldspathic porcelain only, five studies had participants with glass ceramic only, and three studies included participants who received either material. The meta-regression showed no association between ceramic types and the survival rates at five years ($P = 0.12$) and ten years ($P = 0.55$). Evaluation of the homogeneous distribution of the 14 articles reporting 5-year survival rates indicated that there were two outlier articles with lower survival rates reported than in the other 12 studies. A sensitivity analysis revealed that the removal of these two studies would not influence the interpretation of the results. Evaluation of the homogeneous

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	distribution of the eight articles reporting 10-year survival rates found no association between survival rate and study design ($p=0.927$), follow-up time ($p=0.837$), or study setting ($p=0.914$). The combined survival rate of the total pooled sample of feldspathic porcelain and glass ceramic for 5-year follow-up (5,811 restorations) was 95% (95% CI: 91–97%; I^2: 93.6%). At the 10-year follow-up, the survival rate of the sample (2,154) was 91% (95% CI: 88–94%; I^2: 74.5%). For feldspathic porcelain, the survival rates were 92% (95% CI: 80–97%; I^2: 90.9%; 661 restorations) for 5-year follow-up and 91% (95% CI: 83–95%; I^2: 77.4%; 538 restorations) for 10-year follow-up. For glass ceramic, the survival rates were 96% (95% CI: 89–98%; I^2: 91%; 1,579 restorations) for 5-year follow-up and 93% (95% CI: 86–96%; I^2: 75.8%; 605 restorations) for 10-year clinical follow-up. According to 13 of the included studies, which reported 106 failures out of 4,800 restorations, the fracture/chipping rate of teeth and/or inlay, onlay, and overlay restorations was 4% (95% CI: 2–9%). The incidence of endodontic problems was reported as 3% (95% CI: 3–4%; 117 failures out of 3,785 restorations; 11 studies). Because the I^2 value was less than 50% (I^2: 37.7%), the data extracted were those obtained by the fixed effect, showing no difference in incidence of endodontic problems for both materials. The incidence of secondary caries was 1% (95% CI: 1–3%; 48 of 4,644 restorations; 10 studies), and the incidence of debonding was also 1% (95% CI: 0–3%; 4,854 restorations; 6 studies). No severe marginal staining was noted in three studies (0 of 338 restorations). Pulp vitality and endodontic problems were encountered in such restorations (OR: 0.19; 95% CI: 0.04–0.96; 142 of 2,236 restorations in vital teeth; 34 of 132 restorations in non-vital teeth; 3 studies). Failures were not attributable to the type of tooth (premolar compared with molar) (OR: 0.54; 95% CI: 0.17–1.69; 39 of 710 restorations in premolars; 64 of 997 restorations in molars; 5 studies). The I^2 in a number of the meta-analyses indicate high or substantial heterogeneity but the authors have done further analyses and were satisfied that it does not affect their results. The main findings from this review suggest that there is low-quality evidence from a mix of study designs with an unclear or high risk of bias that ceramic inlays, onlays, and overlays produce acceptable high restoration survival rates of over 90% regardless of the ceramic material, study design, or study setting. According to Morimoto <i>et al.</i>, “the pooled estimated survival rate was 95% for 5 years of follow-up and the survival rate decreased but not significantly to 91% after 10 years of follow-up (93% for glass-ceramics and 91% for feldspathic porcelain). One explanation for the similar performance of glass-ceramics and feldspathic porcelain could be the adhesive cementation that likely compensated for the mechanical differences between the two ceramic materials.”²⁹_(p991) The authors also report that “fractures remain the most frequent type of failure. And the type of tooth does not seem to affect survival rates, but restorations survived longer on vital teeth.”²⁹_(p993) There is no evidence with which to draw comparisons between direct and indirect methods of restoration. According to Morimoto <i>et al.</i>, “no study with resin inlays, onlays, and overlays could be selected in this review. Therefore, it was not possible to perform a meta-analysis...[to test] whether resins survive longer than ceramics.”²⁹_(p991)
Significance/direction	Results listed by outcome.
Heterogeneity	The I^2 in a number of the meta-analyses indicate high or substantial heterogeneity but the authors have done further analyses and were satisfied that it does not affect their results.
Comments	GRADE was not used by the review authors. Eleven retrospective studies, two prospective cohort studies, and one randomised controlled trial were included in this review. The authors reported that the percentage likelihood of bias in the individual studies ranged from 46.1% to 76.9%. The table of quality scores was examined, and three (21%) of the 14 included studies had adequate randomisation while two (14%) had adequate blinding of outcome assessors. None of the included cohort studies were not

Parameter	Extraction
	examined for the influence of confounding. The quality of the review was rated as critically low using AMSTAR 2 as the authors combined different study designs in their meta-analysis, and did not address bias in the analysis or discussion. The HRB grades the quality of the evidence as very low for the different outcomes.

Grivas *et al.* (2014)

Parameter	Extraction
First author and year of publication	Grivas <i>et al.</i> (2014)¹¹⁰
Objectives	Evaluated clinical performance (longevity, colour match, and post-operative sensitivity) at twelve months or longer of indirect composite inlays compared with direct composite restorations as well as with ceramic and gold inlays in adults with permanent vital teeth restorations.
Participants	Permanent dentition, cavitated lesions, indirect restoration Adults with permanent vital teeth that have been treated using indirect composite resin or a valid comparator There were 507 participants with 1,326 restorations in the trials. Age and gender were not reported. The follow-up times varied from 3.5 to 11 years.
Setting/context	The clinical settings and study countries were not reported.
Description of interventions/phenomena of interest	Composite inlays and onlays compared with ceramic and gold inlays as well as with direct composite restorations.
Databases and sources searched	Three databases were searched for English-language studies up to November 2013: Ovid MEDLINE (1946 to November 2013), Cochrane Central Register of Controlled Trials (CENTRAL), and Embase (1980 to November 2013). Reference lists of the identified articles and available similar systematic reviews were also screened to find relevant articles. Important prosthodontic journals were hand-searched, focusing on the last 6 months, in order to ensure that no related article had been published and not included yet in the above databases. The authors did not publish a protocol. The review does not state who screened the abstracts and full texts, but two authors did extract the data. Conflict of interest or funding sources for the review were not stated.
Date range (years) of included studies	Fourteen trials (eight randomised controlled trials and six controlled clinical trials) published between 1995 and 2013 were included in the review.
Number of primary studies included in the systematic review	Fourteen trials (eight randomised controlled trials and six controlled clinical trials) published between 1995 and 2013 were included in the review. The sources of funding for primary studies were not reported.
Types of studies included	Randomised controlled trials and controlled clinical trials that evaluate composite resin inlays and onlays for the restoration of posterior teeth were eligible for inclusion. The excluded studies and their reasons for exclusion were not listed.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The authors used a bespoke quality assessment tool used in two other reviews to assess the quality of the 14 included trials. The tool comprised 24 questions to evaluate the scientific power of these studies and distinguish the well-conducted studies from those that were poorly organised.
Appraisal rating	No trial achieved a perfect score of 24. One trial achieved 20 out of 24 (the highest score among the included trials) and two trials achieved 13 out of 24 (the lowest score among the included trials). Only 4 of the 14 trials had adequate randomisation, and 4 trials had adequate blinding for outcome ascertainment. The authors describe the evidence as low quality. The authors discuss publication bias as follows: "A great effort has been made to retrieve all the articles for the purposes of this systematic review. Potential bias could be the exclusion of non-English articles. English abstracts for two of them have been identified but the extraction of useful information was impossible. Authors and manufacturers have not been contacted to confirm whether new trials are due to be published. The identification of the more recent versions of the long-term studies was extremely difficult." ¹¹⁰ (p7)

Parameter	Extraction
Method of analysis	The authors report that "A comprehensive approach should include a meta-analysis and a thorough assessment of the bias. In the present review only eight randomised controlled trials were included. The low quality of the available evidence and the small number of randomised trials as well as the variety of the methodology and the heterogeneity of the trials prevent us from conducting a meta-analysis which could confidently give answers regarding the longevity of the composite inlays. For the above reasons the present study is limited to a qualitative analysis. Finally, authors of the RCT [randomised controlled trial] papers modified the acceptable USPHS clinical criteria according to their needs, making the extraction of the data challenging." ¹¹⁰ (p4)
Outcome assessed	Longevity, colour match, and post-operative sensitivity at 12 months or longer The follow-up times varied from 3.5 to 11 years. Outcome by primary study: Composite inlays compared with ceramic and gold: Manhart 2001; Thordrup 2006; Fasbinder 2013; Gladys 1995; Kaytan 2005. Composite inlays with direct composite fillings: Pallesen 2003; Wassell 2000; Spreafico 2005; Mendonca 2010; Cetin 2009; Manhart 2000; van Dijken 2000. Composite inlays on premolars compared with molars: Manhart 2001; Huth 2011; Pallesen 2003; Manhart 2000; van Dijken 2000.
Results/findings	Five articles have given some evidence on composite inlays compared with ceramic and gold inlays. Five of them were comparing composite with ceramic and only one was comparing composite with gold. The survival rate of composite inlays ranged from 100% after three years to 51% after ten years and was not significantly different to ceramic or gold materials. There was conflicting evidence on colour match over time and there was no difference for post-operative sensitivity at one month follow-up. The authors concluded that there was insufficient evidence to answer whether there was any difference in longevity and aesthetic quality between composite compared with ceramic or gold inlays, while all three substances seem to perform equally with respect to post-operative sensitivity. Five studies that compared indirect composite inlays with direct composite fillings had follow-up periods ranging from 3.5 to 11 years, and the survival rates for indirect composite inlays varied from 100% after 3.5 years to 87.3% after 11 years. The authors report that the studies provide insufficient evidence to identify whether there is a difference in longevity between indirect composite inlays and direct composite fillings. The majority of the studies concur that differences between indirect composite inlays and direct composite fillings with respect to aesthetic quality (colour match and marginal discolouration) and post-operative sensitivity are insignificant. Five studies evaluated composite inlays on premolars compared with molars and the findings of all five agreed that composite inlays performed significantly better on premolars than on molars. However, the available studies could not determine whether cavity size can influence their clinical performance. The authors concluded: "Despite several limitations that have been described in detail above, composite inlays can compete against ceramic inlays, gold inlays and direct composite fillings and it is inevitable that their use will increase in the era of the conservative dentistry." ¹¹⁰ (p8)
Significance/direction	No difference in outcomes.
Heterogeneity	The authors report that "A comprehensive approach should include a meta-analysis and a thorough assessment of the bias. In the present review only eight RCTs [randomised controlled trials] were included. The low quality of the available evidence and the small number of randomised trials as well as the variety of the methodology and the heterogeneity of the trials prevent us from conducting a meta-analysis which could confidently give answers regarding the longevity of the composite inlays. For the above reasons the present study is limited to a qualitative analysis. Finally, authors of the RCT papers modified the acceptable USPHS clinical criteria according to their needs, making the extraction of the data challenging." ¹¹⁰ (p4)
Comments	GRADE was not used by the review authors.

Parameter	Extraction
	Both randomised and non-randomised trials (eight randomised controlled trials and six controlled clinical trials) were included in the review; only randomised controlled trials were included in the pooled narrative analyses. Only four (29%) of the 14 trials had adequate randomisation, and four (29%) trials had adequate blinding for outcome ascertainment. The authors report clinical and methodological heterogeneity. The quality of the review was rated as moderate using AMSTAR 2. The HRB grades the quality of the evidence as low for the different outcomes.

Fron Chabouis *et al.* (2013)

Parameter	Extraction
First author and year of publication	Fron Chabouis <i>et al.</i> (2013)¹¹¹
Objectives	Compared composite inlays and onlays with ceramic inlays or onlays for restoring posterior teeth in adults.
Participants	Permanent dentition, cavitated caries, indirect restorations Population: Adult posterior permanent teeth Two randomised controlled trials involving 138 inlays (no onlays were evaluated) in 80 patients were included in this review. Only one trial reported age range (28–69 years) and gender (19% men).
Setting/context	The settings and countries were not provided.
Description of interventions/phenomena of interest	Composite inlays and onlays were compared with ceramic inlays or onlays. According to Fron-Chabouis <i>et al.</i> , “ceramic inlays and onlays are mainly composed of glass, with some crystals added to increase strength. Composite inlays and onlays are made of a resinous matrix and fillers of different types. Ceramic materials are resistant to compressive forces than composite materials but are susceptible to tensile stresses and more prone to fracture. However, ceramics are harder than composites and more wear-resistant but can induce more wear than usual with the opposing tooth’s surface. Furthermore, adhesive cement interfaces are made of composite material, so the wear of the interface and restoration material should be closer for composites and marginal integrity could be better. Another disadvantage of composites is their resinous matrix and the possible monomer release if it is incompletely polymerized.” ¹¹¹ (p1210)
Databases and sources searched	The authors searched three databases (MEDLINE, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL)) without any restriction on date or language up to 24 December 2012. The full electronic search strategy is provided in an appendix. References of eligible studies and ClinicalTrials.gov were also searched. The authors completed and registered a protocol, which can be accessed on the PROSPERO website. Two authors independently and in duplicate screened the literature. The procedure for extracting the data was not presented. The authors declare no financial support but do not mention other conflicts. The funding source for the review is not mentioned.
Date range (years) of included studies	One of the included trials was published in 2006, and the other was published in three articles in the years 1994, 2001, and 2005.
Number of primary studies included in the systematic review	Two randomised controlled trials involving 138 inlays (no onlays were evaluated) in 80 patients were included in this review. Funding sources for primary studies not reported.
Types of studies included	The inclusion criteria required randomised controlled trials. No list of studies excluded from this review was provided, but the reasons for their exclusion were reported.
Country of origin of included studies	The study countries were not provided.
Appraisal instruments used	The Cochrane Collaboration’s risk of bias instrument was used to assess the risk of bias in primary trials.
Appraisal rating	Based on the Cochrane Collaboration’s risk of bias instrument, both trials were judged to be at high risk of bias. Neither of the two trials was judged to have adequate random sequence generation and only one was considered to have adequate blinding of outcome assessors.

Parameter	Extraction
	The authors planned to assess a possible publication bias by producing a funnel plot of effect estimates against their standard errors if at least 10 trials were included in a meta-analysis; however, “Since this was not the case, identifying and discussing publication bias is awkward. Since most studies are supported by industries in restorative dentistry, such a bias cannot be excluded.”¹¹¹ (p1216)
Method of analysis	The unit of analysis was the tooth. For clinical score outcomes, the authors reported only percentages of restorations assessed with the best grade – that is, 1 for FDI World Dental Federation (FDI) criteria, A for USPHS criteria, and R for CDA [Canadian Dental Association criteria]. For each item, the authors estimated risk ratios for the restoration to be assessed with the best grade (considered the event). To take into account patients with missing outcome data, they assumed that the proportion of patients with the best grade was the same in complete cases and in patients with missing outcome data. For the dichotomous failure outcome, the measure of treatment effect was the risk ratio. To allow for an intention-to-treat analysis, the authors inputted missing outcome data as success. When a study included multiple composite or multiple ceramic groups, all composites were combined into a single composite group and/or all ceramics were combined into a single ceramic group. The authors synthesised trials comparing at least one composite and one ceramic with the same outcome (item score or failure) at a given follow-up time. The decision of whether or not to combine the results of individual studies depended on the assessment of heterogeneity in forest plots and by I^2 coefficients. Combined estimates and associated 95% CIs were calculated using the Mantel–Haenszel fixed-effects method.
Outcome assessed	Outcome: Colour match, occlusal marginal adaptation, or surface finish, failure rate Time frame: The follow-up had to be six months or more. Actual follow-up was three years. Both included studies (Fasbinder 2005; Thordrup 2006) assessed each of the following outcomes: failure, colour match, anatomical form, occlusal marginal adaption, and surface finish.
Results/findings	The authors compared the clinical efficacy (failure and clinical scores) of composite inlays with ceramic inlays in adults using two randomised controlled trials exhibiting a high risk of bias and involving 138 inlays in 80 patients. Using fixed-effects meta-analysis, the 3-year overall failure risk ratio was not statistically significant (relative risk: 2.0; 95% CI: 0.38–10.55; I^2: 0%; two trials; 80 patients; 138 restorations). The overall 3-year success rate was 94.2% for composite inlays and 97.1% for ceramic inlays. The reported clinical acceptable scores (colour match, anatomical form, occlusal marginal adaption, surface finish) for the condition of the indirect restorations (USPHS and California Dental Association) showed considerable heterogeneity between trials and could not be combined; visual examination of the results of the two trials for each measure indicated no difference in outcome. This evidence is insufficient and very low quality, and there is therefore inadequate evidence upon which to judge the performance of composite inlays and onlays compared with ceramic inlays and onlays. According to Fron Chabouis <i>et al.</i>, “although we provide some evidence that ceramic inlays perform better than composite inlays in the short term, this review included only 2 randomized clinical studies and 138 restorations and the 3-year result may not remain in the long term.”¹¹¹ (p1216)
Significance/direction	No statistical difference.
Heterogeneity	No statistical heterogeneity.
Comments	GRADE was not used by the review authors. Both included trials were judged to be at high risk of bias. Neither of the two trials was judged to have adequate random sequence generation and only one (50%) was considered to have adequate blinding of outcome assessors. The authors report no statistical heterogeneity. The quality of the review was rated as critically low using AMSTAR 2 as they did not control for or discuss the influence of risk of bias. The HRB grades the quality of the evidence as low for the different outcomes.

Comparison direct and indirect restoration material

Vetromilla *et al.* (2020)

Parameter	Extraction
First author and year of publication	Vetromilla <i>et al.</i> (2020) ¹¹²
Objectives	Evaluated restorative treatment types and materials for large tooth cavity restorations in permanent posterior teeth in adults with respect to tooth or restoration longevity, and ranked them from best to worst. The studies had to have a minimum of five years of follow-up.
Participants	Permanent dentition, cavitated lesions, restoration materials longevity Adults with large tooth cavity restorations in permanent posterior teeth The characteristics of the 13 randomised controlled trials and 15 prospective studies included were combined (28 studies). These 28 studies included 1,621 participants (with 4,063 teeth) and 40% were male. The mean age range was 15–55 years. The longest follow-ups ranged from 5 to 30 years. Thirteen studies had a 5-year follow-up, 9 studies had 6–10 years follow-up, 4 studies had 11–15 years follow-up, and 2 studies had 26–30 years follow-up. The study countries were Brazil, Denmark, Germany, Italy, Lebanon, Norway, Portugal, Sweden, the Netherlands, and the UK. Additionally, the characteristics of the 15 retrospective studies were presented together. These 15 studies included 904 participants (with 216,996 teeth, one study accounted for 207,690 teeth but did not provide the number of people) and 46% were male. The mean age range was 38–55 years. The longest follow-ups ranged from 5 to 50 years. Four studies had a 5-year follow-up, six studies had 6–10 years follow-up, three studies had 12 years follow-up, one study had more than 18 years follow-up and another had 50 years follow-up. The study countries were Brazil, Canada, Germany, the Republic of Korea, Sweden, the Netherlands, the UK, and Uruguay. In addition, there was one multiregional study.
Setting/context	The study countries were Brazil, Canada, Denmark, Germany, Italy, Lebanon, Norway, Portugal, the Republic of Korea, Sweden, the Netherlands, the UK, and Uruguay. In addition, there was one multiregional study. The clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: A large tooth preparation was defined as any preparation involving the need for a restoration that would encompass two or more surfaces. The clinical studies compared at least two types of restorative materials placed in large tooth preparations in permanent posterior teeth (from two-surface restorations up to full crowns). Materials included: Amalgam, direct resin, feldspathic ceramic, glass ceramic, glass ionomer, gold, indirect resin, metal ceramic, resin sandwich, and zirconia-based ceramic. Comparator: Each other.
Databases and sources searched	Four electronic databases (MEDLINE, Scopus, the Cochrane Library, and Web of Science) were searched up to October 2019. There were no language or year of publication restrictions. The search strategies were presented in a table in the paper. A protocol was registered with PROSPERO. Duplicate screening and extraction were completed. The authors certified that they had no conflicts of interests and funders did not influence the study design or findings. The authors were funded by public institutions.
Date range (years) of included studies	Forty-three studies published between 1989 and 2019 were included in this review.
Number of primary studies included in the systematic review	Thirteen included studies were randomised controlled trials, 15 were prospective cohort studies, and 15 were retrospective cohort studies. As each material should appear in at least two studies, five articles were excluded from analysis because the materials investigated had been evaluated only once. All different types of resin composite were grouped as direct resin composite, which led to six additional studies being excluded from the network meta-analysis because these studies were comparing two types of resin composites. The analysis is based on 32 studies. The sources of primary study funding were not reported.
Types of studies included	Randomised controlled trials, prospective cohort studies, and retrospective cohort studies with a follow-up period of at least 5 years were eligible. The reason for this

Parameter	Extraction																					
	decision was not explained and the language indicated that the authors perceived the variety of study designs as an advantage. A list of studies excluded at full-text screening was not provided but their reasons for exclusion were reported.																					
Country of origin of included studies	The study countries were Brazil, Canada, Denmark, Germany, Italy, Lebanon, Norway, Portugal, the Republic of Korea, Sweden, the Netherlands, the UK, and Uruguay. In addition, there was one multiregional study.																					
Appraisal instruments used	The Cochrane Collaboration’s risk of bias tool was employed to assess the risk of bias in the included trials. The quality assessment for the cohort studies was performed with the Risk Of Bias In Non-Randomized Studies – of Interventions (ROBINS-I) tool and considered confounding, selection of participants, classification of interventions, deviation from intended interventions, missing data, measurement of outcomes, and selection of the reported results.																					
Appraisal rating	Two of the 13 randomised controlled trials were judged to have a high risk of bias and the other 11 trials had an unclear risk of bias. Nine of the 13 randomised controlled trials were judged to have adequate randomisation and 8 had adequate blinding of outcome assessment. Twenty-four of the 30 prospective and retrospective cohort studies were judged to have a serious risk of bias, five had a moderate risk of bias, and only one had a low risk of bias. The main biases were lack of control for confounding and lack of blinding when measuring of outcomes. Publication bias was not discussed in the article.																					
Method of analysis	The primary outcome was restoration survival, recorded either in case of repair or no intervention. Replaced restorations or extracted teeth were considered as failures. The annual failure rate of the investigated restorations was calculated according to the following formula: $(1 - y)z = (1 - x)$, in which y represents mean annual failure rate and x is total failure rate at z years. All data analysis was performed using R, Version 3.5.1 and the packages ‘pcnetmeta’ and ‘meta’ separately for randomised controlled trials and non-randomised prospective and retrospective studies. Pairwise meta-analyses for direct treatment comparisons were performed using the random-effects model, with heterogeneity assessed by calculating the I^2. Multi-arm studies were treated as multiple independent two-arm studies in pairwise meta-analyses, and the effects were estimated as risk ratios. The hierarchical model chosen for the network meta-analysis was the Bayesian framework using the Markov chain Monte Carlo method simulation, with 20,000 iterations for adaptation. The random-effects model was used due to the differences among studies regarding methodology. The convergence was also assessed by the Markov chain Monte Carlo method. A summary network plot was generated in which the nodes represent the competing interventions, and the edges represent the comparison between the interventions. The surface under the cumulative ranking line for each treatment was calculated. In this approach, the closer to 1 the cumulative probability is, the better the treatment.																					
Outcome assessed	Outcomes: Survival rate at 5 years of follow-up or longer The longest follow-ups for the 15 prospective cohort studies and 13 randomised controlled trials ranged from 5 to 30 years. Thirteen studies had a 5-year follow-up, nine studies had 6–10 years follow-up, 4 studies had 11–15 years follow-up, and 2 studies had 26-30 years follow-up. The longest follow-ups for the 15 retrospective cohort studies ranged from 5 to 50 years. Four studies had a 5-year follow-up, six studies had 6–10 years follow-up, three studies had 12 years follow-up, one study had more than 18 years follow-up, and another had 50 years follow-up. Thirty-two studies used in the survival analysis were: <table><tr><th></th><th colspan="2">Survival comparisons</th></tr><tr><th>Randomised controlled trials</th><th>Prospective cohort studies</th><th>Retrospective cohort studies</th></tr><tr><td>Skupien 2016</td><td>Norman 1990</td><td>Felden 1998</td></tr><tr><td>Mannocci 2005</td><td>Rowe 1989</td><td>Wagner 2003</td></tr><tr><td>Bernardo 2007</td><td>Mjor and Jokstad 1993</td><td>Arnelund 2004</td></tr><tr><td>Passia 2013</td><td>Lumley and Fisher 1995</td><td>Opdam 2007</td></tr><tr><td>Fennis 2014</td><td>Mair 1998</td><td>Opdam 2010</td></tr></table>		Survival comparisons		Randomised controlled trials	Prospective cohort studies	Retrospective cohort studies	Skupien 2016	Norman 1990	Felden 1998	Mannocci 2005	Rowe 1989	Wagner 2003	Bernardo 2007	Mjor and Jokstad 1993	Arnelund 2004	Passia 2013	Lumley and Fisher 1995	Opdam 2007	Fennis 2014	Mair 1998	Opdam 2010
	Survival comparisons																					
Randomised controlled trials	Prospective cohort studies	Retrospective cohort studies																				
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Passia 2013	Lumley and Fisher 1995	Opdam 2007																				
Fennis 2014	Mair 1998	Opdam 2010																				

Parameter	Extraction		
	Monaco 2017	Erpenstein 2000 Pallesen and Van Dijken 2000 Wassel 2000 Thordrup 2001 Pallesen and Qvist 2003 Khairallah and Hokayem 2009 Federlin 2010 Santos 2016	Kim 2013 Skupien 2013 Van de Sande 2015 Collares 2016 Laske 2016 Naghipur 2016 Rinke 2016 Olley 2018
Results/findings	The results of randomised controlled trials are the most reliable results because their study design controls for confounding and biases, followed by prospective cohort studies, as these at least control for recall if not for confounding. The retrospective cohort study design has the highest risk of bias and confounding. This should be kept in mind when considering the text-based results and table below. The network meta-analysis results and the annual failure rate values suggest that most of the restorative options have good performance and are suitable for large restorations. Less favourable performances were found for glass ionomer as direct material and glass ceramic and feldspathic ceramic as indirect materials in the ranking of probabilities and surface under the cumulative ranking. Most of the pairwise comparisons between feldspathic and glass ceramic (95% CI: 0.84–1.77 for the prospective cohort studies; 95% CI: 0.87–1.16 for retrospective cohort studies) and direct resin composite and amalgam (95% CI: 0.65–1.15 for randomised controlled trials; 95% CI: 0.93–1.06 for prospective cohort studies; 95% CI: 0.97–1.29 for retrospective cohort studies) did not have significant differences in failure for the comparisons examined. Glass ionomer, either alone or in combination with composite, was found to be more prone to failure than amalgam (95% CI: 0.97–2.20 for prospective cohort studies; 95% CI: 1.36–1.44 for retrospective cohort studies) and direct composite resin in the pairwise meta-analyses (95% CI: 1.06–2.14 for prospective cohort studies; 95% CI: 1.68–1.79 for retrospective cohort studies). Based on the overall results combining the findings of all study designs, the best annual failure rate for direct restorations was resin composite (at 2.2%), and for indirect restorations was gold (at 0.3%). The highest annual failure rate for any method was for glass ionomer restorations (at 10.1%). The highest annual failure rate for the indirect method was for zirconia-based ceramic (at 2.9%), followed by glass ceramic (at 2.5%). Composite glass ionomer sandwich restorations had an annual failure rate of 4.2%, and amalgam had a 2.7% annual failure rate. Indirect metal ceramic restorations had low annual failure rates (at 0.5%), and indirect composite resin (1.8%) had marginally lower failure rates than direct composite resin (2.2%). The failure rate for feldspathic ceramic was 1.6%, similar to that of indirect composite resin. Overall, indirect methods appear to perform better than direct methods. It is important to note that, generally, randomised controlled trials present more reliable evidence and that findings from cohort studies tend to overstate success. The majority of included cohort studies failed to control for bias and confounding. Based on the results of randomised controlled trials, the best annual failure rate for direct restorations was for amalgam (at 1.9%), and for indirect restorations it was metal ceramic (at 0.3%). The highest annual failure rate for any method was for zirconia-based ceramic (at 5.1%). Indirect composite resin (3.5%) had a marginally higher failure rate than direct composite resin (2.7%). The failure rate for gold was 0.75%. For randomised controlled trials, direct methods appear to perform better than indirect methods. It is important to note that, generally, randomised controlled trials present more reliable evidence. However, the randomised controlled trials in this study were at high risk of bias and less than 75% of them had adequate randomisation or blinding for outcome ascertainment.		
Significance/direction	Results listed by outcome.		
Heterogeneity	The authors measured heterogeneity and downgraded the level of evidence in cohort studies. However, they did not discuss the effect of heterogeneity on the trial results.		
Comments	GRADE was used by the review authors. GRADE was overestimated by the review authors for the evidence from trials. The review authors rating did not deduct for the limited number of		

Parameter	Extraction
	trials in each of the five meta-analyses (four meta-analyses were based on one trial, and one meta-analysis was based on two trials), the substantial statistical heterogeneity in the meta-analyses based on two trials, small samples in four of the analyses, and the unclear or high risk of bias in these trial-based studies. Only nine (69%) of the 13 randomised controlled trials were judged to have adequate randomisation and eight (62%) had adequate blinding of outcome assessment. The quality of the review was rated as critically low using AMSTAR 2 as the authors did not control for or discuss the influence of risk of bias. The HRB grades the quality of the evidence as very low for the different outcomes. The review authors graded the evidence from meta-analysis using cohort studies as very low. Twenty-four (80%) of the 30 prospective and retrospective cohort studies were judged to have a serious risk of bias. The main biases were lack of control for confounding and lack of blinding when measuring of outcomes. Six of the ten meta-analyses that had two or more studies had moderate to substantial heterogeneity. The four meta-analyses (direct resin restorations compared with amalgam, direct resin restorations compared with indirect resin, amalgam compared with glass ionomer, and direct resin compared to glass ionomer) with no statistical heterogeneity had inadequate sample sizes. Most of the single study meta-analyses had sample sizes less than 200. The quality of the review was rated as critically low using AMSTAR 2 as the authors did not control for or discuss the influence of risk of bias. The HRB grades the quality of the evidence as very low for the different outcomes, which corresponds with review authors rating

Angeletaki *et al.* (2016)

Parameter	Extraction
First author and year of publication	Angeletaki <i>et al.</i> (2016) ¹¹³
Objectives	Evaluated the clinical parameters of longevity (secondary caries, post-operative sensitivity, marginal discolouration, and colour match) for direct and indirect composite restorations in posterior (molar or premolar) teeth at follow-ups of three years or over.
Participants	Permanent dentition (judged by age and tooth type), cavitated lesions, and direct and indirect resin restorations Three randomised controlled trials published between 2003 and 2014 with 239 participants (with 424 posterior teeth) were included in the review. The mean age range was 23–55 years and the full age range was 20–81 years. Forty-five per cent of participants were male. The longest follow-ups ranged from 5 to 11 years.
Setting/context	The clinical settings were university-based facilities. The study countries were Denmark, the Netherlands, and Turkey.
Description of interventions/phenomena of interest	All direct and indirect composite inlays/onlays, irrespective of the resin and bonding material and the type of tooth. Comparison: Each other
Databases and sources searched	Four electronic databases were searched without restrictions up to 14 December 2015: MEDLINE (via Ovid and PubMed, from 1946), Embase (via Ovid), the Cochrane Oral Health Group Trials Register, and Cochrane Central Register of Controlled Trials (CENTRAL). Unpublished literature was searched on ClinicalTrials.gov, the National Research Register, and ProQuest Dissertations & Theses Global database. The search strategy is presented in an appendix. The reference lists of all eligible studies were hand-searched for additional studies. The protocol is not available. Two reviewers independently screened the abstracts and full texts and extracted the data. The authors declared no conflict of interest and that they did not receive any funding for the review.
Date range (years) of included studies	Three randomised controlled trials published between 2003 and 2014 were included in the review.

Parameter	Extraction
Number of primary studies included in the systematic review	Three randomised controlled trials published between 2003 and 2014 with 239 participants (with 424 posterior teeth) were included in the review. The sources of funding for primary studies were not reported.
Types of studies included	Only randomised clinical trials were eligible for inclusion in the review. The paper that was excluded at full-text screening is listed with its reason for exclusion.
Country of origin of included studies	The study countries were Denmark, the Netherlands, and Turkey.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	One of the three trials was judged to have a high risk of bias and the other two had an unclear risk of bias. One of the three trials was judged to have adequate randomisation and another one had adequate blinding of outcome ascertainment. Statistical analysis of publication bias was not possible, as only two studies were included in the quantitative synthesis. The authors reported that "the present systematic review is not free of limitations. The number of the studies included (2 RCTs [randomised controlled trials] for inlays and one RCT for onlays) and the sample size (157 patients with 176 restorations for direct/indirect onlays and 82 patients with 248 restorations for direct/indirect inlays) may be regarded as relatively small. The included studies, moreover, were found to be at unclear or high risk of bias."¹¹³ (p20)
Method of analysis	For continuous outcomes, mean differences and standard deviations were used to summarise the data from each study. For dichotomous data, the number of participants with events and total number of participants in experimental and control groups were analysed. Regarding meta-analysis for dichotomous data, risk ratios and their 95% CIs were calculated. For continuous data, mean difference and 95% CIs were calculated. The authors assessed clinical heterogeneity by examining the characteristics of the studies, the similarity between the types of participants, the interventions, and the outcomes as specified in the inclusion criteria. The authors planned to conduct meta-analyses if there were studies of similar comparisons reporting the same outcomes at the same follow-up periods. Risk ratios were combined for dichotomous data using fixed-effects models, unless there were more than three studies in the meta-analysis, in which case random-effects models would have been used.
Outcome assessed	Clinical parameters of longevity (secondary caries, post-operative sensitivity, marginal discolouration, and colour match) At three years or over follow-up The longest follow-ups ranged from five to eleven years. Primary studies by outcomes: Pallesen and Qvist 2003; Cetin 2013
Results/findings	One study (Fennis <i>et al.</i>) dealt with onlays, and could not be included in the meta-analyses. Fennis <i>et al.</i> reported an overall 5-year survival rate of 87% (95% CI: 81–93%) of Class II cavity direct and indirect composite restorations. The review authors reported similar high survival rates for direct and indirect composite restorations in premolars. The meta-analysis comparing the incidence of secondary caries for direct inlays compared with indirect inlays over an 11-year period reported no difference between the two materials (odds ratio: 0.93; 95% CI: 0.21–4.04; I^2: 0%; 248 restorations; 2 studies). The pairwise fixed-effects meta-analysis comparing post-operative sensitivity for direct inlays with indirect inlays reported no difference between the two materials (risk ratio: 0.60; 95% CI: 0.19–1.90; I^2: 0%; 2 studies). The meta-analysis comparing marginal discolouration for direct inlays with indirect inlays over an 11-year period reported that direct restorations were statistically significantly less likely to experience marginal discolouration (risk ratio: 0.41; 95% CI: 0.17–0.96; I^2: 0%; two studies). The meta-analysis comparing colour match for direct inlays with indirect inlays over an 11-year period reported no difference between the two materials (risk ratio: 0.62; 95% CI: 0.26–1.47; I^2: 0%; 2 studies). The meta-analysis comparing restoration failure for direct inlays with indirect inlays at five years (risk ratio: 1.54; 95% CI: 0.42–5.58; I^2: 0%; 2 studies) and at

Parameter	Extraction
	eleven years (risk ratio: 0.95; 95% CI: 0.34–2.63; I ² : 0%; 2 studies) reported no difference between the two materials.
Significance/direction	Results listed by outcome.
Heterogeneity	There was no statistical heterogeneity in the meta-analyses. The authors also acknowledge differences in follow-up periods and tooth type.
Comments	GRADE was not used by the review authors. All three trials was judged to have a high or unclear risk of bias. One (33%) of the three trials was judged to have adequate randomisation and another one (33%) had adequate blinding of outcome ascertainment. There was no statistical heterogeneity in the meta-analyses. The sample size (157 patients with 176 restorations for direct/indirect onlays and 82 patients with 248 restorations for direct/indirect inlays) was small. The quality of the review was rated as low using AMSTAR 2 as the authors were unable to control for the influence of risk of bias. The HRB grades the quality of the evidence as low for the different outcomes.

Antonelli da Veiga *et al.* (2016)

Parameter	Extraction
First author and year of publication	Antonelli da Veiga <i>et al.</i> (2016) ¹¹⁴
Objectives	Compared the differences in clinical performance and longevity of direct and indirect resin composite restorations in Class I and Class II cavities in permanent molar and premolar teeth, with at least two years of follow-up
Participants	Permanent dentition, cavitated caries, direct and indirect restorations Population: Humans with Class I and Class II cavities in permanent molar and premolar teeth that were restored with direct and indirect resin composite restorations. Nine randomised clinical trials published between 1998 and 2014 including more than 207 participants (two studies did not report number of participants) and 439 restorations were selected for inclusion. The age range of the participants was 20–81 years; three studies did not report an age range. Just over one-half (51%) of the participants were male.
Setting/context	All nine studies were completed in a university-based dental clinic.
Description of interventions/phenomena of interest	Intervention: Indirect resin composite restorations Comparator: Direct resin composite restorations Direct and indirect resin composite restorations are widely used in contemporary dentistry to restore posterior teeth. Traditionally, the choice between the use of direct and indirect techniques for resin composites in posterior teeth is based on the size of the cavity to be restored. Small and medium cavities are usually restored with direct composite resin restorations. On the other hand, in large cavities, where the width of the isthmus exceeds two-thirds of the distance between the facial and lingual cusp tips, indirect restorations are indicated. However, because of the evidence that direct resin composite restorations have properties suitable for use in posterior teeth, do not require invasive preparation, and are made in only one session at low cost, many dentists are also using them in large cavities, making the clinical decision challenging. BisGMA-based resin composites could have considerable polymerisation linear shrinkage of around 0.36–0.88% and volumetric shrinkage of about 1.5–3.4%. The stress generated by this polymerisation shrinkage in direct resin composites is much higher (13 times higher) than in indirect ones. For indirect resin composite restorations, postcure using light, heat, pressure, or atmosphere of nitrogen and the thin layer of adhesive cement help to relax the stress of the contraction of polymerisation.
Databases and sources searched	Eight data sources were searched, without restrictions, for peer-review papers, grey literature, and unpublished studies up to 18 August 2015: PubMed, the Cochrane Library, Web of Science, Scopus, Latin American and Caribbean Health Sciences Literature database (LILACS) Brazilian Library in Dentistry (BBO), ClinicalTrials.gov, and OpenSIGLE. The search strategies were adapted according to the requirement of the database searched and are described individually. Reference lists of included studies were also searched.

Parameter	Extraction
	The study protocol was registered on the PROSPERO database. Two reviewers independently screened the articles for inclusion. It was not clear who extracted the data. The authors reported no conflicts of interest or additional funding.
Date range (years) of included studies	Nine randomised clinical trials published between 1998 and 2014 were included.
Number of primary studies included in the systematic review	Nine randomised clinical trials published between 1998 and 2014 including more than 207 participants (two studies did not report the number of participants) and 439 restorations were selected for inclusion. The sources of funding for primary studies were extracted but not reported.
Types of studies included	Studies that compared two or more restorative materials in the restoration of carious lesions on root surfaces were included. All randomised controlled trials and non-randomised controlled trials were eligible for inclusion. The reason for this decision was not explained. The authors included randomised clinical trials only. The articles excluded and the reasons for exclusion were presented in the text.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included studies. The authors modified the instrument by excluding operator and participant blinding.
Appraisal rating	Of the nine studies included, three were judged to have a high risk of bias, one an unclear risk of bias, and five a low risk of bias, using the authors adapted Cochrane Collaboration's risk of bias instrument. Using the complete Cochrane Collaboration's risk of bias instrument, all of the studies had a high risk of bias. Five of the nine included studies were judged adequate for randomisation, and seven had adequate blinding of outcome assessor. Publication bias was not assessed.
Method of analysis	A meta-analysis was performed using the Comprehensive Meta-Analysis software to assess differences in the clinical longevity of direct and indirect resin composite restorations. Failure rates for each group and the total number of teeth were included in the meta-analysis. Since the studies had the same follow-up time points, failure rates were obtained and pooled in the meta-analysis by years of follow-up. The overall failure rate was only computed for studies that had a follow-up of 5 years. In addition to the general failure rate, two subgroups were created for comparing analysis – (1) direct resin composite against indirect resin composite, and (2) direct resin composite against direct inlay/onlay– based on 5 years of follow-up. A final analysis was performed comparing the clinical performance of the direct resin composite against the indirect resin composite in molars and premolars at 3-year follow-up. A fixed-effects model was employed. Heterogeneity was assessed using the Inconsistency Index (I^2) and the relative risks were also calculated. The I^2 describes the percentages of total statistical variation across studies that are due to heterogeneity rather than chance. Where necessary, sensitivity analysis and subgroup analysis were completed.
Outcome assessed	At least 2 years of follow-up (predetermined) The follow-up periods ranged from 2 to 11 years. Clinical performance and longevity: Wendt 1996; Wassell 2000; van Dijken 2000; Manhart 2000; Pallesen and Qvist 2003; Bartlett and Sundaram 2006; Cetin 2013; Ozakar-liday 2013; Fennis 2014.
Results/findings	With regard to patient-related variables, such as caries risk and bruxism, only three studies reported such analysis. The most common general failures reported were fracture of restoration, anatomical form, tooth fracture, and marginal adaptation for direct resin composite; marginal discolouration, marginal adaptation, fractures, and debonding of restoration for indirect resin composite; and secondary caries for direct inlay/onlay. The overall risk difference in longevity between direct and indirect resin composite restorations in permanent posterior teeth at 5-year follow-up was not significant, with a relative risk of 1.49 (95% CI: 0.89–2.50; I^2: 5%; 5 trials). The subgroup analysis comparing longevity of direct resin composite with indirect resin composite at 5-year follow-up also found no difference (relative risk: 1.28; 95% CI: 0.66–2.46; I^2: 35%; 2 trials) and low heterogeneity. The subgroup analysis comparing the longevity of direct resin composite with direct inlay/onlay at 5-year

Parameter	Extraction
	follow-up found no statistical difference between the groups, with a relative risk of 1.91 (95% CI: 0.84–4.39; I²: 0%) and no heterogeneity between groups. A pooled meta-analysis compares molars and premolars restored with direct resin composite and indirect resin composite with 3-year follow-up. The heterogeneity was low for both molars (I²: 25%) and premolars (I²: 0%). The overall relative risk was 0.72 (95% CI: 0.18–2.89) without statistical difference. A sensitivity analysis showed that the removal of studies with a high risk of bias did not affect the results. The authors conclude that, “Based on the results of this systematic review and meta-analysis, there is evidence of no difference in terms of clinical longevity between direct and indirect resin composite restorations. This conclusion remains valid even when the type of restored tooth is taken into account. Therefore, it seems more reasonable to suggest that direct restorations should be given preference to indirect restorations in many situations, since the former require less effort and cost.”¹¹⁴ (p11)
Significance/direction	Results listed by outcome.
Heterogeneity	There was no or low heterogeneity in the meta-analysis.
Comments	GRADE was not used by the review authors. All of the studies had a high risk of bias. Five (56%) of the nine included studies were judged adequate for randomisation, and seven (77%) had adequate blinding of outcome assessor. There was no or low statistical heterogeneity in the meta-analyses. The sample size was just over 200. The quality of the review was rated as moderate using AMSTAR 2. The HRB grades the quality of the evidence as moderate for the different outcomes.

Restoration support material

Schenkel *et al.* (2019)

Parameter	Extraction
First author and year of publication	Schenkel <i>et al.</i> (2019)¹¹⁵ Cochrane Review
Objectives	Compared the effects (pain or hypersensitivity, cold response and longevity) of using dental cavity liners with those of not using liners in the placement of Class I and Class II resin-based composite posterior restorations in permanent teeth in children and adults.
Participants	Permanent teeth, cavitated caries, materials to support restoration materials Population: Class I and Class II resin-based composite posterior restorations in permanent teeth in children and adults Eight randomised controlled trials published between 2001 and 2013, comprising 762 participants, were included in this review; the participants included children and adults aged 15–52 years. Only one study reported data on gender and all participants in this single study were male.
Setting/context	All eight studies were conducted in a dental school setting. The studies were completed in Germany, Saudi Arabia, Thailand, Turkey, and the USA.
Description of interventions/phenomena of interest	According to Schenkel <i>et al.</i>, “dental cavity liners are designed to protect the pulp from the toxic effects of dental restorative materials and to prevent the pain of thermal conductivity by placing an insulating layer between restorative material and the remaining tooth structure...The liners most commonly used in restorative dentistry include calcium hydroxide and glass-ionomer cements, both of which are available in either chemical or light-cured formulations.”¹¹⁵ p7 ... in adult posterior teeth.”¹¹⁵ (p19) Comparator: No liner
Databases and sources searched	The authors searched six data sources: Cochrane Oral Health Group Trials Register (to 12 November 2018), Cochrane Central Register of Controlled Trials (CENTRAL; 2018, Issue 10), the Cochrane Library (searched 12 November 2018), MEDLINE Ovid (1946 to 12 November 2018), Embase via Ovid (1980 to 12 November 2018), and Latin American and Caribbean Health Sciences Literature database (LILACS) via BIREME Virtual Health Library (1982 to 12 November 2018). They searched ClinicalTrials.gov and the WHO’s International Clinical Trials Registry Platform for

Parameter	Extraction
	ongoing trials. No restrictions were placed on the language or date of publication when searching the electronic databases. All search strategies are provided in the review's appendices. The reference lists of relevant articles were checked, and the authors contacted known experts in the field. Screening and extraction were completed in duplicate. A protocol was completed. One of the authors had no interests to declare. Analia Veitz-Keenan participated in a study completed by Strober <i>et al.</i> in 2013 as a dental practitioner investigator for the Practitioners Engaged in Applied Research and Learning (PEARL) Network (Strober 2013). The author did not, however, have access to any final collected data and did not participate in the data extraction or risk of bias analysis for this study in this systematic review. The study was funded by New York University College of Dentistry, USA; Cochrane Oral Health Group Global Alliance, UK; and the National Institute for Health Research (NIHR), UK.
Date range (years) of included studies	Eight randomised controlled trials published between 2001 and 2013.
Number of primary studies included in the systematic review	Eight randomised controlled trials published between 2001 and 2013, comprising 762 participants, were included in this review; the participants included children and adults aged 15–52 years. The funding for two primary studies was available to the authors; both were publicly funded.
Types of studies included	Randomised controlled clinical trials were specified in the inclusion criteria. The excluded trials and their reason for exclusion were provided.
Country of origin of included studies	The studies were completed in Germany, Saudi Arabia, Thailand, Turkey, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included trials.
Appraisal rating	Based on the Cochrane Collaboration's risk of bias instrument, the risk of bias was judged to be high in five trials and unclear in the remaining three trials. Four of the eight trials were judged to have adequate randomisation and four were judged to have adequate blinding of outcome assessors. Seven of the eight included studies evaluated post-operative hypersensitivity. All studies were at unclear or high risk of bias. Four of the eight trials measured restoration longevity. Two of the studies were judged to be at high risk and two at unclear risk of bias. Publication bias was assessed as part of the overall quality of the evidence, but there is no specific comment on this bias.
Method of analysis	The analysis plan was a standard Cochrane Review analysis plan and the authors employed random-effects models.
Outcome assessed	Outcome by primary study: Pain or hypersensitivity at 1 week: Akpata 2001; Efes 2006; Burrow 2009. Cold response: Burrow 2009; Strober 2013. Longevity at one or two years: Banomyong 2013; Boeckler 2012; Browning 2006; Efes 2006.
Results/findings	When the use of dental cavity liners was compared with using no liners under the placement of composite resin restorations in permanent teeth, the evidence was judged to be inconsistent and low quality, and there is therefore inadequate evidence upon which to judge the performance of the intervention regarding any difference in post-operative sensitivity at 1 week follow-up (relative risk: 0.56; 95% CI: 0.26–1.17; I²: 0%; 3 trials; 299 teeth; low-quality evidence), and the results for 24 hours and 1 month were similar. Cold response was not different between the two outcomes either (mean: 16 seconds; 6–10 seconds more than without liner; difference not significant). There was no difference between using dental cavity liners compared with using no liners on the longevity of composite resin restorations in permanent teeth at one year (relative risk: 1.00; 95% CI: 0.07–15.00; I²: not applicable; four trials [one trial had failures and was estimatable]; 281 teeth; low-quality evidence), which renders the evidence for this outcome inconclusive. The authors state that “the quality of the evidence for each outcome was considered to be of low quality due to only single studies reporting certain

Parameter	Extraction
	outcomes/time points, a high/unclear risk of bias in the individual studies, and imprecision in the pooled estimate." ¹¹⁵ (p15)
	In conclusion, based on the current evidence, the authors see no reason why the use of liners would add any benefit to the routine resin-based restorations in permanent posterior teeth in adults. There is no evidence for children aged under 15 years.
Significance/direction	Statistical heterogeneity was very low.
Heterogeneity	Results listed by outcome.
Comments	Statistical heterogeneity was very low.
	GRADE was used by the review authors.
	The risk of bias was judged to be high or unclear in all eight trials. Four (50%) of the eight trials were judged to have adequate randomisation and four (50%) were judged to have adequate blinding of outcome assessors. Statistical heterogeneity was very low. The quality of the review was rated as low using AMSTAR 2 as the authors were unable to control for the risk of bias. The review authors and the HRB grade the quality of the evidence as low for the different outcomes.

Reis *et al.* (2015)

Parameter	Extraction
First author and year of publication	Reis <i>et al.</i> (2015) ¹¹⁶
Objectives	Compared the effects of posterior resin composite restorations that were bonded using self-etching with posterior resin composite restorations that were bonded using etch-and-rinse adhesives on the risk and intensity of post-operative sensitivity in permanent dentition (posterior restorations) of adult patients.
Participants	Permanent dentition, cavitated caries, restoration support materials Population: Permanent dentition (posterior restorations) of adult patients The primary studies included at least 799 participants (two studies did not report sample size) and their mean ages, where available, ranged from 23 to 57 years. Eleven primary studies did not report age data. Only seven primary studies reported gender data, and the proportion of males varied across the studies, ranging from 28% to 60%.
Setting/context	Eleven studies reported that the setting was a university clinic. One study was community based, one was conducted solely in private clinics, and one was completed in both university and private clinics. Three studies did not report settings. The study countries were Germany, Japan, Liechtenstein, and the USA.
Description of interventions/phenomena of interest	Posterior resin composite restorations bonded with self-etch adhesives According to Reis <i>et al.</i> , "etch-and-rinse systems employ a phosphoric acid to etch enamel and dentine prior to the application of the bonding solution. As a consequence, the smear layer is removed and the dentine tubules are opened, increasing the dentine permeability and hydraulic conductance of dentine...[in contrast,] self-etch systems are thought to lower the risk of postoperative sensitivity as they do not remove, but incorporate the smear layer in the hybridized complex with the advantage of being less technique-sensitive." ¹¹⁶ (p1053) Comparator: Etch-and-rinse adhesive
Databases and sources searched	A comprehensive search was performed in MEDLINE via PubMed, Scopus, Web of Science, Latin American and Caribbean Health Sciences Literature database (LILACS), Brazilian Library in Dentistry (BBO), and the Cochrane Library without language or date restrictions. The detailed search strategy is provided in a table. The abstracts of the annual conference of the International Association for Dental Research (1990–2014), and unpublished and ongoing trials registry were also searched. Dissertations and theses were searched using the ProQuest Dissertations & Theses Global and the Periódicos CAPES databases. The grey literature was explored using the OpenSIGLE database. To locate unpublished and ongoing trials, the following trials registries were also searched: ISRCTN registry, WHO's International Clinical Trials Registry Platform, ClinicalTrials.gov, Rebec, and the EU Clinical Trials Register.

Parameter	Extraction
	The authors hand-searched the reference lists of all primary studies for additional relevant publications, and searched the 'related articles' link of each primary study in the PubMed database. The full-text articles were screened by two reviewers. The number of reviewers completing data extraction is not clear. The authors completed and registered a protocol. The review was partially supported by the Brazilian Council for Scientific and Technological Development. Conflicts of interest were not declared.
Date range (years) of included studies	Twenty-nine randomised clinical trials published between 1998 and 2013 were included in this review.
Number of primary studies included in the systematic review	Twenty-nine randomised clinical trials published between 1998 and 2013 that compared self-etch with etch-and-rinse adhesives used for direct resin composite restorations in permanent posterior teeth in adult patients were included in this review. The sources of funding for primary studies were not provided.
Types of studies included	The inclusion criteria required randomised clinical trials. The reasons for exclusion at full-text screening were listed, but not linked to study reference.
Country of origin of included studies	The study countries were Germany, Japan, Liechtenstein, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess risk of bias in the primary studies.
Appraisal rating	Based on the Cochrane Collaboration's risk of bias instrument, seven trials were at high risk of bias and 16 were considered to have an unclear risk of bias; the remaining seven trials were at low risk of bias based on the authors' figure reporting the risk of bias for each primary study and using Cochrane Collaboration guidelines. Thirteen (45%) of the 29 included trials were judged to have adequate random sequence generation and 17 (57%) were considered to have adequate blinding of outcome assessors. However, the authors reported that 13 trials were judged to be at low risk of bias considering two measurements, randomisation and allocation concealment, and these 13 trials were used in the meta-analysis. Ten had adequate blinding of outcome assessors (77%). Publication bias is not discussed but the authors did a very comprehensive search and so it is likely to be minimal.
Method of analysis	The extracted data were analysed using RevMan 5. Data from eligible studies were either dichotomous (risk of post-operative sensitivity) or continuous (post-operative sensitivity intensity). The data on the risk of post-operative sensitivity were grouped according to the type of post-operative sensitivity measurement used in each clinical trial into spontaneous and stimuli-induced post-operative sensitivity. To summarise the post-operative sensitivity for each study, the authors calculated the standardised mean difference for the intensity of post-operative sensitivity and relative risk for the risk of post-operative sensitivity. When more than one adhesive of each type was included in a single study, their values were combined to make a single entry. When the data from the original study groups were merged in the study report, the authors were contacted to provide original values. The random-effects pairwise models were employed for the dichotomous and continuous data. Heterogeneity was assessed using the Cochran Q test and I ² statistics. All analyses were conducted using RevMan 5.3.
Outcome assessed	Outcome: Risk and intensity of post-operative sensitivity Spontaneous post-operative sensitivity: Burrow 2009; Perdiago 2009; Sundfeld 2012; Swift 2008. Stimuli-induced post-operative sensitivity: Bottenberg 2007; Burrow 2009; Casselli 2006. Intensity of post-operative sensitivity: Browning 2007; Burrow 2009; Perdiago 2003; Perdiago 2004; Sancakli 2014. Three studies (Ermis 2009; Lopes 2003; Manhart 2010) were excluded from the pairwise meta-analysis as they did not report any event in either study arms. However, the authors could have adjusted the data in these studies to include them in the analysis and the exclusion may bias to results.
Results/findings	The meta-analysis seems robust and included only studies that had a low risk of bias. The main finding from the random-effects meta-analyses suggest that the evidence is inconclusive regarding which type of adhesive strategy – etch-and-

Parameter	Extraction
	rinse or self-etch – is superior, as the use of either adhesive strategy did not affect the risk of spontaneous post-operative sensitivity in posterior resin composite restorations (relative risk: 0.63; 95% CI: 0.35–1.15; I ² : 0%; 544 participants; 326 restorations; 4 trials), stimuli-induced post-operative sensitivity in posterior resin composite restorations (relative risk: 0.99; 95% CI: 0.63–1.56; I ² : 0%; 261 restorations; 3 trials), or intensity of post-operative sensitivity in posterior resin composite restorations (mean difference: 0.08; 95% CI: –0.19 to 0.35; I ² : 57%; 544 restorations; 4 trials). According to Reis <i>et al.</i> , “one may conclude that the type of adhesive strategy (ER [etch-and-rinse] or SE [self-etch]) for posterior resin composite restoration does not seem to influence the risk and intensity of postoperative sensitivity. However further studies should be conducted to evaluate if this is still applied for large and deep posterior resin composite restorations.” ¹¹⁶ (p1065)
Significance/direction	No difference.
Heterogeneity	Low heterogeneity between studies examining spontaneous post-operative sensitivity and stimuli-induced post-operative sensitivity, and high heterogeneity between studies measuring intensity of post-operative sensitivity.
Comments	GRADE was not used by the review authors. The authors included 13 trials in their meta-analyses. The 13 trials were judged to be at low risk of bias considering two measurements, randomisation and allocation concealment. Ten had adequate blinding of outcome assessors (77%). Low heterogeneity between studies examining spontaneous post-operative sensitivity and stimuli-induced post-operative sensitivity, and high heterogeneity (but not over 75%) between studies measuring intensity of post-operative sensitivity. The quality of the review was rated as moderate using AMSTAR 2. The HRB grades the quality of the evidence as high for the different outcomes.

Restoration processes or techniques

Arcanjo Frota Barros *et al.* (2020)

Parameter	Extraction
First author and year of publication	Arcanjo Frota Barros <i>et al.</i> (2020) ¹¹⁷
Objectives	Evaluated the risk or benefit (pulp exposure, dentine deposition, microbiological examination, quality of the restoration, and success of maintaining pulpal health) of selective caries removal for the treatment of dentinal caries in permanent teeth compared with non-selective (complete) or stepwise caries removal.
Participants	Permanent dentition, cavitated caries, direct restoration technique Permanent teeth with dentinal lesions More than 1,021 people (with 1,294 teeth) participated in the studies, and their ages ranged from four to 53 years; however, the majority of participants are children and young adults. Forty-five per cent were male. One study did not report sample size or age and two studies did not report gender.
Setting/context	The studies' settings were not reported. The study countries were Brazil, Indonesia, and Turkey.
Description of interventions/phenomena of interest	Intervention: Selective removal of carious tissue The selective carious tissue removal technique is less invasive, consisting of selective removal of carious tissue from the surrounding cavity walls, allowing the possibility of remineralising the affected dentine in the pulpal wall, after a definitive cavity sealing is executed in the same session. Comparator: Non-selective (complete) caries removal or stepwise carious tissue removal Non-selective (complete) caries removal is complete excavation or total carious tissue removal. Stepwise caries removal consists of the non-selective removal of carious tissue over two sessions. In the first session, all carious dentine is removed from the surrounding walls of the cavity, and then only the most necrotic and contaminated dentine is removed from the pulp wall, with a temporary sealing (lasting 2–6 months) then applied. After this period, the cavity is reopened,

Parameter	Extraction
	remineralisation is evaluated, the softened remaining carious tissue is completely removed, and the final restoration is performed. The purpose of this treatment is to reduce the risk of pulpal exposure by stimulating the deposition of tertiary dentine.
Databases and sources searched	Three databases (PubMed, Embase, and Scopus) were searched until 24 August 2018. The search strategy for PubMed is presented in the paper. All references to related reviews and the list of references of all included studies detected during the electronic survey were searched for eligibility. There was no mention of preparing or publishing a protocol. Screening of search findings and data extraction were completed in duplicate. This study was supported by the Brazilian agency Coordination for the Improvement of Higher Education Personnel, and the authors declared no conflicts of interest.
Date range (years) of included studies	Six studies, in 10 papers published between 2008 and 2018, were included.
Number of primary studies included in the systematic review	Six studies (in 10 papers), published between 2008 and 2018, were included. Of the selected studies, only one was not randomised. Regarding the control group, four papers reported only non-selective or complete caries removal, four papers reported only stepwise caries removal, and two papers reported non-selective and stepwise removal of carious tissue. All studies performed definitive restorations after the interventions – six papers used composite resin as the restorative material, while the other four papers had also used amalgam. The funding sources for primary studies were not reported.
Types of studies included	Controlled clinical trials and cohort studies were eligible for inclusion. There is no rationale to explain the study designs eligible for inclusion in the review. The reasons for exclusion of studies at the full-text screening stage were provided, but a list of the excluded studies was not provided.
Country of origin of included studies	The study countries were Brazil, Indonesia, and Turkey.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies. The Newcastle-Ottawa Scale was used to evaluate the cohort studies.
Appraisal rating	Four of the nine included trial papers were judged to have a high risk of bias. All of these were by the same author reporting different follow-up periods for the same sample. The remaining five trials had an unclear risk of bias. Eight of the nine papers were judged to have adequate randomisation and five had adequate blinding of outcome assessment. There was one retrospective cohort study based on a convenience sample, and it was judged to have an unrepresentative sample but to have adequate assessment of outcome and be adequate for seven other parameters. It scored 8 out of 9 stars. The authors report that "Therefore, the risk of bias assessment showed a moderate heterogeneity among the included studies, ranging from one point not mentioned (unclear risk) or a negative point (low risk of bias) to four points not mentioned (unclear risk)".^{117 (p524)} They continued, "None of the studies included in this systematic review were considered as having low risk of bias in all criteria, decreasing the overall strength of evidence of these studies. However, most studies presented several risk assessment criteria for bias as low risk. In addition, it is possible to define the methodological and sample differences of the studied articles as limitations of this study, rendering meta-analysis of all the outcomes impossible."^{117 (p530)} Publication bias was not measured or discussed.
Method of analysis	Initially, no minimum follow-up period was imposed on the studies for inclusion in the present systematic review, since it was intended to perform several meta-analyses by the different follow-up periods. However, this was not possible because sufficient information was available only for studies with at least 1-year follow-ups, and consequently, only one meta-analysis was performed. The pooled risk ratio was calculated for the overall success of the pulp status, as previously described, using the different techniques for carious tissue removal. Four papers presented data on the same sample, and from this sample, only the data from the 18-month study follow-up was used, since that follow-up time was the most similar to those periods applied in the other selected studies. In order to make comparisons easier, the data on the individuals were included in the meta-

Parameter	Extraction
	analysis were presented. The studies with follow-ups of less than one year were not included in the meta-analysis. The pooled risk ratio and its 95% CI were calculated for the primary outcome, and subgroups were created considering the different techniques for caries removal, such as stepwise excavation and non-selective removal of carious tissue. Heterogeneity was assessed by the Cochran's Q test and quantified by the I^2 statistic. As a higher heterogeneity (determined as $I^2 > 40\%$) was detected, a random-effects model was applied. Meta-analysis was conducted using the software Review Manager (version 5.3).
Outcome assessed	Pulp exposure, dentine deposition, microbiological examination, quality of the restoration, and success of maintaining pulpal health were the outcomes assessed. Initially, no minimum follow-up period was imposed on the studies for inclusion in the present systematic review, since it was intended to perform several meta-analyses by the different follow-up periods. The longest follow-up periods ranged from 1 to 60 months, with two studies reporting a final follow-up of 3 months or less. Outcome by primary study: Microbiological examination outcome: Bitello-Firmino (2018); Orhan (2008). Quality of the restoration: Casagrande (2017); Pratiwi (2017). Pulp exposure: Casagrande (2017); Maltz (2012); Orhan (2010); Rando-Meirelles (2013).
Results/findings	Microbiological evaluation was performed in two studies by counting the number of colony-forming units for total viable microorganisms, <i>Streptococcus</i> species, and <i>Lactobacillus</i> species. In both studies, the selective and non-selective removals of carious tissue were equally effective in reducing the total microbial load. Only one study evaluated the quality of the restorations after the treatments and concluded that no significant difference in the longevity of the restorations was detected ($p=0.163$). Additionally, a single study evaluated the deposition of dentine after the treatments, using mineral trioxide aggregate, as pulp protection material. After 4 weeks, no significant difference in the remineralisation level was found between the groups that performed non-selective or selective removal of carious tissue. Regarding the pulp exposure outcome, the three studies in which the control group was represented by non-selective or stepwise removal of carious tissue presented a greater risk of pulp exposure compared with the selective removal group. However, stepwise removal presented a lower risk of accidental pulp exposure when compared with non-selective removal. One of the studies included in this review reported that pulp exposure occurred during treatments, but these teeth were excluded from the study, so it is not known to which group they belonged. Four studies were included in the random-effects pairwise meta-analysis for overall success of maintaining pulpal health at 12–18 months. It should be noted that there is a mix of randomised and non-randomised trials in the meta-analysis. The overall results found statistically significant differences between selective caries removal and the combined stepwise and non-selective caries removal groups (risk ratio: 1.11; 95% CI: 1.02–1.21; I^2: 34%; 781 participants; four trials). Analysis of the subgroups demonstrated the same higher-risk results for the non-selective removal over selective removal (risk ratio: 1.09; 95% CI: 1.02–1.17; I^2: 0%; 541 participants; three trials). No statistically significant difference was detected for the stepwise excavation compared with selective removal of caries (risk ratio: 1.10; 95% CI: 0.88–1.38; I^2: 68%; 240 participants; 2 trials); however, this analysis had substantial statistical heterogeneity. Selective removal resulted in greater success of maintaining pulp vitality compared with both non-selective (complete) and stepwise excavation.
Significance/direction	Results listed by outcome.
Heterogeneity	The authors recognised clinical heterogeneity in the depth of excavation and the follow-up times.
Comments	GRADE was not used by the review authors.

Parameter	Extraction
	Both randomised and non-randomised trials were included in the meta-analysis. All nine papers were judged to have a high or unclear risk of bias. All nine had adequate randomisation and five (56%) had adequate blinding of outcome assessment. The authors identified clinical heterogeneity in the depth of excavation and the follow-up times. The quality of the review was rated as critically low using AMSTAR 2 the authors included a mix of randomised and non-randomised studies in the meta-analysis and were unable to control for the risk of bias in the meta-analysis. The HRB grades the quality of the evidence as very low for the different outcomes.

Göstemeyer *et al.* (2019)

Parameter	Extraction
First author and year of publication	Göstemeyer <i>et al.</i> (2019)¹¹⁸
Objectives	Evaluated the efficacy of atraumatic restorative treatment compared with conventional restorative treatment for restoring root carious lesions in older adults.
Participants	Permanent dentition, cavitated caries, direct restoration technique Older adults (aged over 60 years) with root carious lesions in need of restorative treatment. Three randomised controlled trials published between 2006 and 2016 were included, with 277 participants (with 636 lesions) aged between 60 and 101 years.
Setting/context	The study countries were Colombia, Hong Kong, and Ireland. The study settings were facilities that care for older people on a day-care or full-time basis.
Description of interventions/phenomena of interest	Intervention: Atraumatic restorative treatment; that is, cavity preparation using hand instruments only. Comparator: Conventional restorative treatment; that is, cavity preparation using rotary burs. No restrictions were applied to the restorative materials used in either group.
Databases and sources searched	Three electronic databases (Embase via Ovid, MEDLINE via PubMed, and Cochrane Central Register of Controlled Trials [CENTRAL]) were screened on 12 August 2017 using a defined search strategy, which was adapted for each database. No restrictions were applied to publication language or date. This search was updated on 7 November 2018 to assess whether further trials had been conducted and published. Unpublished or grey literature materials were not sought. The authors did not mention preparing a protocol for the review. Duplicate screening and extraction were completed. The sources of funding and conflicts of interest were not mentioned in the article.
Date range (years) of included studies	Three randomised controlled trials published between 2006 and 2016 were included in this review.
Number of primary studies included in the systematic review	Three randomised controlled trials published between 2006 and 2016 were included. The funding sources for primary studies were not reported.
Types of studies included	Only randomised controlled trials were eligible for inclusion. Excluded studies and reasons for exclusion were published in an appendix.
Country of origin of included studies	The study countries were Colombia, Hong Kong, and Ireland.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	The authors judged that one study had a high risk of bias, one had an unclear risk of bias, and one had a low risk of bias; however, it appears to the HRB reviewers that all three studies had a high risk of bias. All three studies had adequate randomisation and blinding of outcome assessor. There was no publication bias detected by funnel plot analyses.
Method of analysis	Meta-analysis was performed for the outcome (risk of failure, measured as events per total restorations in each group) using Review Manager (RevMan) version 5.3. Heterogeneity was assessed using both Cochran's Q test and I ² -statistics. Fixed- or random-effects meta-analysis was performed depending on heterogeneity (I ² < 35% or above). Odds ratios and 95% confidence intervals (95% CI) were calculated. Publication bias was assessed graphically via a simple test of asymmetry using funnel plots. The authors assessed the possible impact of

Parameter	Extraction
	attrition on outcome estimates through metaanalysis for four different scenarios: (1) per-protocol analysis, that is assessment of participants based on the intervention they received and that had been followed to the end of the study; Participants who dropped out during follow-up were excluded from this analysis. per-protocol analysis accounts for possible attrition bias and deviations from protocol; (2) intention-to-treat analysis, that is assessment of participants as randomised regardless of whether they received the intervention to end or dropped out during the intervention and follow-up period. For intention-to-treat analysis the authors assumed that all missing participants experienced an event (i.e. restoration failure); (3) and (4) scenario analyses following the intention-to-treat principle. Attrition was handled differently in the experimental and control groups. In the best-case (for atraumatic restorative treatment) analysis (c), we assumed that only dropouts in the control (conventional treatment), but not the experimental (atraumatic restorative treatment) group, experienced events (failures). In the best-case (for conventional treatment) scenario (d), this was reversed. These scenario analyses explore the uncertainty introduced by attrition via the most extreme imputations. In a meta-analysis, Z-values are used to compare two interventions. A Z-value of 0 indicates no difference between two interventions. A Z-value exceeding ± 1.96 corresponds to a P-value of <0.05 (twosided test), which is traditionally assumed to indicate a statistically significant difference. For repeated updates of meta-analyses, as new trials become available to include, a new Z-value is calculated for each update. In trial sequential analysis, this series of Z-values is plotted against the accumulated sample size, events or information. This cumulative Z-curve is then assessed regarding its relation to the conventional significance boundaries ($Z = \pm 1.96$), the required information size and the trial sequential monitoring boundaries for benefit, harm or futility. Trial Sequential Analysis Viewer 0.9.5.10 Beta) was used for conducting the Trial sequential analysis. The required information size was calculated based on an assumed type I error risk of $\alpha = 0.05$, a type II error risk of $\beta = 0.20$ (equivalent to a power of 0.80) and the control event proportion. The relative risk reduction was based on an a priori defined worthwhile interventional effect of 20%. It should be noted that smaller intervention effects may well be relevant. This, however, would increase the required information size even further. Variance-based heterogeneity correction was performed according to the O'Brien-Fleming function and was used for calculating the trial sequential monitoring boundaries. Results of the cumulative Z-value crossing the conventional boundary of significance ($Z = \pm 1.96$) but not the trial sequential monitoring boundaries for benefit or harm were defined as spuriously significant. Firm evidence was assumed to be reached when the Z-curve crossed the outer trial sequential monitoring boundaries for benefit or harm before the required information size was reached. Firm evidence of futility was confirmed when the Z-curve was crossing the inner trial sequential monitoring boundaries for futility and the required information size was reached.
Outcome assessed	Retention of restoration (measured by partial or complete loss). The outcome studied was restoration failure and possible reasons for failure. The longest follow-up was 6–24 months (not predetermined). Cruz Gonzalez 2016; da Mata 2015; Lo 2006;
Results/findings	The per-protocol analysis indicated that there was a significantly greater difference in the failure rates of restorations with the atraumatic restorative technique compared with conventional restorative treatment (fixed-effects pairwise meta-analysis: odds ratio: 2.06; 95% CI: 1.06–4.00; I^2: 0%; 353 restorations; three trials). The intention-to-treat analysis indicated that there was no significant difference in the failure rates of restorations with the atraumatic restorative technique compared with conventional restorative treatment (fixed-effects pairwise meta-analysis: odds ratio: 1.36; 95% CI: 0.92–2.72; I^2: 0%; 463 restorations; 3 trials). There was no firm evidence on atraumatic restorative technique compared with conventional restorative treatment reached, regardless of whether per-protocol (required information size: 931; reached IS: 353) or intention to treat scenario analyses (required information size: 1,545; reached information size 463) were performed.

Parameter	Extraction
	The authors concluded that “This systematic review and meta-analysis found no compelling evidence to support either ART [atraumatic restorative treatment] or CT [conventional treatment] for restoring root carious lesions in older adults. However, based on the limited number of included trials, CT may be more efficacious than ART for this purpose.” ^{118 (p292)} The GRADE summary of the per-protocol analysis revealed that the certainty of the evidence from these findings was low.
Significance/direction	Results listed by outcome.
Heterogeneity	The authors stated that “These studies demonstrated some heterogeneity in terms of clinical technique and the clinical environment where the treatment took place. In particular, different types of GICs [glass ionomer cements] were used for the placement of ART [atraumatic restorative treatment] restorations. It is clear that the type of restorative material may impact restoration survival. However, ART restorations performed worse compared to CT [conventional treatment] (which were all placed using RMGIC [resin-modified glass ionomer cement]) throughout all included trials irrespective of the GIC type used. This indicates that the ART approach might be generally associated with an increased risk of failure in root caries restorations irrespective of which restorative material has been used.” ^{118 (p291)}
Comments	GRADE was used by the review authors. All three studies were judged to have a high risk of bias. All three studies had adequate randomisation and blinding of outcome assessor. The authors identified clinical heterogeneity but no statistical heterogeneity. The quality of the review was rated as critically low using AMSTAR 2 as the authors were unable to control for the risk of bias in the meta-analysis and did not discuss its effects. The HRB grades the quality of the evidence as low for the different outcomes which is higher than the grade assigned by the review author.

Solon-de-Mello *et al.* (2019)

Parameter	Extraction
First author and year of publication	Solon-de-Mello <i>et al.</i> (2019) ¹¹⁹
Objectives	Evaluated whether the survival rates of indirect restorations cemented with self-adhesive resin cement in permanent teeth are influenced by the presence or absence of selective enamel etching.
Participants	Permanent dentition, cavitated caries, restoration technique The number of patients with indirect restorations on their permanent teeth in each of the included studies ranged from 31 to 34. The minimum age of all participants included in the clinical trials was 18 years, and the maximum age was 59 years.
Setting/context	Both studies were undertaken in a university setting; study countries were not reported.
Description of interventions/phenomena of interest	Intervention: Cementation with self-adhesive resin cement after selective enamel etching Comparison: Cementation with self-adhesive resin cement without selective enamel etching The authors described the intervention as follows: “Self-adhesive resin cements are polymerizing cements defined as cements based on filled polymers designed to adhere to the tooth structure without the requirement of a separate adhesive or etchant. They were introduced to dentistry in the beginning of the 21st century and have rapidly gained popularity. This class of cements are generally composed of phosphoric acid and/or carboxylic acid methacrylate monomers. After mixing, the phosphoric acid groups react with the hydroxyapatite of the hard dental tissue, and with basic inorganic fillers incorporated in the luting material. Simultaneously to the cement reaction, radical polymerization is initiated through polymerization of the methacrylate monomers. While the material sets, the acid groups are neutralized, and it turns from hydrophilic to hydrophobic. The major benefit of these materials would appear to be simplicity of application and potential savings in time and chairside costs, since it does not require the etching

Parameter	Extraction
	and bonding steps, presenting many different advantages to the clinician when compared with traditional ones [cements]. The multi-step application technique is complex and rather technique-sensitive, and consequently may compromise bonding effectiveness.” ¹¹⁹ (p328)
Databases and sources searched	Five databases were searched until May 2018: MEDLINE via PubMed, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, Scopus, and LILACS. The terms were searched in the fields title and abstract without application of any filter or limit regards to the idiom. The manuscripts written in idioms other than English were properly translated by the authors. The grey literature was explored for new studies using the OpenGrey database, the CAPES database, the ClinicalTrials.gov database, Opengrey, and the WHO’s International Clinical Trials Registry Platform. The reference lists of the selected articles were hand-searched. Experts were also contacted to identify unpublished and ongoing studies. A study protocol was prepared and registered with PROSPERO. Extraction and screening were completed in duplicate. This study was financed in part by CAPES. The authors declared no potential conflict of interest
Date range (years) of included studies	The two included studies were randomised clinical trials published in 2012 and 2016.
Number of primary studies included in the systematic review	The two included studies were randomised clinical trials, with a split-mouth design, published in 2012 and 2016. The review authors contacted the primary study authors to identify funding sources. However, they did not receive any responses.
Types of studies included	Randomised clinical trials only were eligible for inclusion. The list of excluded studies and their reasons for exclusion were reported in the study paper.
Country of origin of included studies	Study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration’s risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	The two included trials were judged to be at low risk of bias overall. Both trials were at low risk of bias for randomisation and for outcome assessment. Regarding how the risk of bias affected the analysis and quality of the evidence, the authors stated that “In the present review, the evaluation of the risk of bias of the included articles was not exclusively performed based on the written reports. To elucidate these key domains, as allocation concealment and blinding participants, it was necessary to contact the authors by email. Even though all the necessary responses could be obtained, it is important that the CONSORT [Consolidated Standards of Reporting Trials] guidelines are respected for the randomised controlled trial in order to facilitate the standardization and correct interpretation of the data more reliably.”¹¹⁹ (p334) The authors reported that there was no publication bias.
Method of analysis	According to Solon de Mello <i>et al.</i> , “The meta-analysis was performed including the studies that provided the number of fails and the total number of succeeded indirect restorations cemented with self-adhesive resin cement with and without selective enamel etching and the total number of indirect restorations. The meta-analysis was performed using the RevMan Software 5.3. The random-effects model was used as studies did not present the same methodology, and the risk ratio was obtained” ¹¹⁹ (p331) The heterogeneity among studies was tested using the Higgins inconsistency index (I^2). A forest plot was generated for comparisons and the confidence interval was set at the 95% level.
Outcome assessed	Survival rates of the evaluated indirect restorations was the outcome assessed and this was measured by the rate of restoration failure. According to the authors, “Restoration failures were considered by parameters such as problems with the marginal integrity of the restoration, debonding, fracture, recurrent caries, post-operative hypersensitivity, endodontic treatment, or another factor that would lead to the necessity of making a new indirect restoration, which would represent compromise in treatment longevity. The most common general failures reported were fracture of tooth or restoration and debonding of restoration for both studies.”¹¹⁹ (p335) Survival rates: Baader 2016; Peumans 2012.

Parameter	Extraction
Results/findings	The authors reported that “One study reported 36 and 78 months data and the other study reported 36 and 48 months data. Therefore, two distinct meta-analyses were performed, one with the follow-up period of 36 months and the other with the follow-up periods of 48 and 78 months. Considering that the studies did not have the record of failures with the same time of follow-up beyond 36 months, that period was chosen for the first meta-analysis. The second meta-analysis was carried out to evaluate whether the results of 78- and 48-month-long follow-ups of both studies would result in different findings ($p>0.05$). The pooled meta-analysis with 36 months follow-up demonstrated no statistically significant difference in clinical longevity for selective etching in indirect restorations ($p>0.05$). These studies showed a lack of heterogeneity ($I^2=0\%$) and risk ratio of 0.45 [95% CI: 0.16–1.25] for indirect restorations, and the pooled meta-analysis with 48 and 78 months follow-up also demonstrated no statistically significant difference in clinical longevity for selective etching in indirect restorations ($p>0.05$). These studies show an absence of heterogeneity ($I^2=0\%$) and risk ratio of 0.46 [95% CI: 0.19–1.09] for indirect restorations.” ^{119 (p334)}
Significance/direction	According to the authors, “The findings presented here showed that there were no statistical differences in clinical longevity between ceramic restorations cemented with self-adhesive cement without prior enamel conditioning compared to the group that received prior enamel conditioning. Despite the small number of studies included in the review, it is important to highlight that both were well designed, respecting the calculation of sample size, demonstrating moderate quality of evidence by GRADE. Even though the studies have been well conducted and have good methodological quality, the findings were borderline. Thus, it is suggested [that] more well-designed studies [be conducted] with long-term follow-ups and increased sample size.” ^{119 (p336)}
Heterogeneity	The authors commented on heterogeneity as follows: “The pooled meta-analysis with 36 months follow-up demonstrated no statistically significant difference in clinical longevity for selective etching in indirect restorations ($p>0.05$). These studies showed a lack of heterogeneity ($I^2=0\%$) and risk ratio of 0.45 [95% CI: 0.16–1.25] for indirect restorations, and the pooled meta-analysis with 48 and 78 months follow-up also demonstrated no statistically significant difference in clinical longevity for selective etching in indirect restorations ($p>0.05$). These studies show an absence of heterogeneity ($I^2=0\%$) and risk ratio of 0.46 [95% CI: 0.19–1.09] for indirect restorations.” ^{119 (p334)}
Comments	GRADE was used by the review authors, and found that the evidence was of moderate quality. The authors noted that “It is worth mentioning that although the two studies included in the present systematic review address posterior teeth, it is suggested that this result can be applicable to anterior teeth in similar condition, restored indirectly and cemented with self-etching cement; in this sense more studies are necessary in anterior teeth.” ^{119 (p335)}

Deng *et al.* (2016)

Parameter	Extraction
First author and year of publication	Deng <i>et al.</i> (2016) ¹²⁰
Objectives	Evaluated the effects of direct pulp capping using laser treatment in patients who required this treatment for their deep carious lesions on the success of restorations.
Participants	Permanent dentition, cavitated caries, restoration technique All studies included in this review used teeth with deep carious lesions and undergoing direct pulp capping treatment. The ages of the 534 participants ranged from 19 to 74 years. Gender was not reported. The sample sizes ranged from 10 to 200.
Setting/context	The study countries and settings were not reported.
Description of interventions/phenomena of interest	Intervention: Laser (light amplification by stimulated emission of radiation). Comparator: The words ‘control group’ were used through out the article to describe the comparator. The comparator itself was not described until the

Parameter	Extraction
	discussion where the authors say “compared with pulpectomy or pulpotomy”. 120 (p937) The authors defined the intervention as follows: “Laser (light amplification by stimulated emission of radiation) is a manufactured single photon wavelength with concentrated light energy that can exert a strong effect, targeting tissue at an energy level much lower than that of natural light. Owing to their photo-physical characteristics, including their ability to produce good ablation, hemostasis, detoxification, decontamination, and biostimulation effect, lasers have become increasingly popular in direct pulp capping (DPC) treatment in the clinical setting.” 120 (p935–936) Five studies were included using four different laser systems: carbon dioxide (CO₂); diode; erbium, chromium:yttrium-selenium-gallium-garnet (Er,Cr:YSGG); and Erbium-doped Yttrium Aluminium Garnet (Er:YAG). The authors noted that “All of the 5 included studies used a rubber dam during the DPC [direct pulp capping] procedures, which meant excellent conditions for infection control.”^{120 (p940)}
Databases and sources searched	The authors searched four databases (PubMed, the Cochrane Library, Embase, and Chinese National Knowledge Infrastructure (CNKI)) from 1971 through 30 May 2016 for relevant studies. They also conducted manual searches to identify additional studies by using the references of the obtained articles. The preparation and registration of a review protocol was not reported. Extraction and screening were completed in duplicate. Funding: This study was supported by grant from the Key Science and Technology Program of Hubei Province of China and grant from the Building of Oral Health Electronic Information Management System for College Teachers and Students. None of the authors reported any disclosures regarding conflicts of interest.
Date range (years) of included studies	The included studies were published in 1998 (two studies), 2007, 2015, and 2016.
Number of primary studies included in the systematic review	Five randomised controlled trials, published in 1998 (two studies), 2007, 2015, and 2016, were included in this review. Funding: The sources of funding for primary studies were not reported.
Types of studies included	Randomised controlled trials and non-randomised controlled trials were eligible for inclusion. A list of excluded studies with their reason for exclusion was provided in a table.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration’s risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	As noted by the authors, all studies were at high risk of bias for performance bias. Overall, all five studies were at high or unclear risk of bias. Only one study was at low risk of bias for randomisation and the other four were at unclear risk of bias for randomisation. One study was at low risk of bias for outcome assessment and the other four were at unclear risk of bias for outcome assessment. According to the authors, “All included studies met the inclusion and exclusion criteria, but some did not adequately describe their methods in detail (for example, random sequence generation, allocation concealment). Because participant and personnel masking was impossible given the handling characteristics of the lasers, we considered performance bias to be high risk. We determined that 1 study was at a high risk of bias for incomplete outcomes data as it did not give a description of the reason for withdrawals or dropout from the study. We found neither reporting nor other biases in these studies.”^{120 (p937)} The authors stated that “We did not conduct an evaluation of the publication bias due to the limited number of included studies in the final analysis.”^{120 (p936)}
Method of analysis	According to the authors, “We used RevMan 5.2 a statistical program provided by the Cochrane Collaboration, to perform the meta-analysis, and ‘tooth’ was used as the analysis unit. We used the risk ratio and 95% confidence interval as measurable statistics, and we calculated with fixed-effects and random-effects model meta-analysis using the Mantel–Haenszel method for dichotomized data. Significant differences were considered at $p < 0.05$. We evaluated the statistical

Parameter	Extraction
	heterogeneity among the studies using the chi-squared test with a significance set at $p < 0.10$. We used the I^2 statistic to assess the percentage of heterogeneity. When the I^2 value ranges from 0% to 40%, the heterogeneity is mild. When I^2 value ranges from 40% to 60%, the heterogeneity is moderate; when it ranges from 50% to 90%, the heterogeneity is significant; and when it ranges from 75% to 100%, the heterogeneity is extreme. In general, if $p > 0.10$ and $I^2 < 50\%$, all included studies are considered to be homogenous, and the fixed-effects model can be chosen for analysis. If not, the source of heterogeneity should be analyzed. We did not conduct an evaluation of the publication bias due to the limited number of included studies in the final analysis."¹²⁰ p(936)
Outcome assessed	All studies included in this meta-analysis evaluated the outcome of direct pulp capping treatment by clinical criteria (measured as success rate), and some of them combined radiography or laser Doppler flowmetry. Success: Wilder-Smith 1988; Dabrowska 1997; Santucci 1999; Gao 2007; Huth 2012. The follow-up period ranged from six months to four years.
Results/findings	According to the authors' reporting on their meta-analysis, "We used all data of the included studies to calculate the effects of the lasers on the outcome of DPC [direct pulp capping] treatment. Because a heterogeneity test showed that there was low heterogeneity among these studies (Chi-squared test =0.83, $p = 0.99$, $I^2 = 0\%$), we used the fixed-effects model meta-analysis. Based on the results, we found the laser groups had a significantly higher success rate than the control groups (relative risk, 6.28)."¹²⁰ p(937) They continued, "the success rate was approximately 89.9% in the laser aid group, and only 67.2% in the control group. The effective decontamination may be responsible for the high success rate of laser-assisted DPC for caries-exposed pulp tissue."¹²⁰ p(938) The authors also reported that "we found disadvantages reported for using lasers on an exposed pulp surface if inappropriate laser power, time, or technique were used. Most of the laser systems showed great promise for DPC treatment according to previous in vitro and in vivo studies."¹²⁰ p(939) According to Deng <i>et al.</i>, "A direct comparison between different laser systems cannot be made from the data examined in this review and a protocol for the clinical use of lasers for DPC treatment cannot be formulated in this meta-analysis with the limited evidence in the literature."¹²⁰ p(939) They explained that "many of our included studies exhibited small sample sizes, such that their overall veracity is questionable, and their results should be interpreted with caution."¹²⁰ p(940)
Significance/direction	The results showed that the success rate (89.9%) of the laser groups was higher than that of the control groups (67.2%), and the difference was statistically significant (risk ratio: 1.35; 95% CI: 1.23–1.49; $p < 0.00001$). According to the authors' overall conclusion, "Additional well-designed randomized controlled trials with larger sample sizes are needed to draw a more definitive conclusion. Based on the available information, the results of this meta-analysis demonstrated DPC [direct pulp capping] treatment could achieve better clinical outcomes with the aid of lasers."¹²⁰ p(940)
Heterogeneity	Regarding heterogeneity, the authors stated that "We evaluated the statistical heterogeneity among the studies using the Chi-squared test with a significance set at $p < 0.10$. We used the I^2 statistic to assess the percentage of heterogeneity. When the I^2 value ranges from 0% to 40%, the heterogeneity is mild. When I^2 value ranges from 40% to 60%, the heterogeneity is moderate; when it ranges from 50% to 90%, the heterogeneity is significant; and when it ranges from 75% to 100%, the heterogeneity is extreme. In general, if $p > 0.10$ and $I^2 < 50\%$, all included studies are considered to be homogenous, and the fixed-effects model can be chosen for analysis. If not, the source of heterogeneity should be analyzed. We did not conduct an evaluation of the publication bias due to the limited number of included studies in the final analysis."¹²⁰ p(936) Using a fixed-effects model, the authors found no significant heterogeneity between these studies (Chi-squared test =0.83, $p = 0.99$, $I^2 = 0\%$). According to the authors, "we conducted the first meta-analysis, ... to explore the effects of lasers on the DPC [direct pulp capping] treatment."¹²⁰ p(937)

Parameter	Extraction
Comments	GRADE was not used by the review authors.

Appendix I: Data extraction for studies on mixed dentition

Non-cavitated caries

Non-invasive treatment

Khijmatgar *et al.* (2020)

Parameter	Extraction
First author and year of publication	Khijmatgar <i>et al.</i> (2020) ¹³⁵
Objectives	Evaluated the remineralisation potential of NovaMin compared with placebo or no intervention in humans with evidence of demineralisation (white spot lesions and/or cavitation) on teeth.
Participants	Mixed dentition, non-cavitated caries, non-invasive treatment The population comprised humans with evidence of demineralisation (white spot lesions and/or cavitation) on teeth. The authors stated that "The study selected is an RCT [randomised controlled trial] comparing NovaMin in the form of RenNew with a control group. NovaMin was prescribed by researchers to be self-administered in a concentration of 5% to a total of N=48 patients initially. The patients were followed up twice at the third and sixth month after the baseline appointment. During the follow-up process, pictures were taken and several clinical procedures were carried out, such as measurement of decalcification index, modified gingival and plaque index and plaque bacterial counts." ¹³⁵ (p89)
Setting/context	The study countries or clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: Various types of NovaMin-containing vehicles such as toothpaste, mouth rinses, or any prophylactic pastes without any limitation in their formulations, concentration, vehicles, method, duration, and frequency of application. Comparison: Negative control (Crest toothpaste). The authors stated "NovaMin is a bioactive glass that is used in dental care products for remineralization of teeth, hypersensitivity, gingivitis, bleeding, non-carious lesions, carious lesions, and whitening of the teeth... NovaMin consists of calcium sodium phosphosilicate, which is the active ingredient that enables it to bind to the surface of the tooth to initiate the process of remineralization on the enamel. This occurs instantly on contact with saliva or any aqueous media." ¹³⁵ (p88)
Databases and sources searched	Four databases were searched (PubMed, the Cochrane Library, ScienceDirect, and the Trip database) for English-language publications published during the period 1988 to July 2017. Additional automated searches were conducted to review some of the reference lists of the related papers, and review articles pertinent to the topic. The preparation or publication of a protocol was not mentioned. Extraction and screening were completed in duplicate. The authors declared that there was no funding support for the systematic review and there was no conflict of interest for this systematic review.
Date range (years) of included studies	The included study was published in 2015.
Number of primary studies included in the systematic review	One randomised controlled trial, published in 2015, was included in this narrative review. The sources of funding for primary studies were not reported, but in the risk of bias assessment, it was acknowledged that studies of fluoridated toothpaste had a high risk of bias as they were funded or completed by industry.
Types of studies included	Randomised trials were eligible for inclusion. The authors reported that studies excluded were presented in an excluded studies table with reasons for the same. However, the table is not available to view.
Country of origin of included studies	The study countries were not reported.

Parameter	Extraction
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included study.
Appraisal rating	The included study had an overall score of unclear risk of bias. It had an unclear risk of bias for randomisation and a low risk of bias for blinding of outcome ascertainment.
Method of analysis	As only one study was included, the authors provided a narrative description of the study findings.
Outcome assessed	The primary outcome for the chosen study was the remineralisation capacity of NovaMin. The patients in the trial were followed-up at 3 months and again at 6 months. Remineralisation: Hoffman 2015.
Results/findings	The authors stated that "According to the study reviewed, the baseline comparisons using the decalcification index obtained between the NovaMin study group (ReNew) and the control group (Crest) yield a <i>p</i> -value of 0.97, whereas after a 3-month follow-up interval, the value is 0.0403, suggesting there was a trend towards improvement in white spot lesions in the control group, and at the 6 months' time point the <i>p</i> -value is 0.81, concluding that there are no significant differences in the remineralization process obtained by using traditional toothpaste and NovaMin. The study selected also shows that there is no favourable difference in the plaque and gingival health after 6 months." ¹³⁵ (p90)
Significance/direction	In addition, the authors stated "According to this systematic review, there are no statistically significantly different results obtained between the NovaMin group and the control group, even though initially a <i>p</i> =0.0403 suggested that statistically significant values were recorded at the three-month time point. However, this result is based on only one clinical trial. In addition, the RCT [randomised controlled trial] selected was also presented with some drawbacks, such as inaccuracy in assessment of WSL [white spot lesion] due to the presence of gingival hyperplasia and plaque in some patients, dependence on patients' compliance and, finally, the subjectivity of decalcification index on measuring WSL." ¹³⁵ (p91)
Heterogeneity	Heterogeneity was not an issue as there was only one trial included in the review.
Comments	The authors stated "To conclude, this systematic review has its own sets of limitations. Firstly, the articles were searched in English, which might have predisposed them to selection bias. Second, there was only one available RCT [randomised controlled trial] contributing to low [analytic power] for this review, due to the limitation of an extremely low amount of extracted data. Third, the number of studies was relatively low. Finally, within the selected article were a few unclear biases that have further reduced the eligibility of this review." ¹³⁵ (p91) Regarding the quality of evidence, Khijmatgar <i>et al.</i> stated that "Although the study included is a randomized controlled clinical trial, the evidence is regarded as high-quality evidence, but due to factors like selection bias, performance bias and attrition bias, the level of evidence of the study included is graded as low. Therefore, further clinical studies with minimal bias are required to propose recommendations to interested parties." ¹³⁵ (p91)

Ma *et al.* (2019)

Parameter	Extraction
First author and year of publication	Ma <i>et al.</i> (2019) ¹³⁶
Objectives	Evaluated the efficacy of casein phosphopeptide-amorphous calcium phosphate compared with no intervention or placebo for the remineralisation of white spot lesions. Type of dentition not specified. The authors examined 11 laboratory-based studies and two clinical studies; the HRB excluded the laboratory studies from the extraction.
Participants	Mixed dentition (assumption based on age), non-cavitated caries, non-invasive management Population: Humans with early enamel carious lesions, randomised to test or control groups

Parameter	Extraction
	Two randomised controlled trials published in 2014, including 129 participants with a mean age range of 3–15 years and a full age range of 2.5–18 years, were included. It was not clarified whether primary or permanent dentition was examined. The proportion of males in the two studies was 45% and 54%.
Setting/context	The study countries were Denmark and Thailand. The study settings were not reported.
Description of interventions/phenomena of interest	Intervention: Ma <i>et al.</i> described the intervention as follows: “therapeutic dental regimes had to use remineralising agents based on casein phosphopeptide-amorphous calcium phosphate. Any kind of product containing casein phosphopeptide-amorphous calcium phosphate could be included in this meta-analysis, such as MI Paste or Tooth Mousse”.^{136 (p3)} Ma <i>et al.</i> reported that “Casein phosphopeptide-amorphous calcium phosphate, a new type of bioactive material derived from the milk protein casein, can act as a reservoir of bio-available calcium and phosphate, facilitating their precipitation on the enamel surface and thus effectively enhancing remineralisation. Research has indicated that casein phosphopeptide-amorphous calcium phosphate is anticariogenic and capable of reversing the early stages of enamel lesions in vitro and in clinical research.”^{136 (p2)} Comparator: No treatment, placebo treatment, and fluoride toothpaste The actual interventions were tooth mousse or fluoride toothpaste with tooth mousse and the comparators were standard fluoride toothpaste or standard fluoride toothpaste
Databases and sources searched	The search covered a number of electronic sources – the Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Embase, and Ovid – and was conducted in May 2019. The search was restricted to English-language studies and had “certain time restrictions”.^{136 (p2)} Additional records were identified by searching reference lists of included studies. Medical Subject Headings (MeSH) terms and free text words were provided in the article text. Two reviewers independently screened the literature and extracted the data. The authors reported that they prepared a protocol, but it is not published or accessible. This work was supported by the National Natural Science Foundation of China and the Youth Science Foundation of Guangxi Medical University. No funders played a part in the design of the study, data collection, analyses, or interpretation of the results, or in writing the manuscript. The authors declare that they have no financial or non-financial competing interests related to this work.
Date range (years) of included studies	The two included randomised controlled trials were published in 2014.
Number of primary studies included in the systematic review	Two randomised controlled trials published in 2014, including 129 participants with a mean age range of 3–15 years and a full age range of 2.5–18 years, were included. The funding sources for the primary studies were not reported.
Types of studies included	Clinical trials with a comparator group were eligible for study inclusion. The studies excluded at full-text screening are not referenced, but the reasons for exclusion are provided.
Country of origin of included studies	The study countries were Denmark and Thailand.
Appraisal instruments used	The Cochrane Collaboration’s risk of bias instrument was used to assess the risk of bias in the primary studies.
Appraisal rating	The Cochrane Collaboration’s risk of bias instrument was used to assess the risk of bias in the primary studies. One study was judged to have a low risk of bias and the other study to have a high risk of bias. Both studies had adequate randomisation and one study had adequate blinding for outcome assessors. The authors estimate that their research has a low risk of bias, and so does not affect their results. The authors also report that publication bias was not evaluated due to the small number of studies in each meta-analysis.
Method of analysis	The data type for the outcome measurement was mainly continuous data. To avoid errors caused by different measuring instruments, the standardised mean difference was used with a 95% CI to generalise the effectiveness of treatment in each report. Heterogeneity across studies was tested using <i>p</i>-values. If <i>p</i><0.05, the data were considered significantly heterogeneous. The degree of inconsistency of the statistical analysis was assessed with the I² statistic. If the included studies showed good homogeneity, the fixed-effects model was used. When the clinical and methodological heterogeneity was high (<i>p</i><0.05), the authors used the

Parameter	Extraction
	random-effects model to combine the studies. If there were 10 or fewer studies, publication bias was not assessed, because more than 10 studies are required to check funnel plot asymmetry. Sensitivity analysis was performed by the leave-one-out approach in this review. The analysis was carried out using Stata version 14.1.
Outcome assessed	Outcome: Remineralisation efficacy, measured as percentage reduction in fluorescence Timeframe: four weeks to 12 months (not predetermined) Outcome by primary study Remineralisation efficacy: Bröchner 2014; Sitthisettapong 2014.
Results/findings	The values of quantitative light fluorescence were used to assess remineralisation efficacy. Both included studies had patients with white spot lesions on smooth surfaces. When the two clinical studies were pooled, no significant heterogeneity was found (I^2 : 0%); therefore, a pairwise fixed-effects model of analysis was used to compare the interventions and comparators: toothpaste with casein phosphopeptide-amorphous calcium phosphate, and placebo paste without casein phosphopeptide-amorphous calcium phosphate. The reported interventions were tooth mousse with casein phosphopeptide-amorphous calcium phosphate or fluoride toothpaste with active tooth mousse, and the comparators were standard fluoride toothpaste or standard fluoride toothpaste with placebo tooth mousse. There was no significant difference between using the intervention and controls (standardised mean difference: 0.08; 95% CI: -0.91 to 1.08; $p=0.87$; 2 trials; 129 participants).
Significance/direction	No difference
Heterogeneity	There was no heterogeneity.
Comments	GRADE was not used by the review authors. The HRB judged the quality of this evidence as moderate due to the high risk of bias in one of the two included studies; one trial was judged to have inadequate blinding of outcome assessment. In addition, the sample size in the pooled analysis was less than 200. The quality of the systematic review was judged as moderate using AMSTAR 2 as the review had no critical flaws.

Chong *et al.* (2018)

Parameter	Extraction
First author and year of publication	Chong <i>et al.</i> (2018)¹³⁸ (Cochrane Review)
Objectives	Compared the retention, effectiveness, and safety of different types of slow-release fluoride devices on preventing, arresting, or reversing the progression of carious lesions on all surface types of primary (deciduous) and permanent teeth at 12 months following treatment.
Participants	Mixed dentition, non-cavitated carious lesions, and non-invasive fluoride Population: All surface types of primary and permanent teeth One randomised trial published in 2005, with 174 children living in the UK who were assigned either slow-dissolving, fluoride-releasing glass beads or placebo beads, was included. The mean age at the beginning of the study was 8.8 years, and at termination was 10.9 years. Gender was not reported. The setting was an inner-city schools in an area served with low-fluoride water.
Setting/context	The study recruited children from seven schools in an area of deprivation in the UK that had low levels of fluoride in the water.
Description of interventions/phenomena of interest	Clinical trials in children or adults treated with slow-release fluoride devices compared with another type of fluoride treatment (e.g. toothpaste, mouth rinse, gel, or varnish), placebo, or no treatment (usual care). Slow-release fluoride devices or beads have been investigated as a potentially cost-effective method of preventing, arresting, or reversing the progression of carious lesions in people with a high risk of caries.
Databases and sources searched	The authors searched four electronic databases: Cochrane Oral Health Group Trials Register (to 23 January 2018), the Cochrane Central Register of Controlled Trials (CENTRAL) (to 23 January 2018), MEDLINE via Ovid (1946 to 23 January

Parameter	Extraction
	2018), and Embase via Ovid (1980 to 23 January 2018). ClinicalTrials.gov and the WHO's International Clinical Trials Registry Platform were also searched for ongoing trials (23 January 2018). No restrictions were placed on the language or date of publication when searching the electronic databases. Search strategies are presented in appendices. The authors hand-searched reference lists of included studies. Searches were based on the <i>Cochrane Handbook for Systematic Reviews of Interventions</i> guidance. The authors prepared a protocol. Duplicate screening and extraction were implemented. There were no conflicts of interest and funding was provided through the Cochrane Oral Health Group Global Alliance, UK.
Date range (years) of included studies	One randomised trial published in 2005, involving 174 children living in the UK, was included.
Number of primary studies included in the systematic review	One randomised trial published in 2005, involving 174 children living in the UK who were assigned either slow-dissolving, fluoride-releasing glass beads or placebo beads, was included. The included trial was supported by a grant from the Wolfston Foundation.
Types of studies included	Only parallel randomised controlled trials (RCTs) were eligible for inclusion, in order to avoid contamination irrespective of publication status, language, or blinding. The authors excluded five studies and provided details and reasons in the characteristics of excluded studies table.
Country of origin of included studies	The study country was the UK.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess the risk of bias in the primary studies.
Appraisal rating	This study was judged to be at high risk of bias using the Cochrane Collaboration's risk of bias instrument. However, the trial was judged to have adequate random sequence generation and was considered to have adequate blinding of outcome assessors. There was an insufficient number of trials to assess publication bias.
Method of analysis	For dichotomous outcomes (where the outcome of interest was either present or absent), the estimate of treatment effect of an intervention would have been expressed as risk ratios (together with 95% CIs) or as hazard ratios if these were available as time-to-event data. Narrative analysis was completed, as there was only one trial. For continuous outcomes, the authors reported mean differences and CIs for outcomes and percentage retention.
Outcome assessed	Outcome: Arresting or reversing the progression of carious lesions at 12 months: Toumba 2005. Increase in decayed, missing, and filled teeth at two years compared with baseline: Toumba 2005. Increase in decayed, missing, and filled surfaces at two years compared with baseline: Toumba 2005. Progression of carious lesions through enamel or into dentine: No evidence Dental pain due to decay: No evidence Harms of slow-release fluoride devices: Toumba 2005. Participant satisfaction: No evidence Retention of slow-release fluoride devices: Toumba 2005. Time frame: 24 months for included study
Results/findings	A narrative analysis was completed, as there was only one trial. The study attrition rate was high, at 24% (42 children were lost to follow-up). In addition, a further 69 lost their bead devices and were excluded from the final analysis. The bead retention rate among the 132 followed up at 24 months was very low, at 48% (63/132). Only 36% (63) of 174 children recruited to the study were included in the final analysis, as they had retained the beads and were available to participate. Decayed, missing, and filled permanent or primary teeth was greater than 1 at the start of the study, and there were greater than 1,000,000 colony-forming units of <i>Streptococcus mutans</i> per millilitre of saliva at the start of the study. There is insufficient or very low-quality evidence to determine whether slow-release fluoride devices (glass beads) help reduce dental decay. Retention of the beads is a problem. The incidence of decayed, missing, and filled permanent teeth or primary teeth or their surfaces was statistically significantly better in

Parameter	Extraction
	treated than in non-treated populations at 2-year follow-up. Caries increment was significantly lower at 24 months in the intervention group (n=31) than in the control group (n=32) (mean difference: -0.72 decayed, missing, and filled teeth; 95% CI: -1.23 to -0.21; mean difference: -1.52 decayed, missing, and filled surfaces; 95% CI: -2.68 to -0.36). The primary study authors reported no irritations or other harms.
Significance/direction	The incidence of decayed, missing, and filled permanent or primary teeth or their surfaces at two years was statistically significantly different in treated and non-treated populations at two years.
Heterogeneity	Not applicable, as only one trial was included.
Comments	GRADE was used by the review authors. The authors graded the trial as having very low-quality evidence as they identified one eligible trial with a sample size less than 200. The HRB graded the review as having low-quality evidence due to the high risk of bias (with attrition over 20%) and the small sample size. The trial had adequate randomisation and blinding of outcome assessment. The quality of the systematic review was judged as high using AMSTAR 2.

Paula *et al.* (2017)

Parameter	Extraction
First author and year of publication	Paula <i>et al.</i> (2017) ¹⁴¹
Objectives	Compared different remineralisation agents (fluoride products, casein phosphopeptide-amorphous calcium phosphate, and ICON resin) and techniques with each other for the treatment of white spot lesions in both permanent and primary teeth. There was no age cut-off, and both permanent and primary teeth were included.
Participants	Mixed dentition, non-cavitated caries, non-invasive management Population: Patients with white spot lesions in both permanent and primary teeth Age: No age cut-off Age and gender were not reported. Thirteen randomised controlled trials published between 2006 and 2015, with 1,187 participants, were included in this review.
Setting/context	The settings or study countries were not reported.
Description of interventions/phenomena of interest	Remineralisation agents: fluoride products, casein phosphopeptide-amorphous calcium phosphate, and ICON resin Comparator: Each other
Databases and sources searched	The search was conducted on three databases: PubMed, the Cochrane Library, and ScienceDirect. The authors reported a search strategy for each database. The authors searched the references of the selected articles and relevant reviews. Abstract screening was done by one author and full-text screening by two authors. It was not clear who extracted the data. Articles with abstracts published between 29 September 2005 and 29 September 2015, in English and Portuguese, were included. There is no mention that a protocol was prepared. The authors state that their research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors, and that they have no actual or potential conflicts of interest.
Date range (years) of included studies	Thirteen randomised controlled trials published between 2006 and 2015, with 1,187 participants, were included in this review.
Number of primary studies included in the systematic review	Thirteen randomised controlled trials published between 2006 and 2015, with 1,187 participants, were included in this review. The funding sources of primary studies are not mentioned.
Types of studies included	The inclusion criteria were randomised controlled trials. After evaluating the full texts, 32 references were excluded from the study and are listed with the reasons for exclusion in an appendix.
Country of origin of included studies	The study countries were not provided.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess the risk of bias in the primary studies.

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Appraisal rating	Based on the Cochrane Collaboration's risk of bias instrument, according to the authors, eight trials were judged to have a high risk of bias and five trials to have an unclear risk of bias. Using Cochrane guidance, all trials would be judged to have a high risk of bias. However, all 13 trials were judged to have adequate random sequence generation and 9 (69%) were considered to have adequate blinding of outcome assessors. The authors note that the high risk of bias in the primary studies seriously limits the conclusions about products to treat white spot lesions. Publication bias was not discussed.
Method of analysis	The actual analysis is not described in the methods section. The authors reported that "the clinical methodology of all studies was evaluated by the interventions and results obtained. Due to the disparity of methodology, it was not possible to perform a quantitative analysis (meta-analysis)." ^{141 (p30)}
Outcome assessed	Outcome: Remineralisation (regression or disappearance) of white spot lesions Follow-up: 1–20 months (not predetermined) Outcome by primary study: Remineralisation (regression or disappearance) of white spot lesions: Sonesson 2014; Du 2012; Ferreira 2009; Zantner 2006; Jiang 2013; Llena 2013; Memarpour 2015; Robertson 2011; Beerens 2010; Bröchner 2011; Bailey 2009; Andersson 2006; Senestraro 2013.
Results/findings	Based on the disparities between products, method of assessment, and time to follow-up of evaluation methodologies, the authors were unable to do a meta-analysis. Most of the studies included in this narrative analysis reported that therapy with remineralising agents reduces white spot lesions (in terms of their size or visual appearance). Five of six studies concluded that fluoride products were associated with the remineralisation of white spot lesions, although only two demonstrated a statistically significant improvement. Three studies of the effects of casein phosphopeptide-amorphous calcium phosphate on remineralising white spot lesions demonstrated improvements, and the improvements were significant in two of these studies. One study on ICON resin indicated significant regression of white spot lesions, either in size or in their clinical visual appearance. When fluoride was compared with casein phosphopeptide-amorphous calcium phosphate, both products demonstrated improvements but neither product was significantly better than the other. The main finding from this review suggests that there is moderate- to low-quality evidence upon which to assess the effectiveness of the different remineralising agents included in the review, due to heterogeneity in comparisons, outcome measures, and follow-up periods. The authors reported that "the aforementioned limitations have a huge consequence in the high risk of bias, as obtained from the analysis performed in the results chapter." ^{141 (p35)} According to Paula <i>et al.</i>, "More studies are required for scientific evidence in order to reach a conclusion of the most suitable therapeutic method for the treatment of surface and subsurface demineralization of the enamel." ^{141 (p23)}
Significance/direction	Varied by intervention
Heterogeneity	Based on the disparities between products, method of assessment, and time to follow-up of evaluation methodologies, the authors were unable to do a meta-analysis. These afore mentioned differences are a proxy for heterogeneity.
Comments	GRADE was not used by the review authors. The HRB graded the evidence as moderate quality for the main outcomes due to a high or unclear risk of bias in all the included trials. Blinding of outcome ascertainment was considered inadequate. There was methodological heterogeneity in the included trials. The quality of the systematic review was judged moderate using AMSTAR 2.

Gao *et al.* (2016a)

Parameter	Extraction
First author and year of publication	Gao <i>et al.</i> (2016) ¹⁴²

Parameter	Extraction
Objectives	Compared professionally applied fluoride therapy with other active treatments, with placebo, or with no intervention in remineralising and arresting dental caries in primary and permanent teeth in children.
Participants	Mixed dentition, non-cavitated caries, non-invasive management Population: Early enamel caries in primary and permanent teeth of 2,060 children The age range or gender of the children were not reported in the review.
Setting/context	The study settings or countries were not reported in the review.
Description of interventions/phenomena of interest	According to Gao <i>et al.</i> , “professionally applied fluoride therapy is a relatively low-cost and easily operated treatment and has been used to arrest active dental caries...Fluoride inhibits plaque metabolism, alters plaque composition, affects plaque formation, and reduces plaque bacteria’s ability to produce a large amount of acid from carbohydrates”. ^{142 (p2)} Comparator: Other active treatments, placebo, or no intervention
Databases and sources searched	The authors completed a systematic search of publications from 1948 to 2014 using four databases: PubMed, the Cochrane Library, Web of Science, and Embase. They included English-language publications only. Keywords were provided. Searches were performed on the bibliographies of the selected full-text publications in order to identify relevant papers, which were included for assessment. There was no mention that a protocol was prepared. Duplicate screening was completed. It is not clear if extraction was completed in duplicate. The authors declared that they had no competing interests. This research was funded by the General Research Fund of the University Grant Council, Hong Kong.
Date range (years) of included studies	Seventeen randomised controlled trials published between 2001 and 2014 were included in this review.
Number of primary studies included in the systematic review	Seventeen randomised controlled trials published between 2001 and 2014 were included in this review; 10 measured the role of professionally applied fluorides in remineralising early enamel caries among 2,060 participants, and seven measured the role of professionally applied fluorides in arresting dentine caries among 12,145 participants. The funding of primary studies was not discussed.
Types of studies included	The authors were not absolutely clear, but it appears that they intended to include clinical trials and at some stage these became randomised controlled trials. The list of excluded studies was not provided, but a reason for each exclusion was provided.
Country of origin of included studies	The study countries were not reported in the review.
Appraisal instruments used	The risk of bias assessment of each study was undertaken using the Cochrane Collaboration’s risk of bias instrument.
Appraisal rating	The authors do make an overall judgement on the risk of bias in the included studies, and so the HRB has done so using Cochrane guidelines. For the 10 trials measuring the role of professionally applied fluorides in remineralising early enamel caries, eight were judged to have a high risk of bias and two to have an unclear risk of bias. Four of the 10 trials were judged to have adequate random sequence generation, and four were considered to have adequate blinding of outcome assessors. For the seven trials measuring the role of professionally applied fluorides in arresting dentine caries, four were judged to have a high risk of bias and three to have an unclear risk of bias. Three of the seven trials were judged to have adequate random sequence generation, and six were considered to have adequate blinding of outcome assessors. When commenting on the risk of bias, the authors stated that “blinding of outcome measurement and allocation concealment were either not achieved or not mentioned by the researchers. The sample size of some studies was small, while some studies didn’t report the statistical procedure of sample size calculation or justified the sample size used in their studies”. ^{142 (p6)} Publication bias is acknowledged. Only English-language articles were considered in this review. Silver diamine fluoride is mainly used in Asian countries compared with its use in countries

Parameter	Extraction
	elsewhere in the world. This review may not be comprehensive because studies published in Japanese, Chinese, Spanish, or Portuguese were not included.
Method of analysis	Meta-analysis (Stata 13.1) using the pairwise random-effects model was used to evaluate the overall percentage of remineralised early enamel caries and to show the effective weight of each study in this review according to the sample size and calculated percentage of remineralised early enamel caries. Meta-analysis using the pairwise random-effects model was used to compare the proportion of dentine caries being arrested as the caries-arresting proportion.
Outcome assessed	Outcome: Remineralising and arresting dental caries Time frame: 1–36 months (not predefined) Measuring the role of professionally applied fluorides in remineralising early enamel caries at 1–30 months. For meta-analysis, 1,216 with a time frame of between 1 and 9 months. Four of the 10 trials were included. Three trials had more than two arms. Autio-gold 2001; Amorim 2008; Ferreira 2009; Almeida 2011. Measuring the role of professionally applied fluorides in arresting dentine caries at 12–36 months. For meta-analysis, 13,086 with a time frame of between 18 and 36 months. Five of the seven trials had more than two arms. Lo 2001; Chu 2002; Llodra 2005; Ye 2009; Zhi 2012. A number of the trials had more than two arms, so network meta-analysis may be more appropriate.
Results/findings	The authors did not explain their rationale for meta-analysis. A number of the trials had more than two arms, so network meta-analysis may be more appropriate. Random-effects pairwise meta-analyses performed on four papers show that using 5% sodium fluoride varnish is superior to controls in remineralising early enamel caries; the overall percentage of remineralised enamel caries was 63.6% (95% CI: 36–91%; I^2: 96%; 4 trials; 1–30 months follow-up). The level of heterogeneity was very high. According to the authors, “Apart from NaF [sodium fluoride] varnish, there is limited evidence to support the benefits of using other professional-applied fluoride agents such as 0.9% silicon tetrafluoride, 0.42% sodium fluoride gel and 10% SDF [silver diamine fluoride] in remineralising early enamel caries”.^{142 (p7)} Random-effects meta-analyses performed on five papers show that using 38% silver diamine fluoride is superior to controls in arresting dentine caries in both the primary and permanent teeth of children; the overall proportion of arrested dentine caries was 65.9% (95% CI: 41–91%; I^2: 96%; 5 trials; 12–36 months follow-up). The level of statistical heterogeneity was very high, but this is not discussed. Based on the findings of this review, there is low-quality evidence to suggest that 5% sodium fluoride varnish is an effective remineralising agent for early caries and that 38% silver diamine fluoride is effective in arresting the progression of active caries. According to Gao <i>et al.</i>, “professionally applied 5% sodium fluoride varnish shows the capability to remineralise early enamel caries in children. Silver diamine fluoride solution at 38% is effective in arresting active dentine caries.”^{142 (p8)}
Significance/direction	Favours 5% sodium fluoride varnish for remineralisation and 38% silver diamine fluoride for arresting the progression of active caries.
Heterogeneity	Substantial heterogeneity was not discussed by the authors.
Comments	GRADE was not used by the review authors. The HRB graded the evidence as low or very low quality for the two interventions due to a high or unclear risk of bias in the included trials. Blinding of outcome ascertainment was inadequate for one outcome and randomisation was inadequate for both outcomes. There was substantial statistical heterogeneity in the outcome analysis. The quality of the systematic review was judged as critically low using AMSTAR 2 as the authors did not complete a robust meta-analysis including control for risk of bias and addressing heterogeneity.

Lenzi *et al.* (2016)

Parameter	Extraction
First author and year of publication	Lenzi <i>et al.</i> (2016) ¹⁴⁰
Objectives	Evaluated the effectiveness of professional topical fluoride application (gels or varnishes) on the reversal of incipient enamel carious lesions in primary or permanent dentition in children.
Participants	Mixed dentition, non-cavitated carious lesions, non-invasive management Population: Enamel carious lesions in primary or permanent dentition in children Five parallel-group randomised clinical trials, published between 2001 and 2015, were included in the review, and three trials were included in the meta-analysis. The mean age range of the 274 children was 3.4–11.7 years. Gender was not reported.
Setting/context	The study countries were Brazil, Albania, and the USA. The study settings were not reported.
Description of interventions/phenomena of interest	According to Lenzi <i>et al.</i> , “The action of topical fluoride has been verified in in vitro and in situ studies regarding the formation of fluoride and its remineralizing ability; however, there is limited clinical evidence on its actual effectiveness. To the best of our knowledge, a systematic quantitative evaluation of the available evidence on the therapeutic effect of the main modalities of topically applied fluoride has never been undertaken. Moreover, comparisons of regimens and agents for remineralisation of ‘incipient’ carious lesions may provide more useful information for clinical evidence-based decision making”. ¹⁴⁰ (p85) Comparator: No intervention, or a placebo
Databases and sources searched	The search was completed up to July 2015 using PubMed/MEDLINE, the Cochrane Library, Scielo, LILACS, and Scopus databases with no publication year or language limits. The authors searched unpublished trials through the ClinicalTrials.gov database. The references of the included articles were also cross-checked for additional studies. The authors presented their MEDLINE strategy in an appendix. Study screening and extraction were completed by two reviewers. This study protocol was recorded in PROSPERO. The authors declared no conflict of interest but provided no information on funding.
Date range (years) of included studies	Five parallel-group randomised clinical trials, published between 2001 and 2015, were included in the review, and three trials were included in the meta-analysis.
Number of primary studies included in the systematic review	Five parallel-group randomised clinical trials, published between 2001 and 2015, were included in the review, and three trials were included in the meta-analysis. The funding of primary studies is not discussed in the paper.
Types of studies included	The authors specified randomised clinical trials in their inclusion criteria. They provided the reasons for exclusion at full-text screening, but did not reference the excluded studies.
Country of origin of included studies	The study countries were Brazil, Albania, and the USA.
Appraisal instruments used	Two reviewers independently assessed the risk of bias of the three trials included in the meta-analysis using a risk of bias instrument. It is not clear which risk of bias instrument was used.
Appraisal rating	Overall, all three trials were judged to be at high risk of bias. None of the three trials was judged to have adequate random sequence generation or adequate blinding of outcome assessors. The authors reported that, “Although the participants were randomly assigned to experimental groups in two primary studies, a clear statement of the randomization method was not observed. A lack of information about the allocation concealment and masking of participants was verified in the three studies. One study reported a sample characteristics imbalance at baseline”. ¹⁴⁰ (p88) The authors reported that a comprehensive search in several databases was conducted in order to avoid publication bias.
Method of analysis	For the meta-analysis, the authors only included the data from the studies that evaluated the effect of fluoride varnish on the reversal of non-cavitated carious lesions. Pooled-effect estimates were expressed as the weighted mean difference between groups. It was not possible to perform the meta-analysis on studies assessing fluoride gels because there was insufficient information about the factors in the studies to be included in the pooling.

Parameter	Extraction
Outcome assessed	Outcome: Reversal of enamel carious lesions Time frame: Not predefined Outcome by primary study: Reversal of enamel carious lesions (fluoride varnish): Autio-Gold 2001; de Amorim 2008; Xhemnica 2008. Reversal of enamel carious lesions (fluoride gel): Ferreira 2005; Bonow 2013. The follow-up periods varied from 1 to 9 months for trials included in the meta-analysis.
Results/findings	The therapeutic methods ranged considerably regarding the fluoride application protocols. There was a significant trend of effectiveness of fluoride varnish on the reversal of enamel carious lesions (standardised mean difference: -2.04; 95% CI: -3.25 to -0.84; $p < 0.05$; 3 trials; 234 participants). Substantial statistical heterogeneity was reported in the meta-analysis (I^2: 92%). It was not possible to perform the meta-analysis on studies assessing fluoride gels because there was insufficient information about the factors in the studies to be included in the pooling. Fluoride varnish seems to be an effective treatment for the reversal of carious lesions in primary and permanent dentition; however, further clinical trials concerning the efficacy of topical fluorides for treating those lesions are still required, mainly regarding the fluoride gel. Considering the scientific evidence on topical fluorides, paediatric dentists can use fluoride varnishes as an adjuvant for the treatment of active white spot lesions in primary or permanent dentition.
Significance/direction	Significant trend of effectiveness of fluoride varnish on the reversal of enamel carious lesions.
Heterogeneity	Substantial statistical heterogeneity was reported in the meta-analysis (I^2 : 92%).
Comments	GRADE was not used by the review authors. The HRB graded the evidence as very low quality for the two interventions due to small sample size, a high risk of bias in the included trials, and inadequate randomisation and blinding of outcome ascertainment. In addition, there was substantial statistical heterogeneity in the outcome analysis. The quality of the systematic review was judged as low using AMSTAR 2 as the authors were unable to control for the risk of bias in the meta-analysis.

Li *et al.* (2014)

Parameter	Extraction
First author and year of publication	Li <i>et al.</i> (2014) ¹³⁷
Objectives	Compared the use of casein phosphopeptide-amorphous calcium phosphate in any modality with the use of fluoride toothpastes or mouthwashes, placebos, topical creams, and chewing gum in order to assess their long-term (>3 months) remineralising effect on early carious lesions.
Participants	Mixed dentition, non-cavitated caries, non-invasive treatment Population: 2,367 participants adolescents' primary and permanent teeth There were no age limits, but nearly all participants were adolescents. The type of teeth would appear to be both primary and permanent teeth, but again this is not clear. Three studies published between 2008 and 2012 were of interest, as they covered non-cavitated carious lesions, while the other five covered orthodontic secondary carious lesions. The participants' ages ranged from 3.5 to 15 years in the non-cavitated carious lesions studies (two randomised clinical trials and one controlled clinical trial) with follow-ups between 6 and 24 months. Gender was not reported.
Setting/context	The study settings or countries were not reported.
Description of interventions/phenomena of interest	Casein phosphopeptide-amorphous calcium phosphate to remineralising non-cavitated caries Comparator: Fluoride toothpastes or mouthwashes, placebos, topical creams, and chewing gum
Databases and sources searched	Seven databases were searched: MEDLINE via PubMed (1970 to 10 April 2013), Web of Science (1970 to 10 April 2013), Embase (1970 to 16 April 2013), the

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	Cochrane Central Register of Controlled Trials (CENTRAL) (13 April 2013), ScienceDirect (1970 to 10 April 2013), Chinese Biological Medicine Database (CBM), and the Chinese National Knowledge Infrastructure (CNKI) database (1989 to 10 April 2013). Studies written in English and Chinese were considered for inclusion. The reference lists of included studies were also searched for additional studies. Unpublished literature was also searched on ClinicalTrials.gov, the National Research Register, OpenGrey, and the WHO's International Clinical Trials Registry Platform. The search strategy developed for MEDLINE is presented in an appendix. The preparation of a protocol was not mentioned in the review. Screening and data extraction were completed in duplicate. This study was supported by grants from the National Natural Science Foundation of China. The authors reported that they did not have any conflicts of interest.
Date range (years) of included studies	Three studies published between 2008 and 2012 were of interest, as they covered non-cavitated carious lesions, while the other five covered secondary carious lesions in orthodontic patients.
Number of primary studies included in the systematic review	The review included 2,367 participants in six randomised clinical trials and two controlled clinical trials in which casein phosphopeptide-amorphous calcium phosphate was delivered by any method. Three studies published between 2008 and 2012 were of interest, as they covered non-cavitated carious lesions, while the other five covered orthodontic secondary carious lesions. The sources of funding for primary studies were not reported.
Types of studies included	Randomised or quasi-randomised clinical trials with follow-ups of 3 months or more were specified in the inclusion criteria. The 75 studies excluded during full-text screening and the reasons for exclusion were presented in an appendix.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The risk of bias assessment of each study was undertaken using the Cochrane Collaboration's risk of bias instrument.
Appraisal rating	Of the three studies of interest, two had a high risk of bias and one had a low risk of bias. Two of the three trials of interest were judged to have adequate random sequence generation and all three were judged to have adequate blinding of outcome assessors. Substantial differences were found in the intervention measures, time points of outcome assessment, and measurement methods. Meta-analysis was not possible due to both the high risk of bias and clinical heterogeneity of the trials. The authors did not discuss publication bias.
Method of analysis	Mean differences (MDs) and standard deviations (SDs) were used to summarise data in studies with continuous outcomes, and Peto odds ratios and 95% CIs were used for studies with dichotomous outcomes.
Outcome assessed	Outcome: Remineralising effect of casein phosphopeptide-amorphous calcium phosphate on early carious lesions: Time frame: >3 months (predefined) Outcome by primary study: Remineralising effect of casein phosphopeptide-amorphous calcium phosphate on early carious lesions 6–24 months follow-up for the studies of interest: Morgan 2008; Rao 2009; Sitthisetapong 2012.
Results/findings	The findings were presented in a narrative analysis, although the authors considered meta-analysis. The authors reported that "Meta-analysis was impossible both due to high risk of bias and clinical heterogeneity."¹³⁷ (p774–775) Three studies evaluated the effect of casein phosphopeptide-amorphous calcium phosphate on naturally occurring caries, and a significant reduction in caries increment was observed after using casein phosphopeptide-amorphous calcium phosphate compared with placebo. In a 2-year follow-up study, chewing casein phosphopeptide-amorphous calcium phosphate gum significantly enhanced the regression of approximal caries compared with placebo gum. However, no clinical advantage was found for using extra casein phosphopeptide-amorphous calcium phosphate after brushing with fluoridated toothpaste. There appears to be no significant advantage to using casein phosphopeptide-amorphous calcium phosphate as a supplement to fluoride-containing products in

Parameter	Extraction
	these high-risk-of-bias studies; therefore, the evidence for this intervention is low quality. No serious side effects were reported in studies assessing the clinical safety of casein phosphopeptide-amorphous calcium phosphate usage.
Significance/direction	There is low-quality evidence that casein phosphopeptide-amorphous calcium phosphate is better than no intervention; however, it offers no advantage as a supplement to fluoride.
Heterogeneity	Meta-analysis was not possible both due to the high risk of bias and clinical heterogeneity of the included studies.
Comments	GRADE was not used by the review authors. The HRB graded the evidence as low quality for the outcomes assessed due to a high risk of bias in most of the included trials, and to inadequate randomisation. Quasi-randomised trials were included, further reducing the quality of evidence. In addition, there was substantial clinical and methodological heterogeneity in the outcome analysis. The quality of the systematic review was judged as moderate using AMSTAR 2.

Microinvasive treatment

Chen *et al.* (2021)

Parameter	Extraction
First author and year of publication	Chen <i>et al.</i> (2021) ¹⁴³
Objectives	Evaluated the caries-arresting effectiveness of infiltration and sealing for proximal non-cavitated carious lesions and beyond, including different dentition types and caries risk levels in humans.
Participants	Mixed dentition (not stated), non-cavitated lesions, caries arrest Children, adolescents, and adults, with proximal or approximal non-cavitated caries, diagnosed clinically (visually intact surface) or by radiographs. Only studies with caries risk for most people (more than 80%) were collected for further classification. The authors included 17 split-mouth randomised controlled trials published in 22 articles between 2005 and 2020. Ten studies evaluated infiltration and six evaluated sealing, while one study evaluated both. Five studies included participants with primary teeth and 12 studies included participants with permanent teeth. Overall, there were 869 participants with 2,241 non-cavitated carious lesions and a mean age range of 5–26 years. Gender was not reported.
Setting/context	The clinical setting and study countries were not reported.
Description of interventions/phenomena of interest	Infiltration and sealing are microinvasive treatments for arresting proximal non-cavitated carious lesions. However, their efficacies under different conditions remain unknown. Intervention: Infiltration or sealing technology (mainly resin-based infiltration and sealants, one glass ionomer sealant) The two microinvasive strategies were compared with each other and with non-invasive treatments, placebo or no treatment.
Databases and sources searched	Three electronic databases (the Cochrane Library, PubMed, and Embase) and three other data sources (OpenGrey, ProQuest Dissertations & Theses Global, and Web of Science Conference Proceedings Citation Index) were searched without restrictions from inception to 6 April 2020. The search keywords were presented in the article text and an appendix. Full texts of the eligible retrieved studies were assessed for additional references, and authors were contacted for additional information. A protocol was prepared but not published. Two authors selected the eligible studies and extracted the data independently. The authors declared that they had no competing interests and no funding was provided.
Date range (years) of included studies	The authors included 17 split-mouth randomised controlled trials published in 22 articles between 2005 and 2020.
Number of primary studies included in the systematic review	The authors included 17 split-mouth randomised controlled trials published in 22 articles between 2005 and 2020. Ten studies evaluated infiltration and six evaluated sealing, while one study evaluated both. Five studies included

Parameter	Extraction
	participants with primary teeth and 12 studies included participants with permanent teeth. Only six trials had a dropout rate of less than 20% at their last follow-up. The sources of funding for primary studies were not reported.
Types of studies included	Split-mouth randomised controlled trials were eligible for inclusion. The reasons for excluding full-text articles were provided but not a list of their references.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	Eight of the 17 included trials were judged to be at high risk of bias, eight trials had an unclear risk of bias, and one trial had a low risk of bias. Fourteen (82%) of the 17 trials had adequate randomisation and all 17 trials had adequate blinding for outcome ascertainment. Sensitivity analysis for risk of bias was not done. The authors reported that "For this meta-analysis, publication bias was not evaluated due to insufficient studies (fewer than 10) with clinical and methodological homogeneity."¹⁴³ (p10)
Method of analysis	The authors assessed clinical, methodological, and statistical heterogeneity. The meta-analysis was conducted using Stata software, version 16. Effect variables were calculated as odds ratios with 95% CIs for binary data in this research. Meta-regression analysis was conducted to identify the influence of follow-up years on treatment efficacy. The authors conducted the meta-analysis with a random-effects model owing to clinical issues and methodological heterogeneity, regardless of the statistical assessment. The I² Inconsistency Index was used to assess statistical heterogeneity. Since differences among the intervention methods, dentition types, and caries risk levels might have affected the outcome data, the authors analysed these factors using subgroup analysis with a random-effects empirical Bayes model.
Outcome assessed	Lesion progression (arrest) was assessed by digital radiography via digital subtraction radiography, pairwise reading, or lesion stage. Infiltration: Arthur 2017 ; Arslan 2019 ; Ammari 2018; Jorge 2019 ; Bagher 2018; Basili 2017; Ekstrand 2010; Foster Page 2017; Martignon 2012; Meyer-Lueckel 2016; Paris 2020; Meyer-Lueckel 2012; Paris 2010; Peters 2019; Peters 2018; Vaghela 2017; Sealing: Alkilzy 2011; Alkilzy 2009; Gomez 2005; Martignon 2012; Martignon 2010; Martignon 2006; Trairatvorakul 2011. Follow-up periods ranged from 12 to 84 months.
Results/findings	The meta-regression analysis results revealed that different research durations (ranging from 6 to 84 months) did not influence caries progression ($p>0.620$, 95% CI: -0.143 to 0.233). Thus, the authors chose caries progression at the longest follow-up times for randomised controlled trials with more than one follow-up. The overall intervention effects of infiltration and sealing were significantly different from the intervention effects of the control treatments (i.e. non-invasive treatments or placebo treatment) (odds ratio: 0.23; 95% CI: 0.18–0.30; I²: 0%; 17 trials; moderate evidence). The authors analysed the two different measures (infiltration and sealing) using subgroup analysis, and found that both intervention measures reduced the odds of lesion progression compared with the control group (infiltration compared with non-invasive treatments: odds ratio: 0.21; 95% CI: 0.15–0.30; I²: 0%; 11 trials; moderate evidence; sealing compared with placebo: odds ratio: 0.27; 95% CI: 0.18–0.42; I²: 0%; seven trials; moderate evidence). Of note, one trial was included in both the infiltration and sealing interventions. For both primary and permanent dentition, both infiltration and sealing were more effective than non-invasive treatments (primary dentition: odds ratio: 0.30; 95% CI: 0.20–0.45; I²: 0%; five trials; permanent dentition: odds ratio: 0.20; 95% CI: 0.14–0.28; I²: 0%; 13 trials). The overall positive effects of infiltration and sealing were significantly different from the control effects based on different caries risk levels (odds ratio: 0.20; 95% CI: 0.14–0.28; I²: 0%; 9 trials). Except for caries risk at moderate levels (moderate risk: odds ratio: 0.32; 95% CI: 0.01–8.27; I²: not applicable; one trial), there were

Parameter	Extraction
	significant differences between microinvasive and non-invasive treatments (low risk: odds ratio: 0.24; 95% CI: 0.08–0.72; I²: 0%; two trials; low to moderate risk: odds ratio: 0.38; 95% CI: 0.18–0.81; I²: not applicable; one trial; moderate to high risk: odds ratio: 0.17; 95% CI: 0.10–0.29; I²: 0%; 4 trials; high risk: odds ratio: 0.14; 95% CI: 0.07–0.28; I²: 0%; 11 trials). Except for caries risk at moderate levels (moderate risk: odds ratio: 0.32, 95% CI: 0.01–8.27), infiltration was superior to sealing (low risk: odds ratio: 0.24; 95% CI: 0.08–0.72; low to moderate risk: odds ratio: 0.38; 95% CI: 0.18–0.81; moderate to high risk: odds ratio: 0.20; 95% CI: 0.10–0.39; high risk: odds ratio: 0.14; 95% CI: 0.05–0.37; I²: 0%; three trials). The authors concluded that, “In summary, infiltration and sealing were more efficacious than non-invasive treatments for arresting the progression of proximal carious lesions. In both the primary and permanent dentition, infiltration and sealing were effective. For the intervention effects of infiltration or sealing on different caries risk levels, a larger number of trials and more detailed trials are needed”^{143 (p15)}
Significance/direction	Results listed by outcome
Heterogeneity	There was no statistical heterogeneity, and clinical heterogeneity for intervention, comparator, or follow-up time did not influence the results.
Comments	GRADE was used by the review authors. The HRB judged this evidence as moderate quality for the main outcomes, which corresponds with the authors’ rating and low for subgroup outcomes. The HRB’s rating is assigned due to the high or unclear risk of bias in most included studies. The quality of the systematic review was judged as low using AMSTAR 2 due to the inability to control for risk of bias. The subgroup evidence had small sample sizes.

Elrashid *et al.*(2019)

Parameter	Extraction
First author and year of publication	Elrashid <i>et al.</i> (2019) ¹⁴⁴
Objectives	Evaluated the efficacy (clinical performance) of resin infiltration (compared with placebo or control material) on non-cavitated proximal carious lesions in primary and permanent teeth in humans.
Participants	Mixed dentition, non-cavitated caries, minimally invasive or microinvasive treatment Non-cavitated proximal carious lesions in primary and permanent teeth in humans The authors included seven randomised controlled trials with 263 participants (with more than 735 lesions; two studies did not report the number of lesions) published between 2010 and 2017. The age range for children was 5–9 years and for adults was 16–41 years. Gender was not reported. The longest follow-up was between 12 and 36 months.
Setting/context	Clinical settings or study countries were not reported.
Description of interventions/phenomena of interest	Intervention: Resin infiltration is a minimally invasive technique for treating non-cavitated proximal caries. It slows/stops the carious lesion progression rate by creating a diffusion barrier inside the porous enamel lesion body. Comparator: Control material or placebo Examples of control materials include: Fluoridated toothpaste and dental floss (one primary study), fluoride varnish (one primary study), or no treatment (three primary studies)
Databases and sources searched	Seven electronic sources (EBSCOhost, PubMed, Wiley Online Library, the Cochrane Library, Google Scholar, OpenGrey, and OpenThesis) were searched. The search used appropriate MeSH terms and the most reported keywords, as well as an adapted search syntax of each electronic source. The authors prepared a protocol but did not publish it. Studies were limited to English only. The reference lists of included studies were screened to identify additional studies. It is not clear if screening or extraction were completed in duplicate. The authors received no funding for the review and declared that they had no conflicts of interest.

Parameter	Extraction
Date range (years) of included studies	The authors included seven randomised controlled trials published between 2010 and 2017.
Number of primary studies included in the systematic review	The authors included seven randomised controlled trials with 263 participants (with more than 735 lesions; two studies did not report the number of lesions) published between 2010 and 2017. The funding sources for primary studies were not reported.
Types of studies included	Randomised controlled trials with a minimum of a 12-month follow-up were eligible for inclusion. The reasons for exclusion of full-text studies were provided, but not the study references.
Country of origin of included studies	Study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	Two trials were judged to have a high risk of bias, two to have an unclear risk of bias, and three to have a low risk of bias. All seven trials had adequate randomisation and adequate blinding of outcome ascertainment. The authors reported that "In contrast, two trials were at high risk of bias since they failed to mention all their prespecified outcomes...Consequently, those two were excluded from the meta-analysis." ¹⁴⁴ (p214) The authors did not measure publication bias.
Method of analysis	Heterogeneity assessment was performed by analysing clinical, statistical, and methodological heterogeneity. Methodological heterogeneity was examined by assessing the difference in bias risk between the included studies in each meta-analysis. The statistics were performed by RevMan software.
Outcome assessed	Non-cavitated proximal carious lesion progression rate (arrest and remineralisation), assessed by bitewing radiographs with at least 12 months follow-up (predetermined) The longest follow-up was between 12 and 36 months. Primary dentition at 12–24-month follow-up: Ammari 2017; Foster Page 2017. Permanent dentition at 18–36-month follow-up: Arthur 2017; Meyer-Lueckel 2012; Meyer-Lueckel 2016.
Results/findings	Two meta-analyses were conducted to eliminate the limitation of the significant heterogeneity between trials: one for primary teeth (two trials) and the other for permanent teeth (three trials). There was no statistical heterogeneity in the meta-analyses. The risk of carious lesion progression with resin infiltration was significantly lower in primary teeth (risk ratio: 0.48; 95% CI: 0.30–0.75, $p=0.001$; I^2 : 0%; 219 participants; 2 trials; high-quality evidence downgraded by HRB to moderate) and in permanent teeth (risk ratio: 0.19; 95% CI: 0.11–0.33, $p<0.00001$; I^2 : 0%; 478 participants; 3 trials; high-quality evidence downgraded by HRB to moderate) compared with that of control or placebo. The authors concluded that "The available evidence conveys high confidence that proximal resin infiltration has superior efficacy in slowing/arresting the carious lesions' progression rate in comparison to conventional management modalities." ¹⁴⁴ (p218)
Significance/direction	Favours resin infiltration over other methods or no method.
Heterogeneity	There was no statistical heterogeneity but there was clinical heterogeneity (see comparator).
Comments	GRADE was used by the review authors. The HRB judged this evidence as moderate (downgraded from the authors high rating) due to the inclusion of unclear risk of bias studies in the meta-analysis. The quality of the systematic review was judged as low using AMSTAR 2 as the authors did not discuss the influence of the risk of bias on the analysis.

Faghihian *et al.* (2019)

Parameter	Extraction
First author and year of publication	Faghihian <i>et al.</i> (2019) ¹⁴⁵

Parameter	Extraction
Objectives	Evaluated the efficacy (clinical performance) of the resin infiltration technique in arresting initial caries progression in both primary and permanent teeth compared with control groups such as placebo, fluoride therapy, and oral health instruction.
Participants	Mixed dentition, non-cavitated caries, minimally invasive or microinvasive treatment Initial caries in primary and permanent teeth The eight included randomised controlled trials, published between 2010 and 2017, included 408 participants (238 children with 476 lesions and 170 adults with 684 lesions, or a total of 1,160 lesions). Seven studies evaluated lesions on proximal surfaces and one on occlusal surfaces. The children's ages ranged from 5 to 9 years and the adults' ages ranged from 13 to 41 years. Gender was not reported.
Setting/context	The study countries and clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: Resin infiltration is a microinvasive technique for treating early caries. It slows/stops the carious lesion progression rate by creating a diffusion barrier inside the porous enamel lesion body. Comparator: Placebo, fluoride therapy, and oral health instruction
Databases and sources searched	Four databases were searched up to January 2018: Embase, Scopus, the Cochrane Library, and PubMed. Keywords were provided. The search was restricted to English-language publications. A manual search of relevant published reviews was conducted in order to obtain additional articles. The authors registered a protocol with PROSPERO. Duplicate screening was completed, but not duplicate extraction. The source of funding for the review and conflicts of interest were not reported.
Date range (years) of included studies	The eight included randomised controlled trials were published between 2010 and 2017.
Number of primary studies included in the systematic review	The eight randomised controlled trials, published between 2010 and 2017, included 408 participants (238 children with 476 lesions and 170 adults with 684 lesions, or a total of 1,160 lesions). Seven studies evaluated lesions on proximal surfaces and one on occlusal surfaces. The longest follow-up was between 1 and 2 years. The sources of funding for the primary studies were not reported.
Types of studies included	Randomised controlled trials and clinical controlled trials were eligible for inclusion. The three studies excluded during full-text screening and their reasons for exclusion were reported.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	Five of the eight included studies were judged to have a high risk of bias and three studies had an unclear risk of bias. All eight studies were judged to have adequate randomisation and adequate blinding of outcome assessment. The authors described the risk of bias results in the discussion but did not interpret them. A funnel plot and Egger test were used to analyse publication bias. The visual inspection of the funnel plot did not show a clear asymmetry, which might be indicative of a lack of publication bias; however, considering the scarcity of the studies included in the meta-analysis as well as the power of statistical tests. The authors noted that "In general, it seems that the articles had a good quality for entering in the systematic review". ^{145 (p91)}
Method of analysis	Data were analysed using Comprehensive Meta-Analysis software, version 2 software calculating I ² ; the Tau ² and Q indices were used to analyse heterogeneity. A forest plot was applied to show the results of the study. A funnel plot and Egger test were used to analyse publication bias.
Outcome assessed	Effectiveness in arresting initial caries progression Primary dentition: Ekstrand 2010 and 2015; Ammari 2017; Rodrigo 2017 (not in meta-analysis); Bakhshandeh and Foster Page 2017. Permanent dentition: Arthur 2017 (not in risk of bias); Meyer-Lueckel 2012; Meyer-Lueckel 2016; Martignon 2012. The longest follow-up was between 1 and 3 years (not predetermined).

Parameter	Extraction
Results/findings	Eight articles were selected for the quantitative analysis of data and preparation of evidence table. Results of the fixed-effects meta-analysis of all studies estimated a risk ratio of 0.37 (95% CI: 0.29–0.48; I²: 25%; 943 teeth; eight trials) over a 1–3-year period, which revealed that resin infiltration significantly reduced the risk of caries progression compared with the control groups. Two subgroup analyses were completed: length of follow-up and type of dentition. Follow-up after less than 2 years: Risk ratio of 0.30 (95% CI: 0.21–0.43; I²: 27%; 4 trials) over a 12–23-month period Follow-up after 2–3 years: Risk ratio of 0.46 (95% CI: 0.33–0.66; I²: 0%; 4 trials) over a 2–3-year period Primary teeth: Risk ratio of 0.43 (95% CI: 0.31–0.63; I²: 0%; 4 trials) over a 1–3-year period Permanent teeth: Risk ratio of 0.31 (95% CI: 0.21–0.45; I²: 55%; 4 trials) over a 1–3-year period The authors concluded that “Resin infiltration has a significant advantage over non-invasive preventive measures in arresting initial carious lesions in primary and permanent teeth. This technique should be regarded as a viable option for treating initial carious lesions.”^{145 (p93)}
Significance/direction	Results listed by outcome
Heterogeneity	The authors reported that “The results of heterogeneity tests Q (P=0.227), I ² (25%), and Tau2 (P=0.047) indicated acceptable homogeneity of data.” ^{145 (p91)}
Comments	GRADE was not used by the review authors. All trials were judged to have a high or unclear risk of bias for one or more parameters. The quality of the systematic review was judged as critically low using AMSTAR 2, as the authors did not control for high or unclear risk of bias or discuss the implications of the risk of bias. The HRB graded the evidence in this review as moderate.

Chatzimarkou *et al.* (2018)

Parameter	Extraction
First author and year of publication	Chatzimarkou <i>et al.</i> (2018) ¹⁴⁶
Objectives	The objective of this review was to provide a comprehensive synthesis of resin infiltration effects, in vivo, on early proximal carious lesions in primary and permanent teeth.
Participants	Mixed dentition, non-cavitated caries, microinvasive treatment Patients (children and/or adults) with primary or mixed/permanent dentition with proximal carious lesions, extending at enamel to the outer third of dentine. According to the authors, “Four studies were conducted in primary teeth in children, with mean age ranging from 5.8 to 11 years old. The lesions sample size tested by the included studies was between 32 and 84. The rest of the studies were designed to assess lesions in permanent teeth. The mean age of the participants in these studies ranged from 21.1 to 25 years, while the sample size examined was between 44 and 186 lesions.”^{146 (p10)}
Setting/context	The included studies were conducted in Brazil (three studies), Colombia (one study), Denmark (one study), Germany (three studies), India (one study), and the USA (one study). The clinical settings for the studies were not reported.
Description of interventions/phenomena of interest	Intervention: Resin infiltration (with or without non-invasive methods such as dental floss or fluoride). Comparator: Other microinvasive treatment techniques or non-invasive methods (control) such as dental floss or fluoride. The authors defined the intervention as follows: “caries infiltration was introduced as a proximal microinvasive treatment approach, aiming at infiltrating the porous body of the lesion as well as establishing a diffusion barrier within the tooth. Diffusion pathways for cariogenic acids and dissolved minerals are occluded, thus halting the demineralization process before it has reached cavitation. The concept of caries infiltration was first developed at the Charité Berlin as a microinvasive approach for the management of smooth surface and proximal non-non-cavitated carious lesions... Caries infiltration utilizes capillary

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	forces to carry methacrylic resins with high penetration coefficients (infiltrants) into the porous enamel. Enamel is etched using HCL [hydrochloric acid] 15% rather than phosphoric acid to remove the pseudo-intact surface layer. Resin infiltration is a promising technique that could reduce the loss of dental hard tissue and avert costly treatments. Furthermore, resin infiltration depends less on patients' compliance, thus providing increased efficacy. However, there is still uncertainty about the technique's success as compared to standard invasive and non-invasive preventive treatments."¹⁴⁶ (p9) Chatzimarkou <i>et al.</i> explained that "All trials [included in this review] used resin infiltration as the intervention of primary interest which was applied to lesions extending up to one-third of the outer dentin layer and was typically administered in conjunction with other non-invasive instructions for oral hygiene, flossing and application of fluoride and/or fluoride supplements."¹⁴⁶ (p10) The authors described the comparator as follows: "Comparison interventions [in the studies included in this review] mainly comprised non-invasive, placebo control interventions, including flossing, instructions for diet and fluoridation. In one study sealing application methods were used as a comparator."¹⁴⁶ (p10)
Databases and sources searched	The authors searched three databases: MEDLINE via PubMed, the Cochrane Central Register of Controlled Trials (CENTRAL), and LILACS via BIREME Virtual Health Library (VHL). Electronic searches were undertaken on 30 September 2017 and updated on 22 April 2018. No language restrictions were applied to the searches. Unpublished literature was searched in OpenGrey, ClinicalTrials.gov, and the ISRCTN registry Hand-searching of the reference lists of the retrieved full-text articles was also conducted, and the authors of original studies were contacted for data clarification if needed. The authors reported that they did not register a protocol. Extraction and screening were completed in duplicate. Funding: The authors reported that they did not receive funding for this review. The authors stated that "None of the reviewers/authors of the present study has any potential interest to declare with regard to resin infiltration interventions used by any of the eligible articles for inclusion."¹⁴⁶ (p15)
Date range (years) of included studies	The included studies were published from 2010 to 2018.
Number of primary studies included in the systematic review	Nine randomised controlled trials with a split-mouth design (consisting of 10 articles, as one was a follow-up report), published from 2010 to 2018, were considered eligible for inclusion in the review. The review authors noted that "The present review was also prone to industry-related bias as in two of the included trials (3 articles), authors appeared to be actively involved (founders) with one of the products used for resin infiltration; however, it was not possible to estimate whether sponsorship and professional interest on their part was related to the trials' findings and presentation of their published results."¹⁴⁶ (p15)
Types of studies included	Randomised controlled trials or controlled clinical trials were considered. Both parallel and split-mouth designs were eligible for inclusion. A list of excluded full-text studies was not provided but reasons for exclusion were provided. Caries progression: Meyer-Lueckel 2016; Martignon 2012; Paris 2010; Meyer-Lueckel 2012; Sarti 2015; Pereira 2015; Ekstrand 2010; Rai 2016; Ammari 2018; Peters 2017 NCT01496456.
Country of origin of included studies	The study countries were Brazil (three studies), Colombia (one study), Denmark (one study), Germany (three studies), India (one study), and the USA (one study).
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	According to Chatzimarkou <i>et al.</i>, "Overall, risk of bias was rated as unclear in six studies (7 articles), and high in three. Generation of random sequence for treatment allocation was adequately reported in all trials, while for allocation concealment this was the case for half of the studies. Although blinding of participants was adequately described in all but one study, blinding of personnel involved in the trial was not clear and this might potentially bear an impact on the effectiveness of treatment provided (i.e. instructions for oral hygiene measures). Again, only one study failed to report masking of the outcome assessor. For the

Parameter	Extraction
	majority of the studies, attrition bias was not suspected; however, 2 trials reported a significant amount of dropouts during the course of the treatment. Risk of bias due to selective reporting was low in 5 studies. Interestingly, two studies failed to present the results of all pre-specified time points, while in one study, it was not clear whether digital subtraction radiography was performed, although [it was] pre-specified. One study was rated high risk of bias for additional parameters, as although the study followed a randomization scheme, it presented unbalanced allocation of lesions according to ICDAS [International Caries Detection and Assessment System] scoring system. Lastly, two studies were suspected for industry-related bias as the founders of the assigned intervention (i.e. product used) were involved in authorship, while in one study industry funding appeared to play a role on the presentation of the results of the study and/or publication. As such, these studies were rated unclear with regard to other bias domain."¹⁴⁶ (p10) All nine included studies were at low risk of bias for randomisation, and eight of the nine included studies were at low risk of bias for outcome assessment. "Furthermore for the primary teeth, no robust conclusions could be drawn for the effect of resin infiltration, mainly due to the scarcity of the available studies, the inherent risk of bias and the apparent heterogeneity in trial settings and means/ time points of outcome evaluation."¹⁴⁶ (p13) The authors noted that "Publication bias could not be explored either graphically or statistically as no more than 4 studies were combined within the syntheses overall."¹⁴⁶ (p11)
Method of analysis	Chatzimarkou <i>et al.</i> stated that "Only studies at unclear or low risk of bias overall were included in meta-analyses. Random-effects meta-analyses were conducted as they were considered more appropriate to better approximate expected variations in trial settings. Treatment effects were calculated through odds ratios (ORs) for lesion progression along with associated 95% confidence intervals (95% CIs)...Sensitivity analyses were predetermined to explore and isolate the effect of studies with unclear risk of bias on the overall treatment effect if both low and unclear risk of bias studies were included."¹⁴⁶ (p10) The authors also said that "As only trials with unclear risk of bias were included in the syntheses, no additional sensitivity analyses were undertaken, although [it was] prespecified."¹⁴⁶ (p11)
Outcome assessed	The outcomes assessed were survival rate (number of restorative failures based on clinical criteria such as FDI and USPHS) and proximal carious lesion progression after application of treatment (assessed with any type of radiographic or clinical measure). The evaluation period for outcome assessment ranged from 3 months to 3 years. Caries progression: Meyer-Lueckel 2016; Martignon 2012; Paris 2010; Meyer-Lueckel 2012; Sarti 2015; Pereira 2015; Ekstrand 2010; Rai 2016; Ammari 2018; Peters 2017 NCT01496456.
Results/findings	According to the authors, "The outcome of interest (i.e. lesion progression) was assessed in two time-spans: one included 18 months to 2 years assessment, and the other 3 years assessment. Both syntheses consisted of comparisons between resin infiltration plus oral hygiene measures (i.e. flossing, fluoridation, etc.), and merely non-invasive oral hygiene measures reported as control. Based on availability of information from the original studies, lesion progression assessed through pairwise conventional radiography is presented as the pooled overall outcome and only studies pertaining to permanent teeth were eligible for data synthesis in the present review. With regard to the 18-month to 2-year follow-up period, there was strong evidence that treatment with resin infiltration combined with non-invasive oral hygiene measures resulted in significantly lower odds for lesion progression as compared to pure non-invasive methods (control). In fact, resin infiltration had 86% lower odds for progression of lesions (3 studies: OR=0.14; 95% CI: 0.08, 0.25; $p<0.001$. No significant statistical heterogeneity was detected for this synthesis ($I^2=0.0\%$; $p=0.77$). Considering 3 years follow-up, again there was strong evidence to support that lesion progression was less likely to occur after treatment with resin infiltration (4 studies: OR=0.15; 95% CI: 0.06, 0.36; $p<0.001$). There was no evidence of statistically significant heterogeneity for this comparison as well ($I^2=16.6\%$; $p=0.31$)."¹⁴⁶ (p10–11)

Parameter	Extraction
Significance/direction	The authors found that “The use of resin infiltration for sealing of early interproximal lesions when combined with oral hygiene measures was promising and more effective than oral hygiene measures alone for follow-up periods of up to 3 years in permanent teeth (low- to moderate-quality evidence). However, no solid conclusions can be drawn with regard to primary teeth.” ¹⁴⁶ (p15)
Heterogeneity	Regarding heterogeneity, the authors stated that “Clinical heterogeneity of included studies was assessed through the examination of individual trial settings, eligibility criteria, treatment methods used and data collection methods. Statistical heterogeneity was examined through visual inspection of the confidence intervals (CIs) for the estimated treatment effects on forest plots. Also, a chi-square test was applied to assess heterogeneity; a <i>p</i> -value below the level of 10% (<i>p</i> <0.1) was considered indicative of significant heterogeneity. The <i>I</i> ² test for homogeneity was also undertaken to quantify the extent of heterogeneity.” ¹⁴⁶ (p9) The authors also stated that “The four studies performed in primary teeth were heterogeneous with regard to study settings or evaluation periods or suffered from inherent high risk of bias and could not be mathematically combined.” ¹⁴⁶ (p11)
Comments	GRADE was used by the review authors. In terms of evidence quality, Chatzimarkou <i>et al.</i> stated that “The assessment of the quality of evidence on proximal lesion progression in permanent teeth (lesions extending up to the outer one-third of dentin) revealed that the level of the existing evidence was moderate for the short-term evaluation period (i.e. 18 months to 2 years). The findings suggest that further research is likely to have an important impact on our confidence in the effect estimate and may change the estimate. The level of existing evidence was low for the long-term follow-up period (i.e. 3 years), showing that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.” ¹⁴⁶ (p11) However, the authors noted that “the level of evidence for the outcome lesion progression for proximal lesions in permanent teeth was downgraded for both periods of evaluation (i.e. 18 months to 2 years and 3 years). For the time period involving 18 months to 2 years follow-up, the level of evidence was downgraded one level due to imprecision, as all available studies involved correlated data not accounted for (i.e. multiple teeth nested within the same quadrant). For 3 years follow-up, the level of evidence was downgraded twice, as apart from the likelihood for imprecision on the estimated outcome, risk of bias was also suspected. Specifically, the high level of dropouts contributed to the rating of unclear risk for attrition bias.” ¹⁴⁶ (p14–15) According to the authors, “To our knowledge, this is the first systematic review that includes a thorough and quantitative synthesis on the effectiveness of resin infiltration for proximal caries management.” ¹⁴⁶ (p15)

Krois *et al.* (2018)

Parameter	Extraction
First author and year of publication	Krois <i>et al.</i> (2018) ¹⁴⁷
Objectives	Evaluated microinvasive treatments compared with each other, non-invasive treatments, placebo or no treatment to arrest early non-cavitated proximal carious lesions in primary and permanent teeth of children, adolescents, and young adults.
Participants	Mixed dentition, non-cavitated caries, microinvasive treatments Age: Children, adolescents, and young adults (mean age: 15 years) Population: Primary and permanent teeth of children, adolescents, and young adults Fifteen reports of 13 randomised controlled trials published between 2010 and 2017, with 486 participants, were included in this review. Four trials assessed lesions in primary teeth and nine trials assessed lesions in permanent teeth. Participants comprised children, adolescents, and young adults with a mean age of 15 years. Gender was not reported.
Setting/context	The study countries were Brazil, Chile, Colombia, Denmark, Germany, Greenland, New Zealand, and Thailand. Eight studies were completed in dental schools while

Parameter	Extraction
	the remaining five were conducted in different locations (a public health clinic, a community setting, a private practice, a public school, and a navy clinic).
Description of interventions/phenomena of interest	According to Krois <i>et al.</i> , “microinvasive strategies (sealing and infiltration) remove a few micrometers of tissue during application, usually when conditioning the tooth surface with acids, and install a diffusion barrier onto (lesion sealing) or within (lesion infiltration) the carious tissue. The barrier (of resins or glass ionomer cements) impedes acid diffusion into the hard tissue and further mineral loss from it, thereby arresting the lesion...Non-invasive strategies remove no carious tissue at all and include dietary control, biofilm control, or control of de- and remineralisation (via fluorides etc.) often combined with each other.” ¹⁴⁷ (p15) Comparator: Each other, non-invasive treatment, no intervention, or placebo
Databases and sources searched	Three electronic databases (MEDLINE, Embase, and the Cochrane library) were searched, and these searches were complemented by examining the references of retrieved full-text studies. No search date or language limits are reported. The search terms are provided, but not the search strategy. It is not clear if two independent reviewers screened the abstracts but two reviewers did screen full texts, and extraction was completed by two independent reviewers. This review had a registered protocol. This study was funded by the authors and their institution. One author has been giving lectures for the manufacturer of the infiltration kit, Chemisch-Pharmazeutische Fabrik, in Hamburg. The Charité–Universitätsmedizin holds patents on the infiltration technology, and was hence involved in two trials on caries infiltration. Nearly all trials on infiltration were sponsored by the manufacturers of the treatments, and two trials were conducted by the inventors of the treatments. The authors of this review, however, do not have any direct association with these patents or trials.
Date range (years) of included studies	Fifteen reports of 13 randomised controlled trials published between 2010 and 2017, with 486 participants, were included in this review.
Number of primary studies included in the systematic review	Fifteen reports of 13 randomised controlled trials published between 2010 and 2017, with 486 participants, were included in this review. Four trials assessed lesions in primary teeth and nine trials assessed lesions in permanent teeth. The funding for seven primary studies was provided by industry, and four primary studies were funded through public funding. The funding sources for the remaining two studies were not available to the review authors.
Types of studies included	Randomised controlled trials were specified in the inclusion criteria. The reasons for and list of full-text exclusions were provided.
Country of origin of included studies	The study countries were Brazil, Chile, Colombia, Denmark, Germany, Greenland, New Zealand, and Thailand.
Appraisal instruments used	The Cochrane Collaboration’s risk of bias instrument was used to assess bias in the included trials.
Appraisal rating	Nine trials were judged to be at high risk of bias and four to be at unclear risk of bias. All trials showed a low risk of bias with regard to blinding of the assessment, but there were limited indications of selective reporting or issues of random sequence generation. In contrast, blinding of operators or participants was always rated as having an unclear or high risk of bias, and allocation concealment was rated as having an unclear risk of bias in seven of the 13 trials. Twelve of the 13 trials of interest were judged to have adequate random sequence generation and eight were judged to have adequate blinding of outcome assessors. An asymmetric funnel plot indicates possible publication bias.
Method of analysis	Pairwise random-effects meta-analyses, used for direct treatment comparisons, were implemented using the metafor package in R. As described, all included studies used a split-mouth design, but reported data only in marginal form. To compute odds ratios, the authors applied the Becker-Balagtas method, setting the inter-class correlation at 0.2. Indirect and mixed comparisons were performed using Bayesian random-effects modelling and Markov chain Monte Carlo simulations using JAGS implemented in the R package gemtc 0.8-2. Networks of interventions were constructed by plotting different treatments (as nodes) and comparisons (as edges). Binomial likelihood was used to model the data. To fit the model, the authors used non-informative priors for the basic parameters from a

Parameter	Extraction
	normal distribution for the random-effects standard deviation. The first 20,000 iterations were discarded as 'burn-in' and then a further 80,000 iterations were undertaken for 4 chains with a thinning of 1. The convergence was assessed based on the Brooks-Gelman-Rubin criteria and inspection of trace plots. Median odds ratios and their 95% credible intervals were reported. Different strategies were ranked according to their probability of having the lowest compared with the highest odds of arresting lesions, and the average rank calculated. The surface under the cumulative ranking line was plotted and the area under the plot (curve) calculated. In pairwise meta-analyses, the authors estimated different heterogeneity variances for each pairwise comparison. In the network meta-analysis, the authors assumed a common estimate for the heterogeneity variance across the different comparisons. Trial sequential analysis was also completed.
Outcome assessed	Outcome: Arrest early non-cavitated proximal carious lesions in primary and permanent teeth (arrest caries progression) Time frame: Mean: 25 months (range: 12–43 months) (not predefined) Outcome by primary study: Arrest caries progression: Sealing: Alkilzy 2011; Basili 2017; Gomez 2014; Gomez 2005; Martignon 2006; Martignon 2010; Martignon 2012; Trairatvorakul 2011. Arrest caries progression by infiltration: Ammari 2017; Arthur 2017; Ekstrand 2010; Foster 2017; Martignon 2012; Meyer-Lueckel 2012; Paris 2010; Meyer-Lueckel 2016.
Results/findings	The approach to meta-analysis and synthesis is very well explained and justified. Firm evidence on the superior efficacy of sealing combined with infiltration over non-invasive treatment was reached. Firm evidence was also reached on the superior efficacy of sealing and infiltration as separate interventions over non-invasive treatment. One study compared infiltration to sealing and found no significant difference. Based on Bayesian network meta-analyses, infiltration was ranked first in 80% of the simulations (sealing: 20%; non-invasive treatment: 0%). There is moderate- to high-quality evidence that sealing (odds ratio: 0.29; 95% CI: 0.18–0.46; seven trials; moderate-quality evidence) or infiltration (odds ratio: 0.22; 95% CI: 0.15–0.33; seven trials; high-quality evidence downgraded by HRB to moderate) are likely to be more efficacious for arresting early (non-cavitated) proximal lesions after a mean of 25 months than non-invasive treatment. The authors reported that their findings showed low heterogeneity and high consistency. The included studies were judged to be at unclear or high risk of bias and the authors stated that this was "due to unclear allocation concealment (lack of concealment has been found to significantly affect the findings of randomized trials) and lack of participant and operator blinding."¹⁴⁷ (p18) Based on the findings of this review, there is adequate evidence that sealing/infiltration is superior to non-invasive treatment. In addition, there is adequate evidence to suggest that either sealing or infiltration, used separately, is superior to non-invasive treatment. The evidence is inconclusive regarding the superiority of sealing compared with infiltration. According to Krois <i>et al.</i>, "sealing or infiltration instead of non-invasive (NI) treatment would avoid 278 per 1,000 treated lesions to progress (44% NI and 16% sealed or infiltrated lesions would progress). The certainty of the evidence was graded as moderate. Sealing instead of NI would avoid 282 per 1,000 treated lesions to progress. The certainty of the evidence was graded as moderate. Infiltration instead of NI would avoid 266 per 1,000 treated lesions to progress (as the control group event proportion was lower). The certainty of the evidence was graded as high...Based on this review and analysis, microinvasive treatment should be chosen over NI treatment (strong recommendation)...we are hence confident in this conclusion".¹⁴⁷ (p18)
Significance/direction	Favours sealing or infiltration over non-invasive treatments.
Heterogeneity	The authors reported that their findings showed low heterogeneity and high consistency.
Comments	GRADE was used by the review authors.

Parameter	Extraction
	Nine trials were judged to be at high risk of bias and four at unclear risk of bias. There were issues with respect to blinding of outcome assessor. The quality of the systematic review was judged as low, as the authors did not complete a sensitivity analysis to control for the effect of the risk of bias. The HRB graded the evidence in this review as moderate downgrading it from the review authors' rating of high or moderate to high.

Liang *et al.* (2018)

Parameter	Extraction
First author and year of publication	Liang <i>et al.</i> (2018) ¹⁴⁸
Objectives	Compared the effectiveness of microinvasive interventions with non-invasive measures (e.g. fluoride), a placebo, or no treatment in arresting non-cavitated proximal carious lesions and analysed their effectiveness in acting on carious lesions of different depths.
Participants	Mixed dentition, non-cavitated caries, microinvasive treatments Population: Non-cavitated proximal carious lesions The type of teeth (permanent or primary) is not stated, but the HRB assumed mixed dentition based on the ages of the trial participants. The trials involved 303 participants with an age range of 6.5–39 years. Gender was not reported.
Setting/context	The study countries of the trials are not reported in the review. The trial settings were not reported.
Description of interventions/phenomena of interest	The study authors stated that microinvasive interventions primarily belong in two categories: sealants and resin infiltration. The authors go on to state that “the reported sealing materials were classified into three types: resin sealant (which included adhesives and pit-and-fissure sealant), glass ionomer cement, and polyurethane tape...Resin infiltration, a low-viscosity resin, can fill the pores of demineralized enamel and create a barrier by capillary action after enamel pretreatment to block further bacterial diffusion and lesion development.” ¹⁴⁸ (p2676) Comparator: Non-invasive measures, placebo, or no treatment
Databases and sources searched	The authors searched the Cochrane Library, PubMed, Embase, and Web of Science on 25 May 2017 without date or language restrictions. The search strategy for each database is provided in an appendix. Two authors screened the literature and completed data extraction. This authors of the review do not mention completion of a protocol. This review was supported by the Science and Technology Program of Shenzhen, China and the Science and Technology Program of Guangzhou, China. All authors declare that they have no conflicts of interest.
Date range (years) of included studies	Eight articles covering seven trials (six randomised and one non-randomised) published between 2005 and 2016, with follow-up periods ranging from 12 to 36 months, were included in the review.
Number of primary studies included in the systematic review	Eight articles covering seven trials (six randomised and one non-randomised) published between 2005 and 2016, with follow-up periods ranging from 12 to 36 months, were included in the review. The funding of primary studies is not reported in the article.
Types of studies included	Randomised controlled trials were the study design specified in the inclusion criteria. The authors provided the reasons for study exclusions, but not a listing of excluded studies.
Country of origin of included studies	The study countries of the trials are not reported in the review.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess the risk of bias in the included trials.
Appraisal rating	Of the seven trials assessed using the Cochrane Collaboration's risk of bias instrument, two trials were judged to have a low risk of bias, four to have a high risk of bias, and one to have an unclear risk of bias. All seven trials were judged to have adequate random sequence generation and blinding of outcome assessors. The authors reported that the included studies had no obvious publication bias.

Parameter	Extraction
Method of analysis	The meta-analysis was conducted using Stata 12.0. The caries progression numbers were binary data, so the authors used the odds ratio with 95% CIs as the effect variable. A meta-regression analysis was performed with the intention of identifying possible sources of variability, including follow-up times and methods of microinvasive interventions, between studies. The quantity of heterogeneity between the studies was measured using the I ² Inconsistency Index with a <i>p</i> -value. If the I ² value was greater than 50%, a random-effects model was adopted; otherwise, a fixed-effects model was used. Different methods of microinvasive intervention and caries depths may be the potential factors that affected the outcome data, so the authors completed a subgroup analysis of the two factors.
Outcome assessed	Outcome: Arresting non-cavitated proximal carious lesions, and the effectiveness of different interventions in acting on carious lesions of different depths at between 12 and 36 months (not predetermined) Outcome by primary study: Arresting non-cavitated proximal carious lesions (resin sealants and infiltration): Ekstrand 2010; Gomez 2005; Martignon 2006; Martignon 2012; Meyer-Lueckel 2016; Paris 2010; Meyer-Lueckel 2012; Trairatvorakul 2011. Arresting non-cavitated proximal carious lesions (glass ionomer cement): Martignon 2012; Meyer-Lueckel 2016; Meyer-Lueckel 2012.
Results/findings	The main finding from this review suggests that there is adequate evidence that resin infiltration and resin sealants are effective microinvasive interventions in arresting the progression of non-cavitated proximal caries. The fixed-effects meta-analysis showed that microinvasive interventions significantly reduced the possibility of caries progression compared with the control (odds ratio: 0.20; 95% CI: 0.14–0.29; I ² : 0%). The authors performed a subgroup analysis to assess the three different microinvasive interventions. Both resin infiltration (odds ratio: 0.15; 95% CI: 0.09–0.24) and resin sealant (odds ratio: 0.33; 95% CI: 0.19–0.58) were statistically significantly effective at reducing the possibility of caries progression, whereas there were no significant differences between the glass ionomer cement and control group's effects on caries progression (odds ratio: 0.13; 95% CI: 0.01–2.65). Three trials related to resin infiltration reported caries progression numbers for different depths of non-cavitated proximal caries at follow-ups of 18–36 months. For enamel caries or caries around the enamel-dentine junction, there was a significant difference in the caries progression rate between the resin infiltration group and the control group (enamel: odds ratio: 0.05; 95% CI: 0.01–0.35; I ² : 38.4%; enamel-dentine junction: odds ratio: 0.07; 95% CI: 0.01–0.70; I ² : 38.4%). There was no difference in caries progression of proximal caries that involved the dentine between the resin infiltration and control group (odds ratio: 0.42; 95% CI: 0.16–1.10; I ² : 38.4%). Two trials related to resin sealant reported caries progression numbers for different depths of non-cavitated proximal caries at follow-up periods of 24–36 months. In the subgroup analysis, no significant differences were found between the resin sealant group and control group regardless of the depths of caries (enamel: odds ratio: 0.62; 95% CI: 0.13–3.00; enamel-dentine junction: odds ratio: 0.44; 95% CI: 0.09–2.15; dentine: odds ratio: 0.43; 95% CI: 0.07–2.63). There is inadequate evidence upon which to judge the effectiveness of glass ionomer cements, as, according to Liang <i>et al.</i> , "it remains unclear whether GIC [glass ionomer cement] is effective...more clinical studies are needed to further explore this issue." ¹⁴⁸ (p2681) Further analysis of the interventions for carious lesions of different depths indicated that there is adequate evidence that resin infiltration could arrest progression of enamel caries and caries around the enamel-dentine junction. However, when the outer third of the dentine was involved, resin infiltration did not yield significantly different results compared with the control group. In contrast, according to Liang <i>et al.</i> , "The subgroup analysis showed that resin sealant was ineffective for reducing the caries progression rate at different depths, even for enamel caries, which was contradictory to the overall effect. This contradiction may be associated with limited original studies that focused on different depths of non-cavitated proximal caries". ¹⁴⁸ (p2682) For dentine caries as distinct from enamel caries, the therapeutic effectiveness of resin infiltration was not significantly different from the control group. According to Liang <i>et al.</i> , "based

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	on existing evidence, dentists should carefully select appropriate microinvasive interventions according to the different depths of non-cavitated proximal caries.” 148 (p2675)
Significance/direction	Varied by outcome.
Heterogeneity	Low to moderate.
Comments	GRADE was not used by the review authors. The authors included both randomised and non-randomised trials in the review, but only randomised trials were included in the meta-analysis. Most trials were judged to be at high or unclear risk of bias. The quality of the systematic review was judged as moderate using AMSTAR 2. The confidence intervals were wide for the subgroup analysis. The HRB graded the evidence as moderate for the main outcome and low for the secondary outcomes.

Dorri *et al.* (2015)

Parameter	Extraction
First author and year of publication	Dorri <i>et al.</i> (2015) ¹⁴⁹ (Cochrane Review)
Objectives	Compared microinvasive treatments with non-invasive measures, invasive measures, no intervention, or a placebo for managing proximal carious lesions in primary and permanent dentition in children and adults.
Participants	Mixed dentition, non-cavitated carious lesions, microinvasive treatments Population: Proximal carious lesions in primary and permanent dentition in with 365 children or adults Age: 4–39 years Gender was not reported.
Setting/context	Five trials were carried out in university settings and two in secondary-level healthcare settings. The setting for one trial was not reported. The studies were completed in Brazil, Chile, Denmark, Germany, Greenland, and Thailand.
Description of interventions/phenomena of interest	According to Dorri <i>et al.</i> , “microinvasive treatments involve conditioning the tooth surface using organic acids prior to treating the caries lesion. The conditioning involves the loss of few micrometers of tooth enamel. There are two types of microinvasive treatments: sealing and resin infiltration.” ¹⁴⁹ (p6) Comparator: Non-invasive measures, invasive measures, no intervention, or placebo.
Databases and sources searched	The authors searched 11 sources to 31 December 2014: the Cochrane Oral Health Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE via Ovid, Embase via Ovid, LILACS via BIREME Virtual Health Library, Web of Science Conference Proceedings Citation Index, ProQuest Dissertations & Theses Global, ClinicalTrials.gov, OpenGrey, and the WHO’s International Clinical Trials Registry Platform. They searched the metaRegister of Controlled Trials to 1 October 2014. There were no language or date restrictions in the searches of the electronic databases. All search strategies are provided in appendices. The authors also did hand-searching of journals and reference chasing within included articles. The literature was screened and data were extracted by at least two independent reviewers. A protocol was prepared by the authors. The authors had no conflicts of interest. The review was funded by the School of Dentistry, the University of Manchester, UK and the National Institute for Health Research, UK.
Date range (years) of included studies	Eight randomised controlled trials published between 2005 and 2011, with 365 participants, were included in this review.
Number of primary studies included in the systematic review	Eight randomised controlled trials published between 2005 and 2011, with 365 participants, were included in this review. Four studies received industry support to carry out the research or had other conflicts of interests.

Parameter	Extraction
Types of studies included	The authors specified randomised controlled trials for inclusion with at least 6-month follow-up, as this is the shortest recommended length of intervals between radiographic exposures. Both parallel-group and split-mouth study designs were eligible for inclusion. The authors provide a list of excluded studies and their reasons for exclusion.
Country of origin of included studies	The studies were completed in Brazil, Chile, Denmark, Germany, Greenland, and Thailand.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess risk of bias.
Appraisal rating	Based on assessment using the Cochrane Collaboration's risk of bias instrument, the authors judged seven of the eight included trials to be at high risk of bias, primarily due to lack of blinding of participants and personnel. All eight trials were judged to have adequate randomisation and blinding of outcome assessment. Publication bias was assessed as part of the overall quality of the evidence, but there is no specific comment on this bias.
Method of analysis	The authors evaluated the efficacy of microinvasive treatments in different subgroups of interventions. Moreover, they synthesised studies according to the measure of radiographic progression used (i.e. digital subtraction radiography, pairwise reading, visual scoring). To calculate one effect estimate for all microinvasive interventions compared with control interventions regardless of the measure used, they combined different measures, preferring more sensitive rather than less sensitive methods for studies where more than one measure was available (digital subtraction radiography over pairwise reading over scoring). The authors calculated the number needed to treat for an additional beneficial outcome for the overall pooled estimates. For the split-mouth studies, the authors calculated odds ratios for differences of paired tooth surfaces being carious or not, along with the appropriate standard errors and 95% CIs. The authors chose the Becker-Balagtas method because in this review they also included studies that reported data only in marginal form (as parallel-group studies), and this method facilitated data synthesis. The authors used the intracluster correlation coefficient when analysing studies. In the studies with data presented as tooth pairs, they calculated the intracluster correlation coefficient from the data. They conducted the meta-analyses with RevMan 2011, using the generic inverse-variance method with either the fixed-effects or the random-effects model. In meta-analyses including two or three studies, they used the fixed-effects model, and in meta-analyses including four or more studies, they used the random-effects model. For the sensitivity analyses, they evaluated the effect on the results of split-mouth studies with high numbers of pairs compared to the number of subjects, as well as the risk of bias grading. They were unable to conduct a meta-analysis of the data from split-mouth studies with different numbers of lesions in each group. Other subgroup analyses and investigation of heterogeneity were done where feasible.
Outcome assessed	Outcome: Arrest of non-cavitated enamel and initial dentinal lesions at least 6 months following treatment Outcome by primary study: Arrest of non-cavitated enamel and initial dentinal lesions at least 6 months following treatment Gomez 2005; Martignon 2006; Ekstrand 2010; Martignon 2010; Paris 2010a; Alkilzy 2011; Trairatvorakul 2011; Martignon 2012. Progression of existing carious lesion into enamel or dentine over 6 months or more: Martignon 2006; Ekstrand 2010; Martignon 2010; Paris 2010a; Alkilzy 2011; Trairatvorakul 2011; Martignon 2012. Change in decayed, missing, and filled teeth at surface, tooth, and whole mouth level. Studies were to assess this over a minimum period of 6 months: No studies measured this outcome Material deficiency (e.g. retention loss, or number of retreatments): Alkilzy 2011. Participant and operator perception, as measured by standardised/validated questionnaires: No evidence Adverse events: Gomez 2005; Paris 2010a; Alkilzy 2011; Trairatvorakul 2011.

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	Costs: No evidence
Results/findings	The random-effects meta-analysis showed that microinvasive treatment significantly reduced the odds of lesion progression compared with non-invasive treatment or oral hygiene advice (odds ratio: 0.24; 95% CI: 0.14–0.41; I²: 32%; 602 lesions; 7 trials; moderate evidence). Measures were reported at time frames of between 12 and 36 months. The changes in lesions were measured by digital subtraction radiography, pairwise comparison of radiographs obtained at baseline and follow-up, and visual scoring using an international classification system. There was no evidence of differences in subgroup findings by methods used to classify the lesions. It remains unclear which microinvasive treatment is more advantageous, or if certain clinical conditions or patient characteristics are better suited for microinvasive treatments than others. No adverse events for microinvasive treatment or non-invasive controls were reported. The findings in this review suggest that there is adequate evidence that microinvasive treatment of proximal carious lesions arrests non-cavitated enamel and initial dentinal lesions and is significantly more effective than non-invasive professional treatment (e.g. fluoride varnish) or advice (e.g. to floss). This finding is based on moderate evidence according to the GRADE levels of evidence, and the authors are “moderately confident that further research is unlikely to substantially change the estimate of effect”.^{149 (p2)} However, the evidence is inconclusive regarding which microinvasive technique offers the greatest benefit, due to the small number of studies available for analysis.
Significance/direction	Favours microinvasive treatment over non-invasive treatment or oral hygiene advice
Heterogeneity	Moderate
Comments	GRADE was used by the review authors. Most of the trials were judged to be at high risk of bias, primarily due to lack of blinding of participants and personnel. The quality of the systematic review was judged as low using AMSTAR 2 as the authors did not control for the high risk of bias in their meta-analysis. The HRB graded the evidence in this review as moderate which corresponds with the authors’ ratings.

Ammari *et al.* (2014)

Parameter	Extraction
First author and year of publication	Ammari <i>et al.</i> (2014) ¹⁵⁰
Objectives	Evaluated effectiveness (caries arrest and control) of sealing and/or infiltration compared with placebo or other materials or techniques to treat non-cavitated proximal lesions in primary and permanent teeth.
Participants	Mixed teeth, non-cavitated caries, microinvasive treatments Population: Children and adults with non-cavitated proximal caries, either in primary molar or posterior permanent teeth Ten trials (8 randomised and 2 non-randomised) with 451 participants (1,114 lesions) aged 4–39 years, published between 2005 and 2012, were included in the review; 7 were published articles and 3 were ongoing studies with partially published results. Gender was not reported. The follow-up period for the studies was 1–5 years.
Setting/context	The setting was not reported. The study countries were Brazil, Chile, China, Colombia, Germany, Greenland, and the USA.
Description of interventions/phenomena of interest	Intervention: Sealing and/or infiltration of proximal caries “The use of fissure sealants has been considered a successful procedure not only to prevent occlusal caries, but also to control the progression of active initial caries or even radiographically evident caries with moderate depth in the occlusal surface.”^{150 (p1218)} Comparator: Different materials/techniques or placebo Actual comparators: Placebo in four studies, fluoride in three studies, and flossing in three studies
Databases and sources searched	The electronic searches were conducted up to June 2013 and used the following electronic bibliography databases: PubMed, Scopus, Web of Science, the

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	Cochrane Library, LILACS, OpenSIGLE, and ClinicalTrials.gov. The electronic databases and search strategy are summarised in a table. Researchers were contacted to identify unpublished and ongoing studies. Efforts were made to obtain conference proceedings and abstracts when possible. A complementary hand-search was performed by screening the references of the selected articles. There was no mention of the preparation of a protocol. Duplicate screening was completed. It is not clear who or how many reviewers extracted the data. Conflicts of interest and funding source were not reported.
Date range (years) of included studies	Ten trials (8 randomised and 2 non-randomised) published between 2005 and 2012 were included in the review; 7 were published articles and 3 were ongoing studies with partially published results.
Number of primary studies included in the systematic review	Ten trials (8 randomised and 2 non-randomised) with 451 participants (1,114 lesions) aged 4–39 years, published between 2005 and 2012, were included in the review; seven were published articles and three were ongoing studies with partially published results. The sources of funding for the primary studies were not reported.
Types of studies included	Study design: Randomised controlled trials and controlled clinical trials with at least 12 months of follow-up The studies excluded at full-text screening were referenced with their reasons for exclusion.
Country of origin of included studies	The study countries were Brazil, Chile, China, Colombia, Germany, Greenland, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included trials.
Appraisal rating	Of the 10 included studies, 6 were judged to have a high risk of bias and 4 had an unclear risk of bias. Eight of the 10 studies had adequate randomisation and all 10 had adequate blinding of outcome assessment. Only four randomised trials were included in the meta-analysis. Publication bias was not mentioned in the article.
Method of analysis	The meta-analysis was performed on the studies considered to have a low risk of bias and on those with pairwise visual reading results through RevMan software. As the results were presented by the authors as the percentage of teeth in each group where caries had progressed, the number of events of progression was calculated for each study. The random-effects model was used, as studies were not functionally equivalent and there is an objective to generalise the results from this meta-analysis. A subgroup analysis was performed among the studies that used infiltration compared with placebo, and the data inserted into the software were: number of units of analysis in which there was caries progression and total number of units analysed in each group. The heterogeneity among studies was tested through the I^2 Inconsistency Index and a forest plot was generated for this comparison. With respect to methods, the authors reported that “four studies met the best requirements features, including randomization and blinding of participants, personnel and outcome assessment”.^{150 (p1224)} These four studies compared infiltration with a placebo. The authors felt that they had dealt with the high risk of bias in studies.
Outcome assessed	Outcome: Caries arrest or progression detected by bitewing radiographs at follow-up after least 12 months. The follow-up periods for the included studies were 1–5 years. Outcome by primary study: Caries arrest or progression: Martignon 2012; Paris 2013; Correa 2013; Peters 2013.
Results/findings	The meta-analysis showed a favourable outcome for the use of infiltration compared with placebo. The chance of caries progression when infiltration was used was significantly lower (odds ratio: 0.22; 95% CI: 0.09–0.057; $p=0.002$; I^2: 29%; 189 lesions; four trials) than when placebo was used. The statistical heterogeneity was rated low. The time frame was not clear, but it was between one and three years. The authors concluded that “This assessment, based on scientific information available at present, concluded that sealing non-cavitated proximal carious

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	lesions, both in primary and permanent teeth, seems to be effective in controlling caries progression in the short and medium term." 150 (p1226)
Significance/direction	Favours infiltration over placebo to arrest caries.
Heterogeneity	The statistical heterogeneity was rated as low.
Comments	GRADE was not used by the review authors. Only four studies that were considered to have minimised the risk of bias were included in the meta-analysis. The sample size for meta-analysis was less than 200. The quality of the systematic review was judged as moderate using AMSTAR 2 as the systematic review has no critical flaws. The HRB graded the evidence in this review as moderate.

Non-cavitated and cavitated caries

Non-invasive treatment

Marcílio Santos *et al.* (2020)

Parameter	Extraction
First author and year of publication	Marcílio Santos <i>et al.</i> (2020) ¹⁵¹
Objectives	Evaluated the effectiveness (antimicrobial effect and lesion progression or regression) and safety (adverse events) of ozone therapy compared with no treatment, sham, or any other antibacterial intervention (including pharmacological and non-pharmacological treatments) for treating cavitated and non-cavitated dental caries in participants of any age.
Participants	Mixed dentition, non-cavitated and cavitated caries, non-invasive treatment Non-cavitated and cavitated proximal carious lesions in primary and permanent teeth in humans Twelve randomised controlled trials published in 13 articles between 2003 and 2020 were included in this review. There were 696 participants with 1,284 lesions, comprising 262 adults (with 492 lesions), 392 children (with 634 lesions), and 42 individuals whose age was unknown (with 158 lesions). Four studies included adults with an age range of 16–82 years, seven studies (eight papers) included children with an age range of 5–16 years, and one study did not report age range. The proportion of males in each study ranged from 49% to 65%; two studies did not report gender. The longest follow-up ranged from immediately after treatment for two studies to 18 months for another two studies.
Setting/context	The study settings were not reported. The study countries were Germany, India, Saudi Arabia, Serbia, Sweden, Switzerland, Turkey, and the UK.
Description of interventions/phenomena of interest	Intervention: Oxidation caused by ozone on biomolecules present in dental disease leads to a disruptive effect on bacteria, damaging the bacterium cell wall and cytoplasmic membrane, thereby increasing the permeability of ozone molecules within bacterial cells. Therefore, theoretically, the application of ozone therapy should be effective in reducing bacterial count and in arresting or reversing the progression of dental caries, and may provide an alternative management strategy to the traditional drill and fill approach. Comparators: No treatment, sham, or any other antibacterial intervention (including pharmacological and non-pharmacological treatments)
Databases and sources searched	The authors completed searches in five electronic databases from inception to 4 April 2020 and without restrictions: MEDLINE (via PubMed), the Cochrane Central Register of Controlled Trials (CENTRAL) (via Wiley), Embase (via Ovid), LILACS (via BIREME Virtual Health Library), and Bibliografia Brasileira de Odontologia (via Biblioteca Virtual em Saúde). Ongoing studies were searched in the trial registry ClinicalTrials.gov and the WHO's International Clinical Trials Registry Platform. They also searched OpenGrey. The search strategies defined for each database are detailed in a supplementary file for the paper. The authors also screened the bibliographic references of the included studies and other relevant literature aiming to identify any further studies not found through electronic searching. They asked advice

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	from experts in the field about any ongoing or awaiting publication studies. They also searched for conference abstracts in the International Association for Dental Research Abstract Archive. The review protocol was registered with PROSPERO. Duplicate screening and extraction were completed. The authors reported no conflicts of interest and they did not receive funding for this review.
Date range (years) of included studies	Twelve randomised controlled trials published in 13 articles between 2003 and 2020 were included in this review.
Number of primary studies included in the systematic review	Twelve randomised controlled trials published in 13 articles between 2003 and 2020 were included in this review. The longest follow-up ranged from immediately after treatment for two studies to 18 months for another two studies. The primary studies' funding sources were public funding for two studies, industry funding for one study, no funding for six studies, and not reported for three studies. The study settings were not reported. The study countries were Germany, India, Saudi Arabia, Serbia, Sweden, Switzerland, Turkey, and the UK.
Types of studies included	Randomised controlled trials with a minimum of a 12-month follow-ups were eligible for inclusion. The excluded studies and reasons for exclusion were provided.
Country of origin of included studies	The study countries were Germany, India, Saudi Arabia, Serbia, Sweden, Switzerland, Turkey, and the UK.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was adapted and employed to assess the risk of bias in the included studies.
Appraisal rating	One of the 12 trials was judged to have a high risk of bias and 9 had an unclear risk of bias. Two studies were judged to have a low risk of bias, but for both of these studies blinding of participants and outcome measurement was not done. Using the full Cochrane Collaboration guidance, the HRB has graded these studies as having a high risk of bias. Five (42%) of the 12 studies were judged to have adequate randomisation and only 2 (2%) had adequate blinding of the outcome assessment. Publication bias was addressed in the comprehensive search and GRADE assessment.
Method of analysis	The authors considered the individual participants as the unit of analysis. For the treatment effects estimate, they planned to calculate mean difference for continuous outcomes and risk ratios for dichotomous outcomes (considering a 95% CI). When possible, treatment effects were combined using a random-effects model meta-analysis. The authors performed a subgroup analysis comparing the results from different forms of application of ozone therapy and between children and adults.
Outcome assessed	Effectiveness (antimicrobial effect and lesion progression or regression) and safety (adverse events) The longest follow-ups ranged from immediately after treatment for two studies to 18 months for another two studies. The authors considered all time points reported by the randomised controlled trials, but they pooled similar time points: short term (0–3 months, by eight studies), intermediate term (more than 3 months to 6 months, by four studies), and long term (more than 6 months, by five studies); time frame not predetermined. Outcome by primary study: <i>Ozone therapy compared with no ozone (compressed air) or no treatment:</i> Antimicrobial effects: No studies Adverse events: Baysan 2007; Huth 2005; Holmes 2003. Clinical severity, lesion progression or remineralisation: Yazicioglu 2014; Baysan 2007; Huth 2005. <i>Ozone therapy compared with chlorhexidine digluconate:</i> Antimicrobial effects: Mese 2020; Durmus 2019; Krunic 2019; Anumula 2017; Hauser-Gerspach 2009. Adverse events: Krunic 2019. Lesion progression or remineralisation: No studies <i>Ozone therapy compared with sealant:</i> Antimicrobial effects: Mese 2020; Durmus 2019; Safwat 2017; Safwat 2018. Adverse events: Baysan 2007. Lesion progression or remineralisation: Safwat 2017; Yazicioglu 2014; Baysan 2007.

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	<i>Ozone therapy added to sealant, compared with sealant only:</i> Antimicrobial effects: No studies Adverse events: Baysan 2007. Lesion progression or remineralisation: Unal 2015; Baysan 2007. <i>Ozone therapy compared with fluoride:</i> Antimicrobial effects: No studies Adverse events: Johansson 2014. Clinical severity, lesion progression or remineralisation: Yazicioglu 2014; Johansson 2014.
Results/findings	Comparison 1: Ozone therapy compared with no ozone (compressed air) or no treatment None of the studies in Comparison 1 evaluated antimicrobial effects of ozone therapy. Three studies (209 participants, 402 lesions) assessed adverse events outcomes, and reported no adverse events during or following treatment (low-quality evidence). Three studies (162 participants, 283 lesions) assessed lesion progression using a laser fluorescence score system. Each study presented a different follow-up time point, which precluded the combination of data in meta-analysis. Two studies reported statistically significantly positive findings with respect to ozone therapy at short-, medium-, and long-term follow-ups, and one reported no difference at short-term follow-up (low-quality evidence). Three studies assessed changes in clinical severity of lesions using an index (classified as soft, leathery, or hard lesion), but owing to the lack of numerical data and different time points (one short term, two medium term, and two long term), it was not possible to pool the findings in a meta-analysis. Ozone reduced the clinical severity of the lesions when compared with the controls, and this was statistically significant in all five comparisons tested (low-quality evidence). Comparison 2: Ozone therapy compared with chlorhexidine digluconate Five studies (219 participants, 239 lesions) compared the antimicrobial effect of ozone therapy with that of chlorhexidine digluconate on treating carious lesions. However, owing to the discrepancies related to the type of ozone application, different population age, and different outcome measures, it was not possible to pool the data from these studies in a meta-analysis. Only one of the three comparisons was statistically significantly different, and the difference was in favour of ozone over chlorhexidine digluconate (low-quality evidence). A meta-analysis of two studies (210 children, one lesion each, aged between 6 and 13 years) found that chlorhexidine digluconate was significantly better than ozone in reducing the total bacterial number immediately after application (mean difference: -33.07; 95% CI: -46.32 to -19.83; $p < 0.00001$; I^2: 0%; 2 trials; low-quality evidence) and 4 months after treatment, when temporary restoration was removed (mean difference: -5.65; 95% CI: -9.79 to -1.51, $p = 0.007$; I^2: 0%; 2 trials; low-quality evidence). After final excavation, with complete removal of the remaining carious dentine, no significant difference between ozone and chlorhexidine digluconate was observed (mean difference: -0.10; 95% CI: -1.07 to 0.88; $p = 0.85$; I^2: 0%; two trials; low-quality evidence). When the assessment was based on bacteria species, chlorhexidine digluconate was more effective in reducing both <i>Streptococcus mutans</i> and <i>Lactobacillus</i> spp. than ozone ($p = 0.000$ and $p = 0.002$, respectively; low-quality evidence). Two studies assessed total bacterial number in adults following ozone therapy compared with chlorhexidine digluconate. The findings were mixed, with one study (48 adults, one lesion each, aged between 20 and 48 years, very low-quality evidence) reporting no difference in <i>Lactobacillus</i> spp. count between ozone and chlorhexidine digluconate following application and the other study (46 participants, one lesion each, aged between 16 and 30 years, very low-quality evidence) reporting in favour of ozone having a lower bacterial (<i>Streptococcus mutans</i>) count after 14 days. Only one study (48 participants, one lesion each) assessed adverse events and reported no events during or after treatment (very low-quality evidence). Comparison 3: Ozone therapy compared with sealant In a meta-analysis of two studies (210 participants, one lesion each, aged between 6 and 13 years, low-quality evidence), ozone therapy showed a

Parameter	Extraction
	significantly higher reduction in the total bacterial counts than sealant after 4 months of treatment at the time of temporary restoration removal (mean difference: 12.60; 95% CI: 3.86–21.34; $p=0.005$; I^2: 0%; two trials; low-quality evidence). This difference was not observed after final excavation and permanent restoration (mean difference: -0.00; 95% CI: -0.01 to 0.01; $p=1.00$; I^2: 0%; 2 trials; low-quality evidence). Another study (40 participants, 80 lesions) found no difference between ozone therapy and sealant regarding bacterial counts after 6 months of treatment (<i>Streptococcus mutans</i>: $p=0.68$; <i>Lactobacillus</i> spp.: $p=0.32$; <i>Candida</i>: $p=1.00$) or after 12 months (<i>Streptococcus mutans</i>: $p=0.34$; <i>Lactobacillus</i> spp.: $p=0.18$; <i>Candida</i>: $p=0.32$; very low-quality evidence). One study (79 participants, 110 lesions) reported that no adverse events were registered (very low-quality evidence). Three studies (161 participants, 249 lesions) assessed lesion progression using the laser fluorescence score system. One study showed a non-significant difference between ozone and sealant treatments at short-term follow-up (3 months) (mean difference: -2.18; 95% CI: -5.58 to 1.22; 110 lesions; $p=0.21$; very low-quality evidence). Results from meta-analyses presented a non-significant difference at medium-term follow-up (6 months) (mean difference: -5.92; 95% CI: -19.91 to 8.07; 2 trials; 190 lesions; I^2: 0%; $p=0.41$; low-quality evidence), and a significant decrease in lesion progression favouring the sealant group at long-term follow-up (12–18 months) (mean difference: 4.89; 95% CI: 1.66–8.12; 2 trials; 238 lesions; I^2: 1%; $p=0.003$; low-quality evidence). There was no heterogeneity in the meta-analyses. Comparison 4: Ozone therapy added to sealant, compared with sealant only One study (79 participants, 110 lesions) reported that no adverse events were registered. Two studies (139 participants, 230 lesions) investigated the effects of ozone therapy added to sealant application compared with sealant alone. One trial did not present a significant difference between groups at short-term follow-up (3 months) (mean difference: -3.35; 95% CI: -8.98 to 2.28; $p=0.24$; very low-quality evidence). Regarding the long-term follow-up (6–12 months), one three-arm trial compared different types of sealant. An overall meta-analysis was performed combining all types of sealants (considering that they all have the same therapeutic purpose). The results showed no significant difference in laser fluorescence values between ozone therapy added to sealant and sealant alone (mean difference: 1.29; 95% CI: -0.91 to 3.49; I^2: 47%; $p=0.25$; 230 participants; 2 trials; low-quality evidence). There was moderate to high heterogeneity in the analysis. Comparison 5: Ozone therapy compared with fluoride One study reported that no adverse events associated with ozone therapy were observed during or after the study period (very low-quality evidence). One study (21 participants, 70 lesions) compared lesion progression following ozone therapy with lesion progression following fluoride varnish, and showed no significant difference in laser fluorescence values between groups at long-term follow-up (after 12 months) ($p=0.05$; very low-quality evidence). Another study (42 participants, 158 lesions, mean age not reported) assessed the effects of ozone therapy compared with fluoride gel and presented improvement in favour of ozone therapy for lesion progression at long-term follow-up (after 18 months) (mean difference: -10.85; 85% CI: -18.63 to -3.07; $p=0.006$; very low-quality evidence). Two studies (63 participants, 130 lesions) assessed clinical severity of carious lesions by visual examination. The meta-analysis of these two trials found no statistically significant difference between ozone and fluoride with respect to the severity of carious lesions following treatment (risk ratio: 0.85; 95% CI: 0.38–1.88; two trials; 130 lesions; I^2: 0%; $p=0.68$; low-quality evidence).
Significance/direction	Results listed by outcome
Heterogeneity	The authors reported that “The main limitations were the heterogeneity between included studies and the small sample size. Another concern was the large number of unpublished studies, available only in abstract form or conference proceedings, which did not provide enough data to draw any conclusions.” ¹⁵¹ (p15)

Parameter	Extraction
Comments	GRADE was used by the review authors. The authors reported that “For all comparisons, the certainty of evidence was considered very low for all primary outcomes. The main reasons were risk of bias (downgraded by 1 level) and imprecision (downgraded by 2 levels). For the domain risk of bias, the main reasons were the unclear risk of bias, specifically related to high risk of performance bias for subjective outcomes. In addition, only two studies presented a prospective protocol, and the others were judged as unclear risk of selective reporting and/or allocation concealment procedures. For the domain imprecision, the main reasons were the few small studies included in each comparison. When presented, confidence intervals were wide, and the direction of the effect was not clear.”¹⁵¹ (p14) The HRB also noted that less than 75% of trials were judged to have adequate random sequence generation and blinding of outcome assessment. In addition, the authors reported high heterogeneity among the included studies. The quality of the systematic review was judged as low, as the authors could not control for high or unclear risk of bias in their analyses. Generally, sample sizes were less than 200 participants, and in some cases less than 100 participants. The HRB graded the evidence in this review as low or very low for all outcomes, and this corresponds somewhat with the review authors’ own scores.

Chibinski *et al* (2017)

Parameter	Extraction
First author and year of publication	Chibinski <i>et al.</i> (2017) ¹⁵²
Objectives	Evaluated the efficacy of silver diamine fluoride in controlling (arresting) caries progression in children’s primary or permanent teeth when compared with active treatments (different doses of silver diamine fluoride, fluoride varnish, sealant, atraumatic restorative technique) or placebos (water or saline).
Participants	Mixed dentition, non-cavitated and cavitated caries, non-invasive management Population: Children’s primary (eight studies), mixed (two studies), or permanent (one study) molar dentition with caries Eleven randomised controlled trials published between 2002 and 2016, with 4,328 children, were included. The children’s age ranges were aligned with the type of dentition: the age range for nine studies on children with treated primary dentition was 3–9 years, the age range for mixed dentition studies was 6–15 years, and the age range for the permanent dentition study was 6–8 years. Gender was not reported. The follow-up periods were 12–36 months.
Setting/context	The study countries or settings were not reported.
Description of interventions/phenomena of interest	Intervention: Different percentages of silver diamine fluoride (38%, 30%, and 12%) application at various frequencies (once-off, every 6 months, every year) to non-cavitated carious lesions Comparator: Active treatments (fluoride varnish, resin sealant, atraumatic restorative technique, or glass ionomer sealant) or placebos (water or saline)
Databases and sources searched	Six data sources (PubMed, Scopus, Web of Science, LILACS, Brazilian Library in Dentistry (BBO), and the Cochrane Library) and several sources of grey literature were searched up to 8 March 2016. There were no restrictions on time or languages. The authors presented their search strategy in a table. The references of the included primary studies were screened for additional studies. The authors prepared and registered a protocol. Duplicate screening and extraction were completed. The authors declared no conflicts of interest and the study was funded through public funding.
Date range (years) of included studies	Eleven randomised controlled trials, published between 2002 and 2016, were included.
Number of primary studies included in the systematic review	Eleven randomised controlled trials published between 2002 and 2016, with 4,328 children, were included. The primary studies’ funding sources were not reported.
Types of studies included	Randomised clinical trials were eligible for inclusion.

Parameter	Extraction
	The studies excluded at full-text screening, with the reasons for exclusion, are referenced in the text.
Country of origin of included studies	The study countries or settings were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included trials.
Appraisal rating	Five of the 11 trials were judged to have a high risk of bias, two of the trials had an unclear risk of bias, and four had a low risk of bias. Seven of the 11 trials were judged to have adequate randomisation and 9 had adequate blinding for outcome ascertainment. Meta-analysis was performed on studies considered to have a low or unclear risk of bias.
Method of analysis	Meta-analysis was performed on studies considered to have a low or unclear risk of bias. A random-effects model, measuring statistical heterogeneity and presenting relative risks and their 95% CIs following the Cochrane Collaboration's protocol, was followed. No sensitivity or subgroup analyses were completed.
Outcome assessed	Outcome: Arresting carious lesions The follow-up period was six months or more (predetermined) The follow-up periods were 12–36 months. Outcome by primary study: Arresting carious lesions: *Dungthip 2016; dos Santos 2014; Seberol and Okte 2013; Zhi 2012. *The Dungthip 1998 study is incorrectly labelled and is taken as the 2016 study.
Results/findings	The studies from which the information could be extracted were included for meta-analysis. The caries arrestment in primary teeth at 12 months promoted by silver diamine fluoride (38%, 30%, and nanosilver fluoride) was 66% higher (relative risk: 1.66; 95% CI: 1.41–1.96; I^2 : 0%; 2,079 participants; 2 trials; high level of evidence) than that observed for other active materials, but it was 154% higher (relative risk: 2.54; 95% CI: 1.67–3.85; p <0.00001; I^2 : 20%; 243 participants; 2 trials; high-quality evidence downgraded by the HRB to moderate) than that observed for placebos. Overall, the caries arrestment using for silver diamine fluoride was 89% higher (relative risk: 1.89; 95% CI: 1.49–2.38; p <0.00001; I^2 : 70%; 2,322 participants; 4 trials; high-quality evidence downgraded by the HRB to moderate) than using active materials and placebos combined. The authors reported that no heterogeneity was detected. In addition, the authors treated studies at unclear risk of bias the same as studies at low risk of bias. The authors graded the evidence as high quality. However the HRB down graded the evidence to moderate for a number of reasons (see comment section). The authors concluded that “The use of silver diamine fluoride (38%, 30% and nanosilver fluoride at various frequencies: once off, once every six months or once every year) is 89% more effective in controlling/arresting caries than other treatments or placebos [in primary teeth]. The quality of the evidence was graded as high.” ^{152 (p527)} There was not enough evidence to assess the effectiveness of silver diamine fluoride in permanent molars.
Significance/direction	Favours silver diamine fluoride (38%, 30%, and nanosilver fluoride) for treatment of caries in primary teeth at various frequencies: once off, once every 6 months, or once every year.
Heterogeneity	The authors reported that no heterogeneity was detected. The HRB authors noted that there was no statistical heterogeneity detected in the silver diamine fluoride (38%, 30% and nanosilver fluoride) compared with other active treatment subgroups, but that there was low heterogeneity in the silver diamine fluoride (38%, 30%, and 12%) compared with placebo interventions subgroup. However, there was high heterogeneity in the overall analysis.
Comments	GRADE was used by the review authors. The authors graded their quality of evidence as high; however, the HRB disagrees with their rating for a few reasons. Less than 75% of included trials were judged to have adequate random sequence generation. Meta-analysis was performed on studies judged to have a low or unclear risk of bias, and no sensitivity analysis was completed to assess the influence of unclear risk of bias on the results. The quality of the systematic review was judged as low using AMSTAR 2 as the authors did not control for bias in their meta-analyses. The HRB graded the evidence in this review as moderate.

Gao *et al.* (2016b)

Parameter	Extraction
First author and year of publication	Gao <i>et al.</i> (2016) ¹³⁹
Objectives	Evaluated the effectiveness of silver diamine fluoride in arresting dental caries in primary or permanent teeth in children, using prospective clinical studies.
Participants	Mixed dentition, non-cavitated and-cavitated caries, non-invasive management Population: Primary and permanent teeth with non-cavitated and-cavitated caries The 19 primary prospective studies included were published between 1969 and 2016, and comprised 3 studies on permanent teeth (with 13,350 participants) and 16 on primary teeth (with 253 participants). Age, gender, and study setting were not reported. The study countries were not provided, but studies were written in English (eight studies), Chinese (four studies), Japanese (three studies), Spanish (one study), and Portuguese (three studies).
Setting/context	The study countries or settings were not provided.
Description of interventions/phenomena of interest	Intervention: Various strengths of silver diamine fluoride were used in the retrieved literature: 14 studies used 38% silver diamine fluoride, three used 30% silver diamine fluoride, and two used 10% silver diamine fluoride. Comparator: A negative control (no treatment) or a placebo (treatment with water). Some clinicians have suggested using silver diamine fluoride for caries management. It is a colourless ammonia solution containing silver and fluoride ions. As neutral silver fluoride is unstable, it is commonly dissolved in water containing ammonia to form a more stable complex ion. Fluoride has proven to be effective in enhancing the remineralisation of dental hard tissue. Silver ion acts as an antibacterial agent in silver diamine fluoride. Laboratory studies have shown that 38% silver diamine fluoride is effective in inhibiting dentine demineralisation and preserving collagen from degradation. After being treated with silver diamine fluoride, a highly remineralised surface zone rich in calcium and phosphate can be found on the arrested cavitated carious lesion. The dentine collagens are protected by the remineralised mineral materials. Silver diamine fluoride also has antibacterial properties and inhibits the growth of cariogenic bacteriw. One significant limitation of silver diamine fluoride treatment is that it will stain carious lesions black. This appearance may not be acceptable for some children and their parents. Hence, it is necessary to inform patients of this outcome of silver diamine fluoride treatment. A primary tooth with its caries arrested can act as a space maintainer and sustain chewing function until the tooth is replaced with a permanent successor tooth. Silver diamine fluoride at 38% has high fluoride content (44,800 ppm). Some clinicians were concerned about the use of silver diamine fluoride in young children because of the risk of causing dental fluorosis. However, since only a very small amount of silver diamine fluoride solution is applied onto a carious lesion, researchers concluded that occasional application of silver diamine fluoride is well below the fluoride concentrations associated with toxicity.
Databases and sources searched	A systematic search of the literature was performed in seven databases containing articles written in English, Chinese, Japanese, Portuguese, and Spanish. English publications were searched in PubMed, Embase, and Scopus; Chinese literature was searched using the China National Knowledge Infrastructure (CNKI) database; Japanese papers were searched using Ichushi-web; and Spanish and Portuguese publications were searched using Biblioteca Virtual en Salud España (BVSE) and Biblioteca Virtual em Saúde (BVS).No limit on the date of publication was set, and the last search was conducted at the end of March 2016. The reference lists of included studies were also searched. The preparation of a protocol was not mentioned. Duplicate screening and extraction were completed. The study was supported by a grant from the General Research Fund of the Research Grants Council of Hong Kong. The authors declared no potential conflicts of interest with respect to the authorship and/or publication of this article.
Date range (years) of included studies	The 19 primary prospective studies were published between 1969 and 2016.

Parameter	Extraction
Number of primary studies included in the systematic review	The 19 primary prospective studies were published between 1969 and 2016, and comprised 3 studies on permanent teeth (with 13,350 participants) and 16 on primary teeth (with 253 participants). The study countries were not provided, but studies were written in English (eight studies), Chinese (four studies), Japanese (three studies), Spanish (one study), and Portuguese (three studies). The sources of funding for primary studies were not reported.
Types of studies included	Prospective clinical studies were eligible for inclusion. This included randomised controlled trials and non-randomised controlled trials. The reasons for selecting these study designs were not explained. A list of excluded studies and their reasons for exclusion were not presented.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included studies.
Appraisal rating	Using Cochrane guidelines, 10 studies were judged as having a high risk of bias and nine as having an unclear risk of bias. Four (21%) of the 19 included studies were judged adequate for randomisation and five (26%) were adequate for blinding of outcome assessment. Publication bias was not measured, although it was an important part of this paper.
Method of analysis	All studies included in the final review were summarised in a table for qualitative evaluation. Pairwise random-effects and fixed-effects meta-analyses were performed on studies measuring the caries-arresting rate after using 38% silver diamine fluoride solution on primary teeth over time. The logistic-normal random-effects model was adopted to evaluate the caries-arresting proportions at different follow-up time points, which referred to the period of the baseline and follow-up examination. The overall caries-arresting proportions were extracted from appropriate studies.
Outcome assessed	Arresting dental caries in primary teeth following treatment with 38% silver diamine fluoride: Chu 2002; Fukumoto 1997; Llodra 2005; Wang 1984; Yang 2002; Ye 1995; Yee 2009; Zhi 2012. Arresting dental caries in permanent teeth following treatment: Braga 2009; Mauro 2004; Oliveira 1985. Time frame: 3 months to 48 months (not predetermined)
Results/findings	The two studies investigating the caries-arresting effect of 38% silver diamine fluoride in permanent teeth did not find that 38% silver diamine fluoride was better than its comparators. Meta-analysis was conducted on eight studies which used 38% silver diamine fluoride to arrest dentine caries in primary teeth in children and had reported adequate data. The results showed that the caries-arresting rate of silver diamine fluoride treatment was 86% at 6 months (95% CI: 47–98%; $p=0.06$), 81% at 12 months (95% CI: 59–93%; $p=0.01$), 78% at 18 months (95% CI: 70–85%; $p<0.001$), 65% at 24 months (95% CI: 35–86%; $p=0.32$), and 71% at or beyond 30 months (95% CI: 56–83%; $p=0.01$). The overall proportion of arrested dental caries after silver diamine fluoride treatment was 81% (95% CI: 68–89%; $p<0.001$). It is noteworthy that the application frequency of silver diamine fluoride varied in different studies. Heterogeneity was not significant. Apart from staining the arrested carious lesions black, the 19 clinical trials did not report any significant complications of silver diamine fluoride use among children.
Significance/direction	Results listed by outcome
Heterogeneity	Heterogeneity was not significant.
Comments	GRADE was not used by the review authors. The review included a mix of randomised and non-randomised trials. The numbers of participants of individual primary studies were not reported. All trials scored high or unclear for risk of bias for one or more parameters. Less than 75% of trials were judged to have adequate random sequence generation and blinding of outcome assessment. The quality of the systematic review was judged as critically low. The HRB graded the evidence in this review as very low for all outcomes.

Microinvasive and invasive treatment

de Amorim *et al.* (2018)

Parameter	Extraction
First author and year of publication	de Amorim <i>et al.</i> (2018) ¹⁵³
Objectives	The authors evaluated the survival rate of atraumatic restorative treatment glass ionomer restorations and atraumatic restorative treatment sealants in primary and permanent posterior teeth. The aim of the present study is to update the results of two previous meta-analyses, published in 2006 and 2012, on the survival percentages of atraumatic restorative treatment restorations and sealants.
Participants	Mixed dentition, non-cavitated and cavitated caries, microinvasive and invasive management Forty-three publications (examining 34 clinical trials), published from 1999 to 2017, were evaluated in this review. It is not clear from the reporting in the review how many randomised controlled trials were included, but from the risk of bias table, it seems as though there were approximately 18. Twenty-eight trials were exclusively focused on children, three were focused on both children and adults, and three were focused on adults. The age range of the included participants was 2–39 years. Gender was not reported. The numbers of participants or teeth were not reported.
Setting/context	The studies were conducted in dental clinics (14 studies) or in the field (20 studies). Twenty-two countries were included in the review: Argentina, Brazil, China, Ecuador, Egypt, Hong Kong, India, Iraq, Kuwait, Latvia, Malaysia, Mexico, Nigeria, Panama, Pakistan, South Africa, Suriname, Syria, Tanzania, Turkey, Uruguay, and Zimbabwe.
Description of interventions/phenomena of interest	Atraumatic restorative treatment is done using hand tools, not the drill and fill method. Its restorative component is based on the selective removal of carious tissues down to the soft dentine in deep or very deep lesions, and to firm dentine in shallow lesions. According to de Amorim <i>et al.</i>, “the rationale for the widespread use of ART [atraumatic restorative treatment] lies in the fact that principles of ART are in accordance with the contemporary philosophy of dental caries management, which is minimal intervention dentistry.”¹⁵³ (p2704)
Databases and sources searched	The literature search comprised publications indexed in English-language databases (PubMed and Embase), which included publications written in Dutch, German, and French. Portuguese- and Spanish-language databases (LILACS and BBO), and Chinese-language databases (CNKI and China Science Journal Database [VIP]), were also searched. Keywords are provided. The lists of references of selected publications were cross-checked for additional studies suitable for inclusion. All publications listed until 1 February 2017 were analysed. The protocol for this systematic review with meta-analysis were registered on PROSPERO. It is not clear if duplicate screening was completed. Two investigators independently extracted the data related to the outcomes. The review was partially supported by the Brazilian Council for Scientific and Technological Development. The authors stated conflicts of interest and none were related to the dental industry.
Date range (years) of included studies	The 43 included articles were published from 1999 to 2017.
Number of primary studies included in the systematic review	The review included 43 publications examining 34 clinical trials from 22 countries published between 1999 and 2017. It is not clear from the reporting in the review how many randomised controlled trials were included. Twenty-eight trials were exclusively focused on children, three were focused on both children and adults, and three were focused on adults. The funding sources for primary studies were not provided.
Types of studies included	It is not exactly clear from the reporting, but it appears that the study inclusion criteria specified clinical trials. The authors provide a table listing excluded publications and the reasons for exclusion.

Parameter	Extraction
Country of origin of included studies	Twenty-two countries were included in the review: Argentina, Brazil, China, Ecuador, Egypt, Hong Kong, India, Iraq, Kuwait, Latvia, Malaysia, Mexico, Nigeria, Panama, Pakistan, South Africa, Suriname, Syria, Tanzania, Turkey, Uruguay, and Zimbabwe.
Appraisal instruments used	A modified version of the Cochrane Collaboration's risk of bias instrument was used to assess the risk of bias in the primary studies.
Appraisal rating	Only 1 trial scored low for risk of bias across all parameters, while 33 trials scored high or unclear for risk of bias for one or more parameters. Eighteen (53%) of the 34 trials were judged to have adequate random sequence generation, and six (18%) were considered to have adequate blinding of outcome assessors. The authors reported that "the results of the current meta-analysis should be interpreted with caution. Even though these results are based on the best available evidence, their validity is to a certain extent compromised by the lack of more methodologically refined [rigorous] trials." ¹⁵³ (p2716) Publication bias was not examined in this review.
Method of analysis	The analyses were carried out by a statistician. If only survival percentages and number of sealants/restorations had been presented in the included publications, the 95% CI had to be obtained from the statistical tables. CIs were used to calculate the standard error for the survival percentages. Survival percentages per year within selected groups were combined by meta-analysis. If survival percentages showed homogeneity, a fixed-effects model was applied. In case of heterogeneity, a random-effects model was used. The decision criterion was the <i>p</i> -value for the homogeneity test. <i>I</i> ² values were used to grade the level of heterogeneity of the survival percentages per survival year. Categorisation of the level of heterogeneity followed the suggestion presented by the Cochrane Research Group. The meta-analyses were performed in R version 3.3.1 using the <i>survcomp</i> package.
Outcome assessed	Survival of single-surface and multiple-surface atraumatic restorative treatment restorations for one year or more Outcome by primary studies: Single-surface atraumatic restorative treatment restorations in primary posterior teeth: Honkala 2003; Louw 2002; Luo 1999; Lo 2001; Taifour 2002; Yip 2002; Yu 2004; Ersin 2006; Van Gemert-Schriks 2007; Menezes 2006; Yassen 2009; Deepa and Shobha 2010; Hilgert 2014; Molina 2017. Multiple-surface atraumatic restorative treatment restorations in primary posterior teeth: Ersin 2006; Honkala 2003; Louw 2002; Luo 1999; Lo 2001; Taifour 2002; Yip 2002; Yu 2004; Ersin 2006; Van Gemert-Schriks 2007; Menezes 2006; Yassen 2009; Deepa and Shobha 2010; Hilgert 2014; Molina 2017. Single-surface atraumatic restorative treatment restorations in permanent posterior teeth: Cefaly 2007; Ercan 2009; Farag 2011; Frencken 1998; Frencken 2006; Van Gemert-Schriks 2007; Ho 1999; Kikwilu 2001; Lo 2007; Loh 2003; Luo 1999; Mickenautsch 1999; PAHO 2006; Estupiñán-Day 2013; Rahimtoola and Van Amerongen 2002; Yip 2002; Gao 2003; Ziraps and Honkala 2002; Ibiyemi 2011; Zanata 2011; Molina 2017. Multi-surface atraumatic restorative treatment restorations in permanent posterior teeth: Cefaly 2007; Ercan 2009; Farag 2011; Zanata 2011; Molina 2017. Atraumatic restorative treatment sealants: Frencken 1998; Vieira 2006; Holmgren 2013; Luengas-Quintero 2013; Liu 2014; Zhang 2017; Hilgert 2017.
Results/findings	The survival rates of single-surface and multiple-surface atraumatic restorative treatment restorations in primary posterior teeth over the first two years were 94.3% (±1.5%; high survival rate) and 65.4% (±3.9%; medium survival rate), respectively. Heterogeneity is high or substantial. Single-surface atraumatic restorative treatment restorations in permanent posterior teeth over the first three years had a survival rate of 87.1% (±3.2%; high survival rate), and multiple-surface atraumatic restorative treatment restorations in permanent posterior teeth over the first five years had a survival rate of 77% (±9.0%; medium survival rate). Heterogeneity is high or substantial. The weighted mean annual failure rates of completely lost atraumatic restorative treatment sealants in permanent posterior teeth over the first 3 and 4 years were 10.7% and 9.6%, respectively. Mean annual dentine-carious-lesion failure

Parameter	Extraction
	percentages in previously sealed pits and fissures using atraumatic restorative treatment sealants in permanent posterior teeth were 0.9% at 3 years and 1.9% at five years. Heterogeneity is high or substantial. According to de Amorim <i>et al.</i> , "Twelve years after the publication of the first meta-analysis, the atraumatic restorative treatment approach has been consistently shown as an effective evidence-based option for managing carious lesions. The time has come to consider atraumatic restorative treatment as no longer an alternative option, but, for some cases, the treatment of first choice." ¹⁵³ (p2720)
Significance/direction	Varied by outcome; see above.
Heterogeneity	Heterogeneity was substantial for most of the weighted mean survival percentages of all types of atraumatic restorative treatment restorations and sealant retention, whereas the level of heterogeneity for the weighted mean survival percentages for the dentine-caries-lesion-preventive effect of atraumatic restorative treatment sealants was lower, even showing full homogeneity (survival years 1 and 3).
Comments	GRADE was not used by the review authors. The review appears to have included a mix of randomised and non-randomised trials. The numbers of participants or teeth were not reported. Most trials scored high or unclear for risk of bias for one or more parameters. Less than 75% of trials were judged to have adequate random sequence generation and blinding of outcome assessment. Heterogeneity was high or substantial among the studies. The quality of the systematic review was judged as critically low. The HRB graded the evidence in this review as very low.

Non-invasive and microinvasive treatment

Urquhart *et al.* (2019)

Parameter	Extraction
First author and year of publication	Urquhart <i>et al.</i> (2019) ¹⁵⁴
Objectives	Mixed dentition, non-cavitated and cavitated caries, non-invasive and microinvasive Compared non-restorative treatments with other active intervention(s), or with no treatment or a placebo, for the arrest or reversal of non-cavitated and cavitated carious lesions in primary and permanent teeth in children and adults.
Participants	Population: Primary and permanent teeth in children and adults Forty-three randomised controlled trials (33 with a parallel study design and 10 with a split-mouth design) based on 48 reports, which involved 7,378 participants and assessed the effectiveness of 22 interventions, were included in this review. Twelve trials involved participants with primary dentition, 21 involved participants with permanent dentition, and nine involved participants with mixed dentition; one study did not report dentition status. The ages varied by dentition. Studies examining primary dentition reported a mean age range of 2–7 years (9 out of 12 studies), studies examining mixed dentition reported a mean age range of 6–23 years (6 out of 9 studies), and studies examining permanent dentition reported a mean age range of 6–83 years (18 out of 21 studies). Gender was not reported.
Setting/context	The 43 included trials were published between 1984 and 2018 and were conducted in 22 countries: Australia, Brazil, Canada, Chile, China, Colombia, Cuba, Denmark, Estonia, Germany, Greenland, Hong Kong, India, Kuwait, Nepal, the Netherlands, Poland, Spain, Sweden, Thailand, the UK, and the USA. Primary study settings were not reported.
Description of interventions/phenomena of interest	According to Urquhart <i>et al.</i> , non-restorative treatments include "sodium fluoride, stannous fluoride toothpaste or gel, acidulated phosphate fluoride, difluorsilane, ammonium fluoride, polyols, chlorhexidine, calcium phosphate, amorphous calcium phosphate (ACP), casein phosphopeptide-ACP (CPP-ACP), nano hydroxyapatite, tricalcium phosphate, prebiotics and/or 1.5% arginine, probiotics, silver diamine fluoride, silver nitrate, lasers, resin infiltration, sealants, sodium bicarbonate, calcium hydroxide, and carbamide peroxide". ¹⁵⁴ (p15)

Parameter	Extraction
Databases and sources searched	Comparator: Other active interventions, no treatment, or a placebo The search for this review was based on a previous search by Wright <i>et al.</i> 2016 (described in an appendix in the review). The authors searched four databases: MEDLINE (1946–2017) and Embase (1974–2017) via Ovid, as well as the Cochrane Central Register of Controlled Trials (CENTRAL) and the Cochrane Database of Systematic Reviews (inception to 2017). The searches were not limited by language or study design. The authors also searched the reference sections of relevant primary studies, systematic reviews, and guidelines to identify additional studies. The review was not registered in PROSPERO and there is no mention of preparing a protocol. Duplicate screening and extraction were completed. The review was supported by industry involved in producing some of the products evaluated.
Date range (years) of included studies	The 43 included trials were published between 1984 and 2018.
Number of primary studies included in the systematic review	Forty-three randomised controlled trials (33 with a parallel study design and 10 with a split-mouth design) based on 48 reports, which involved 7,378 participants and assessed the effectiveness of 22 interventions, were included in this review. Twelve trials involved participants with primary dentition, 21 involved participants with permanent dentition, and nine involved participants with mixed dentition; one study did not report dentition status. The ages varied by dentition. Studies examining primary dentition reported a mean age range of 2–7 years (9 out of 12 studies), studies examining mixed dentition reported a mean age range of 6–23 years (6 out of 9 studies), and studies examining permanent dentition reported a mean age range of 6–83 years (18 out of 21 studies). Primary study funding details were provided in an appendix: nine studies were supported by industry and 17 were funded by public or university grant funding. The funding sources for the remaining 17 trials were not reported to the review authors.
Types of studies included	Studies included parallel or split-mouth randomised controlled trials, with follow-ups of any length. Excluded trials and their reasons were reported.
Country of origin of included studies	The 43 included trials were conducted in 22 countries: Australia, Brazil, Canada, Chile, China, Colombia, Cuba, Denmark, Estonia, Germany, Greenland, Hong Kong, India, Kuwait, Nepal, the Netherlands, Poland, Spain, Sweden, Thailand, the UK, and the USA.
Appraisal instruments used	The risk of bias in the included trials was assessed using the Cochrane Collaboration's risk of bias instrument. The authors note that "information to judge most risk of bias domains was often incomplete or missing." ^{154 (p17)}
Appraisal rating	Overall, one trial was judged to have a low risk of bias, 23 were judged to have an unclear risk of bias, and 19 were judged to have a high risk of bias. The authors reported that "The domain of allocation concealment was judged to be the most serious methodological issue, and overall most studies had serious issues of risk of bias", ^{154 (p17)} Twenty-four (56%) of the 43 included trials were judged to have adequate random sequence generation and 32(74%) were considered to have adequate blinding of outcome assessors. The authors acknowledge that publication bias was an issue.
Method of analysis	The authors conducted network meta-analysis to obtain estimates of the relative effectiveness of all interventions on the primary outcome by combining direct and indirect evidence using random-effects models that assumed a common between-study heterogeneity parameter across the network and a frequentist approach. Bayesian network meta-analysis SUCRA values and the equivalent <i>p</i>-values were also obtained. These represent the average certainty that a treatment is better than all of the other treatments. The authors assessed global incoherence of the network using the design-by-treatment interaction model. The details about the assessment of local incoherence and intransitivity in the context of the assessment of the certainty in the evidence are provided. The authors conducted network meta-analysis using the package netmeta in the software R (version 3.1.1). For studies on root surfaces, data on non-cavitated and cavitated lesions, when separately reported, were combined within one network, as these may be difficult to distinguish in clinical practice and in the research context.

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	Within each network, if studies reported dissimilar follow-up times or lacked a common comparator or if pairwise meta-analysis was not possible, the authors categorised this as unpooled data and prioritised the calculation and reporting of relative risks and mean differences (and 95% CIs) at an individual study level. When the authors failed to obtain these measures of association, they also considered these data unpooled and reported the results as described by the primary study authors. For studies on root surfaces, the authors conducted subgroup analysis at a pairwise level by lesion type, and for studies on coronal surfaces, by dentition. The authors used a test for interaction to explore the extent to which the effect of any included intervention varied according to the type of dentition or lesion. A level of significance of 0.05 was used for the interaction test. When there were no differences in treatment effects among primary, permanent, and mixed dentition, the authors combined the results.
Outcome assessed	Outcome: Arrest or reversal of non-cavitated and cavitated carious lesions Time frame: Any length of time Outcome by primary studies: Non-cavitated carious lesions on occlusal surfaces: Autio-Gold and Courts 2001; Florio 2001; Borges 2010; Agrawal and Pushpanjali 2011; da Silveira 2012; Bakhshandeh and Ekstrand 2015; Honkala 2015. Non-cavitated carious lesions on approximal surfaces: Gomez 2005; Martignon 2006; Ekstrand 2010; Martignon 2010; Paris 2010; Martignon 2012; Meyer-Lueckel 2012. Non-cavitated carious lesions on facial/lingual surfaces: Bailey 2009; Autio-Gold 2001; Agrawal and Pushpanjali 2011. Non-cavitated carious lesions on any coronal surface: Autio-Gold and Courts 2001; Agrawal and Pushpanjali 2011; Sitthisettapong 2012. Advanced cavitated lesions on any coronal surface: Fung 2018; Duangthip 2016; Duangthip, Wong, 2018. Non-cavitated and cavitated lesions on root surfaces: Schaeken 1991; Lynch. 2000; Baysan 2001; Ekstrand 2008; Baca 2009; Ekstrand 2013; Li 2016. Adverse events: Bailey 2009; Baca 2009; Fung 2016; Fung 2018; Duangthip 2016; Duangthip, Fung, 2018; Duangthip, Wong, 2018.
Results/findings	The authors completed four network meta-analyses stratified by lesion location, then by tooth surface, and finally by lesion type. The authors identified eight studies reporting the effectiveness of interventions in arresting or reversing non-cavitated carious lesions on occlusal surfaces, seven of which were suitable to be included in the network meta-analysis. The relative effectiveness of six active interventions was assessed in the studies included in the network meta-analysis. These studies followed a total of 1,575 lesions in primary and permanent teeth for 8–12 months. Network estimates for 0.2% sodium fluoride mouth rinse and supervised tooth brushing; 1.23% acidulated phosphate fluoride gel; 5% Sodium fluoride varnish; resin infiltration and 5% sodium fluoride varnish; sealants and 5% sodium fluoride varnish; and sealants alone showed a two- to three-times-greater chance of arresting or reversing lesions as compared with no treatment (moderate certainty for all comparisons). The combination of sealants and 5% sodium fluoride varnish was the most effective in arresting or reversing lesions compared with no treatment (non-cavitated carious occlusal lesions: relative risk: 3.35; 95% CI: 2.42–4.64; 7 studies; 1,575 lesions; moderate certainty downgraded by the HRB to low). The authors identified 13 studies (14 reports) reporting the effectiveness of interventions in arresting or reversing non-cavitated carious lesions on approximal surfaces, with six studies (seven reports) that could be included in the network meta-analysis. The relative effectiveness of four active interventions was assessed in the studies included in the network meta-analysis, which followed a total of 565 lesions in primary and permanent teeth for 12–36 months. Studies included lesions with radiolucencies ranging from the enamel to lesions in the outer third of the dentine. Network estimates for resin infiltration and sealants after short-term tooth separation showed a two-times-greater chance of arresting or reversing lesions as compared with no treatment (low certainty for all comparisons). Additionally, for the combination of resin infiltration and 5% sodium fluoride varnish, the network estimate suggested that there may be a five-

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	times-greater chance of arresting or reversing lesions compared with no treatment (relative risk: 4.59; 95% CI: 1.00–20.88; six studies; 565 lesions; very low certainty). For 5% sodium fluoride varnish alone, there was a non-significant two-times-greater chance of arresting or reversing lesions as compared with no treatment (relative risk: 2.29; 95% CI: 0.74–7.10; six studies; 565 lesions; very low certainty). The authors identified five studies reporting the effectiveness of interventions in arresting or reversing non-cavitated carious lesions on facial/lingual surfaces, three of which could be used to calculate relative risks. The authors did not create a network with the data coming from the three studies, due to the follow-up times being too dissimilar. In sum, 5% sodium fluoride varnish compared with no intervention (low certainty) and 1.23% acidulated phosphate fluoride gel compared with oral health education (moderate certainty downgraded by the HRB to low) showed a two- to three-times-greater chance of arresting or reversing lesions in primary and permanent teeth. Ten per cent casein phosphopeptide-amorphous calcium phosphate, when compared with placebo cream, may increase the chance of arresting or reversing lesions in primary and permanent teeth; however, these results were neither statistically nor clinically significant (low certainty). Some studies did not report data by a specific coronal surface and instead reported the total number of arrested or reversed lesions on a combination of non-cavitated carious lesions on any coronal surface. The authors identified seven studies reporting the effectiveness of interventions in arresting or reversing non-cavitated lesions on any coronal surface, with three that could be included in the network meta-analysis. The relative effectiveness of three active interventions was assessed in the three studies. These studies followed a total of 4,672 lesions in primary and permanent teeth for 9–12 months. Network estimates for 5% Sodium fluoride varnish and 1.23% acidulated phosphate fluoride gel showed a two-times-greater chance of arresting or reversing lesions compared with no treatment (moderate certainty for all comparisons downgraded by the HRB to low). Ten per cent casein phosphopeptide-amorphous calcium phosphate may increase the chance of arresting or reversing lesions by only 3%; however, these results were neither statistically nor clinically significant (relative risk: 1.03; 95% CI: 0.90–1.18; three studies; 4,672 lesions; low certainty). The authors identified four studies that reported the effectiveness of interventions in arresting advanced cavitated lesions on any coronal surface, from which relative risks (two studies) and mean differences (two studies) were obtained. The lack of a common comparator across interventions prevented the authors from creating a network. After 30 months of follow-up, 30% silver diamine fluoride solution applied annually on primary teeth showed a 1.5-times-greater chance of arresting advanced cavitated lesions in primary teeth compared with 30% silver diamine fluoride solution applied once a week for 3 weeks (relative risk: 1.45; 95% CI: 1.21–1.73; high certainty downgraded by the HRB to low). Also, 30% silver diamine fluoride solution applied annually on primary teeth is superior to 5% sodium fluoride varnish applied once a week for three weeks (relative risk: 1.41; 95% CI: 1.20–1.66; high certainty downgraded by the HRB to low). Additionally, after 30 months of follow-up, 38% silver diamine fluoride solution applied biannually on primary teeth was superior to 12% silver diamine fluoride solution applied biannually (relative risk: 1.29; 95% CI: 1.21–1.38; high certainty downgraded by the HRB to low) and 38% silver diamine fluoride solution applied annually (relative risk: 1.13; 95% CI: 1.07–1.20; moderate certainty downgraded by the HRB to low). The authors identified 11 studies reporting the effectiveness of interventions in arresting or reversing non-cavitated and cavitated lesions on root surfaces, with seven that could be included in a network meta-analysis. The relative effectiveness of five active interventions was assessed in the studies included in the network meta-analysis. These seven studies followed 1,304 lesions in permanent teeth for 3–12 months. The network estimate for 5000 ppm fluoride (1.1% sodium fluoride) toothpaste or gel showed a three-times-greater chance of arresting or reversing lesions as compared with no treatment (relative risk: 2.62; 95% CI: 1.49–4.63; low certainty). Also, network estimates for 1% chlorhexidine in

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	combination with 1% thymol varnish; 38% silver diamine fluoride solution applied annually; 38% silver diamine fluoride in combination with potassium iodide solution applied annually; and 5% sodium fluoride varnish showed a two- to three-times-greater chance of arresting or reversing lesions compared with no treatment; however, these results were not statistically significant (very low certainty). Descriptions of adverse events were reported in only four studies (seven reports) and included black staining, tooth pain, gum pain, gingival swelling, gingival bleaching, and bitter taste. One study stated that 86% of the participants reported at least one adverse event but did not provide specifics regarding which treatment group experienced these events (the 10% casein phosphopeptide-amorphous calcium phosphate group or the placebo group). Other adverse events of interest – including nausea, fluorosis, vomiting, allergic reactions, tooth sensitivity, symptomatic progression, pulpal health, premature loss or extraction, or secondary caries – were not reported in the included studies, and thus no evidence was available to inform their occurrence. Among the studies examining the effect of sealants on occlusal non-cavitated lesions, retention ranged from 41% to 89%, while no studies reported retention of sealants applied on approximal non-cavitated lesions. The authors' summary of findings was as follows: "Study-level data show that when compared with no intervention, 5% NaF [sodium fluoride] varnish could be the most effective treatment for arresting or reversing non-cavitated facial/lingual lesions on primary and permanent teeth (low to moderate certainty downgraded by the HRB to low). Also, study-level data compared the use of 1.23% acidulated phosphate fluoride gel with oral health education on facial/lingual lesions, although this treatment was effective only at longer follow-up times (12 months, moderate certainty). For arresting advanced cavitated carious lesions, study-level data suggest that 38% silver diamine fluoride solution applied biannually was more effective on any coronal surface of primary teeth when compared with both 12% silver diamine fluoride solution applied biannually and 38% silver diamine fluoride solution applied annually (moderate to high certainty downgraded by the HRB to low). Finally, four studies reported adverse events across the different interventions, including black staining, tooth/gum pain, gingival swelling and bleaching, and a bitter taste".^{154 (p23)} According to Urquhart <i>et al.</i>, "the certainty in the evidence ranged from very low to high for the outcome of arrest or reversal across all surfaces, types of lesions, and dentition. We predominantly downgraded the certainty due to serious issues of risk of bias and imprecision".^{154 (p23)}
Significance/direction	Varied by outcome
Heterogeneity	Heterogeneity or inconsistency was only an issue for resin infiltration compared with no treatment.
Comments	GRADE was used by the review authors. Most trials scored high or unclear for risk of bias for one or more parameters. Less than 75% of trials were judged to have adequate random sequence generation and blinding of outcome assessment. The quality of the systematic review was judged as low as they did not control for risk of bias in their analysis. The HRB graded the evidence in this review as low for most outcomes and very low for two outcomes while the authors graded the evidence as high to very low.

Microinvasive and restorative treatment

Marzouk *et al.* (2019)

Parameter	Extraction
First author and year of publication	Marzouk <i>et al.</i> (2019) ¹⁵⁵
Objectives	Evaluated bisphenol A exposure in humans from resin-based dental sealants and restorations which contain bisphenol A glycidyl methacrylate by retrieving all clinical studies that measured urinary BPA (uBPA) concentrations in patients before and after resin-based dental treatments. In addition, the authors explored

Parameter	Extraction
	the degree to which baseline bisphenol A concentrations were associated with prior resin-based dental treatments.
Participants	Mixed dentition, non-cavitated caries and cavitated, micronvasive and restorative treatments The study participants were humans of any age who were exposed to Bisphenol A from dental treatment. The authors stated that “the 7 studies included that measured urinary BPA concentration before and after dental treatment involved 348 participants, with sample sizes ranging from 9 to 172. Of the 7 studies, 5 involved <25 participants. Two studies were of adults; 4 were of children; and 1 study included adolescents and adults. Among the 7 studies, 2 examined resin-based sealants; 2, composite restorations; 1, composite restorations and sealants; and 2, orthodontic adhesives. All studies had measures just before treatment. All studies had urinary BPA measured at 24 h post-treatment.”^{155 (p109)}
Setting/context	The study countries were Brazil, Republic of Korea (South), and the USA. Studies were carried out in different settings, including university, military, academic, research, private practice, and community dental clinics.
Description of interventions/phenomena of interest	Intervention: Bisphenol A from dental treatment Comparator: Pretreatment levels The authors defined the intervention as follows: “Bisphenol A (BPA) is a synthetic chemical that is used to make a wide range of products, including many types of resin-based dental materials. BPA is the starting ingredient in the manufacturing of BPA glycidyl methacrylate (BisGMA), the most common resin-based oligomer matrix component used in many dental composite restorations, dental sealants, and orthodontic adhesives. Because BPA is used to make BisGMA, it may be present after the manufacture of BisGMA as an impurity or by-product of the manufacturing process. Additionally, leaching of BPA from BisGMA -based restorations may occur due to incomplete polymerization during the initial setting period or over time due to mechanical, bacterial, thermal, or salivary enzymatic biodegradation in the oral cavity...Despite the widespread use of resin-based dental materials, the extent to which patients are exposed to BPA from these materials is unclear. BPA is an endocrine-disrupting chemical with potential toxicity in vitro and in vivo. Endocrine-disrupting chemicals perturb normal hormonal processes in the body with harmful downstream health effects. BPA is a known xenoestrogen that can affect the reproductive, psychological, cognitive, or endocrine-related health of children and adults. Specific health conditions that have been associated with BPA exposure include alterations in child behavior, diabetes, hypertension, and obesity.”^{155 (p106–107)}
Databases and sources searched	The authors searched seven databases: PubMed, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, Virtual Health Library (VHL), ScienceDirect, ClinicalTrials.gov, and ProQuest Dissertations & Theses Global. The search was conducted up to 1 May 2018 with no date or language restrictions. The reference listings of eligible studies were also searched. The authors did not report preparing a protocol. Extraction and screening were completed in duplicate. Funding: The study was funded by the National Institute of Dental and Craniofacial Research and the National Institutes of Health. The authors declared no potential conflicts of interest with respect to the authorship and/or publication of this article.
Date range (years) of included studies	The included studies were published in 2005, 2006, 2011, 2012, 2015, 2016, and 2017.
Number of primary studies included in the systematic review	Seven before-and-after studies, published in 2005, 2006, 2011, 2012, 2015, 2016, and 2017, were included in this review. The funding sources for primary studies were not reported.
Types of studies included	Prospective clinical studies were eligible for inclusion. A list of excluded studies and reason(s) for exclusion were provided.
Country of origin of included studies	The studies were conducted in Brazil (one study), Republic of Korea (two studies), and the USA (four studies).
Appraisal instruments used	The authors reported that “Because the identified assessment tools were deemed to not adequately capture study quality and risk of bias for the scope of this type

Parameter	Extraction
	of review, we created a tailored list of assessment criteria to measure relevant study quality metrics deemed appropriate to our specific question.” ^{155 (p109)} This list of measures included important clinical and technical measures but did not include an assessment of research practice (randomisation, representativeness, control of confounding, blinding of patients, provider or assessors)
Appraisal rating	On the topic risk of bias, the authors reported that, “Six of the 7 studies reported inclusion and exclusion details for the sample and high rates of follow-up. No studies included participants who did not receive dental treatment as a comparison group. Most studies reported the materials used, the material that contained BisGMA, and detailed their laboratory methods. Five studies reported using BPA [bisphenol A]-free containers for collection and storage. Four studies reported a limit of detection of BPA, but only 2 reported the number of samples below the limit of detection. Four studies analyzed urinary BPA concentration by demographics and treatment characteristics. Three studies collected information about other sources of BPA, but only 1 study examined other potential sources of BPA in the analysis. All but 2 studies considered urinary dilution as part of their analysis. Only 1 study reported that laboratory analysts were blinded to the collection scheme, sample-numbering system, and material brand used.”^{155 (p109)} “Our risk-of-bias assessment suggests that the studies included had methodologic limitations that could have influenced findings. The small sample sizes of most studies make it difficult to assess associations. Moreover, studies were carried out in different settings, including university, military, academic, research, private practice, and community dental clinics. The potential health implications of an increase in urinary BPA concentrations may vary among different populations.”^{155 (p113)} Publication bias was not measured or discussed
Method of analysis	Marzouk <i>et al.</i> reported that “For all measures, we report ng/mL (nanograms per milliliter) as the unit of measurement for BPA [bisphenol A] concentrations... Because of the heterogeneity in type of materials, laboratory methodologies, time points, and reporting of outcomes, we chose not to perform quantitative comparisons and instead performed a qualitative synthesis”.^{155 (p109)}
Outcome assessed	Urinary BPA concentrations before and after dental treatment with any type of resin-based dental material. Urinary bisphenol A concentrations: Martin (2005); Joskow (2006); Kang (2011); Kingman (2012); Kim (2015); Maserejian (2016); Moreira (2017).
Results/findings	According to the authors, “All 7 studies reported a substantial increase in mean urinary BPA concentrations 24 hours after treatment, with the increase ranging from 43% to 354% compared with pretreatment. The percentage increase varied for the different types of materials. The increase in mean urinary BPA concentrations 24 hours after treatment was between 43% and 51% for dental composite restorations, 30% and 113% for dental sealants, and 95% and 319% for orthodontic adhesives. The 1 small study that combined dental sealants and dental composite restorations is the oldest and reported the highest increase at 354%. Findings may be affected by outliers.”^{155 (p109)} The authors also stated that “In all studies, BPA [bisphenol A] concentrations increased 24 hours after treatment. The 2 studies with the largest sample sizes found statistically significant increases >40% in urinary BPA concentrations at 24 hours post-treatment (both <i>p</i>-values <0.01). The 1 study to examine urinary BPA concentrations beyond 1 month post-treatment found that concentrations returned to baseline by 14 days after treatment and remained at baseline 6 months after treatment.”^{155 (p106)}
Significance/direction	Marzouk <i>et al.</i> reported that “Across all studies, we observed an increase in urinary BPA concentrations 24 hours after treatment. There was also some suggestion of an increase at 7 days post-treatment. Beyond 1 week of treatment, the evidence is mixed.”^{155 (p112)}
Heterogeneity	According to Marzouk <i>et al.</i>, “There was substantial heterogeneity among the studies included in this review, and a limitation is that we were not able to combine estimates across studies.”^{155 (p113)} The authors also stated that “Despite the heterogeneity in study design and methods, results show a consistent increase in urinary BPA between baseline and

Parameter	Extraction
	24 hours following dental treatment. This consistency suggests the release of BPA during dental treatment from resin-based dental materials.” ¹⁵⁵ (p112)
Comments	According to the authors, “This is the first comprehensive assessment of systemic BPA exposure from dental treatment in humans.” ¹⁵⁵ (p112)

Paula *et al.* (2019)

Parameter	Extraction
First author and year of publication	Paula <i>et al.</i> (2019) ¹⁵⁶
Objectives	Estimated the release of bisphenol A, after the use of composite resins and/or dental sealants, to determine if the increase is higher than the acceptable daily exposure and may cause harmful effects to the health of children, adolescents, and pregnant adults. However, harmful effects were not examined.
Participants	Mixed dentition, non-cavitated caries and cavitated, micronvasive and restorative treatments Children, adolescents, and pregnant adults following use of composite resins and/or sealants in dental treatments The sample sizes are completely different, ranging from 4 to 1,001 patients, with a mean of 171.6 participants (and ±268.19 standard deviations). The age of patients ranged from children to adults aged 55 years. Gender was not reported.
Setting/context	The countries and clinical settings for the included studies were not reported.
Description of interventions/phenomena of interest	Release of bisphenol A following the use of composite resins and/or dental sealants In dentistry, monomers with a bisphenol A core are commonly used in resin-based materials such as root canal sealers, adhesives, composites, and sealants. Although dental materials typically do not contain pure bisphenol A, the presence of this compound can be the result of the manufacturing process, or a byproduct of degradation of bisphenol A-glycidyl methacrylate or other components, such as ethoxylated bisphenol. In the intraoral environment, these materials are exposed to extreme thermal changes, pH variances, mechanical erosion, and degradation occurrence from bacterial and salivary enzymes, which can cause bisphenol A release. During or just after resin placement, its leaching can also occur by incomplete monomer polymerisation. Bisphenol A and its derivatives are classed as endocrine active substances, and can cause estrogenic activity that may affect human health. As early as the 1930s, bisphenol A was recognised as an endocrine disruptor that mimics estrogen and alters hormonal function. The increased emphasis on bisphenol A release can be attributed to the fact that it plays a role in the pathogenesis of several endocrine disorders, including female and male infertility; hormone-dependent tumours, such as breast and prostate cancer; polycystic ovary syndrome; precocious puberty; several metabolic disorders, including obesity; and teratogenic effects, even at a low dose. The United States of America’s (USA’s) Environmental Protection Agency set a reference value for acceptable daily bisphenol A exposure at <50 (microgram of medication per kilogramme body weight) µg/kg per day. However, temporary tolerable daily intake for bisphenol A, calculated by the USA’s Environmental Protection Agency as well as by the European Food Safety Authority, was reduced from 50 µg/ to 4 µg/kg body weight per day in 2015, increasing the importance of control in release of this compound or even its integration into the composition of various materials. For surfaces treated with resins, there is no specific recommendation and there exist only a few studies, such as those reported. The scientific community has already started discussing this problem, but has not yet made clinical recommendations. Several sources of bisphenol A were examined, such as adhesives, resin composites, dental sealants, and acrylic resins used to make several types of treatments, such as restorations, fissure sealants, or bonded orthodontic appliances. For evaluating the release of bisphenol A after these treatments, the investigators used three mediums for measurement: 15 studies analysed the bisphenol A levels in saliva, 4 analysed levels in blood, and 8 analysed levels in urine. The bisphenol A evaluation method of choice was high-pressure liquid chromatography in most studies, but gas chromatography,

Parameter	Extraction
	enzyme-linked immunosorbent assay, estrogenic assay, and flow cytometry (immune and renal function) were also used. The follow-up periods were similar, with evaluations immediately after the treatment, in the first hour after the treatment, and in the first day after the treatment. Later follow-up times ranged from 1 month to 5 years.
Databases and sources searched	Three electronic databases were searched: PubMed, Cochrane (specific details not provided), and Embase. The research included English-, Spanish-, and Portuguese-language filters, using a combination of the keywords. The search end date is not reported, but is likely to be some time in 2018. The discussion mentions that only studies published after 1990 were included. Additional search methods included the reference lists of relevant studies, which were scrutinised manually. The systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) database. Three independent reviewers scrutinised the studies based on the inclusion criteria and subsequently extracted the data. The research received no external funding and the authors declared no conflict of interest.
Date range (years) of included studies	The 20 included studies were published between 1996 and 2018.
Number of primary studies included in the systematic review	The 20 included studies were published between 1996 and 2018. The study designs were randomised controlled trials (16 studies), prospective cohort studies (3 studies), and case-control studies (1 study). The sources of funding for primary studies were not reported.
Types of studies included	Randomised controlled trials, prospective cohort studies, and case-control studies were included. The reasons for selecting these study designs were not explained. The list of excluded studies and reasons for exclusion were not provided.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included randomised controlled trials, and the Risk Of Bias In Non-Randomized Studies – of Interventions (ROBINS-I) was used for the prospective cohort and case-control studies.
Appraisal rating	Twelve of the 16 randomised controlled trials were judged to have a high risk of bias, and 4 had an unclear risk of bias. Seven of the 16 randomised controlled trials had adequate randomisation and 14 had adequate blinding of assessment outcome. The quality assessment of the four non-randomised studies included in this systematic review considered them to have a low to moderate risk of bias. Bias due to confounding was low risk for all four studies. Bias in outcome measure was considered moderate risk due to missing or unclear information. The authors reported that “However, the quality assessment of the studies, both randomised controlled trials and cohort studies, demonstrated low risk of bias in most parameters, with some moderate risk of bias, concluding a systematic review with strong clinical evidence”.^{156 p1627} indicating an underestimate in the risk of bias in the primary studies. Publication bias was not measured.
Method of analysis	The authors reported that “As the assays’ measurement units were different with very disparate follow-ups, it was impossible to perform a meta-analysis”. ^{156 (p1627)}
Outcome assessed	Estimated the release of bisphenol A, after the use of composite resins and/or dental sealants, to determine if the increase is higher than the acceptable daily exposure and may cause harmful effects to the health of children, adolescents, and pregnant adults. However, harmful effects were not examined. Release of bisphenol A: Randomised controlled trials: Kingman 2012; Kang 2011; Zimmerman-Downs 2010; Sasaki 2005; Chung 2012; Fung 2000; Maserejian 2016; McKinney 2014; Lee 2017; Moreira 2017; Berge 2017 ; Raghavan 2017; Manoj 2018 ; Arenholt-Bindslev 1999; Michelsen 2012; Olea 1996.
Results/findings	All 15 studies of salivary content showed an increase in the levels of bisphenol A within 1 hour of the treatments, either with composite resins or with sealants. This increase in bisphenol A in most studies ranged from 2 to 42 ng/mL, although there are some reports of extreme values ranging from 120 to 931 ng/mL. In follow-ups, the levels decrease over time, for example from treatment to after 1 week. Some studies have evaluated the levels of bisphenol A by the number of

Parameter	Extraction
	surfaces restored or sealed, with an exponential increase in levels from six surfaces upwards. On the other hand, one study performed the evaluation after the treatment followed by mouthwash, demonstrating an abrupt decrease in levels. Two of the four studies that evaluated levels of bisphenol A in the blood reported that it was not detected in serum at any of the study follow-up time points. Five studies evaluating urinary levels of bisphenol A immediately after treatment reported that levels increase slightly after resin-based treatments, but not as markedly as levels detected in saliva. One study measured the estrogenic assay, and an increase immediately after treatment from 0.1 to 1.43 ppm was observed, with only one type of fissure sealant (Delton®); however, levels decreased to below 0.1 ppm after 24 hours. The authors recommended that “some clinical precautions should be taken to decrease the release of bisphenol A, namely the use of rubber dam, the immediate polishing of all resins used, or the use of glycerin gel to avoid non-polymerisation of the last resin layer, and mouthwash after treatment.”^{156 (p1)} In addition, they advised “use of the smallest possible number of restorations or sealants, a maximum of four per appointment”.^{156 (p1)} These measures are even more important in children and adolescents, and in particular for pregnant women to avoid potential teratogenic effects.
Significance/direction	The interpretation of the findings depends on chemical cut-off for bisphenol A.
Heterogeneity	Authors make no comment on heterogeneity.
Comments	GRADE was not used by the review authors. Both randomised and non-randomised studies were included in the review. All 16 trials were judged to have a high or unclear risk of bias. Seven (44%) of the 16 randomised controlled trials had adequate randomisation and 14 (88%) had adequate blinding of assessment outcome. The quality assessment of the four non-randomised studies included in this systematic review considered them to have a low to moderate risk of bias. Bias due to confounding was low risk for all four studies. Bias in outcome measure was considered moderate risk due to missing or unclear information. The quality of the review was rated as critically low using AMSTAR 2 as the authors made no comment on heterogeneity and did not discuss the effects of high or unclear risk of bias on the analysis. The HRB grades the quality of the evidence as low.

Treatment technique

Wang *et al.* (2016)

Parameter	Extraction
First author and year of publication	Wang <i>et al.</i> (2016)¹⁵⁷ (Cochrane Review)
Objectives	Compared the effects (survival and failure) of rubber dam isolation compared with other types of isolation (cotton roll) used for direct and indirect restorative treatments in children’s molars.
Participants	Mixed dentition, both non-cavitated carious lesions and cavitated caries, materials to support application of microinvasive and invasive restorations Population: Children’s primary or permanent molars or premolars Four randomised controlled trials (including split-mouth trials), published between 2010 and 2013, analysed 1,270 participants (among which 233 participants were lost to follow-up) to compare the effects of rubber dam isolation with other types of isolation used for restorative treatments in dental patients. The four trials included participants with different age ranges and receiving various restorative treatments. For the three trials where both age and gender were known, ages ranged from 5.9 to 16.9 years while mean age ranged from 6.3 to 12.3 years, and 60% of the participants were male.

Parameter	Extraction
Setting/context	The studies were conducted in Brazil, China, Germany, and Kenya. One study was carried out in a private dental clinic setting, one in a dental hospital setting, and two in school settings.
Description of interventions/phenomena of interest	Successful restorations in dental patients depend largely on the effective control of moisture and microbes during the procedure. The rubber dam technique has been one of the most widely used isolation methods in dental restorative treatments. Creating a physical barrier around a treatment site to reduce contamination due to moisture and microbes is common practice in medical and dental procedures. Isolating the tooth to be restored from the contamination of moisture or saliva in restoration placement may promote the bonding of the restorative materials to the tooth. Comparator: Other types of isolation (cotton roll usage)
Databases and sources searched	The authors searched nine electronic sources: Cochrane Oral Health Group Trials Register (up to 17 August 2016), the Cochrane Central Register of Controlled Trials (CENTRAL) (2016, Issue 7) (17 August 2016), MEDLINE via Ovid (1946 to 17 August 2016), Embase via Ovid (1980 to 17 August 2016), LILACS via BIREME Virtual Health Library (1982 to 17 August 2016), Scielo via BIREME Virtual Health Library (1998 to 17 August 2016), Chinese Biomedical Literature Database (CBM) (1978 to 30 August 2016), China Science Journal Database (VIP) (1989 to 30 August 2016), and China National Knowledge Infrastructure (CNKI) (1994 to 30 August 2016). The authors searched ClinicalTrials.gov, the WHO's International Clinical Trials Registry Platform, OpenGrey, and Sciencepaper Online (in Chinese) for ongoing trials. There were no restrictions on the language or date of publication when searching the electronic databases. The search strategy is in Appendix 1 of their paper. A protocol was prepared for this review. This review was supported by the National Institute for Health Research, through funding to the Cochrane Oral Health Group Global Alliance, UK.
Date range (years) of included studies	The four randomised controlled trials were published between 2010 and 2013.
Number of primary studies included in the systematic review	Four randomised controlled trials (including split-mouth trials) were included, which analysed 1,270 participants (among which 233 participants were lost to follow-up) to compare the effects of rubber dam isolation with other types of isolation used for restorative treatments in dental patients. Two review authors independently screened the studies and extracted the data. One study did not state its funding source, and one study stated that it received both industry and non-industry funding. The remaining studies stated that they received either industry funding or non-industry funding The trials were published between 2010 and 2013 and included participants with different age ranges and receiving various restorative treatments. For the three studies where both age and gender were known, ages ranged from 5.9 to 16.9 years, while mean age ranged from 6.3 to 12.3 years, and 60% of the participants were male. One study was carried out in a private dental clinic setting, one in a dental hospital setting, and two in school settings. The studies were conducted in Brazil, China, Germany, and Kenya. This review was supported by the National Institute for Health Research, through funding to the Cochrane Oral Health Group Global Alliance, UK.
Types of studies included	All randomised controlled trials or quasi-randomised controlled trials (including split-mouth/crossover trials) were to be included. The list of excluded studies and the reasons for exclusion are presented in a table in the review.
Country of origin of included studies	The studies were conducted in Brazil, China, Germany, and Kenya.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess risk of bias.
Appraisal rating	All four studies were found to be at high risk of bias using the Cochrane Collaboration's risk of bias instrument. Three of the four trials were judged to have adequate randomisation and two were judged to have adequate blinding for outcome assessment. The authors excluded one trial from the analysis due to inconsistencies in the presented data. The authors warned that the proportion of

Parameter	Extraction
	information from studies at high risk of bias is sufficient to affect the interpretation of results, and this was considered during the GRADE assessment. Publication bias was partially dealt with in the search strategy and considered as part of the GRADE assessment.
Method of analysis	The data available were inadequate for the planned meta-analysis, sensitivity analysis, or subgroup analysis. For the primary outcome of survival/success rate of the restorative treatment, the authors calculated hazard ratio or risk ratio with a 95% CI. For the primary outcome of incidence of adverse events, the authors calculated relative risks and a 95% CI to estimate the treatment effect. For the secondary outcomes, they calculated relative risks and a 95% CI for dichotomous data, and mean difference and a 95% CI for continuous data. The authors standardised the data results and did a narrative analysis as the trials measured the same outcome at different time points or different outcomes.
Outcome assessed	Time frame: six months or more Outcome by primary study: Survival and failure rates: Ma 2012 (6 months); Kemoli 2010 (24 months). Adverse events: None of the included studies reported adverse events Restoration's quality: No evidence Cost: No evidence Participant satisfaction: No evidence
Results/findings	The results indicated that dental restorations had a significantly higher survival rate in the rubber dam isolation group compared with the cotton roll isolation group at six months in participants receiving composite restorative treatment of non-carious cervical lesions (risk ratio: 1.19; 95% CI: 1.04–1.37; 1 trial; 162 participants; very low-quality evidence). The rubber dam group had a lower risk of failure at two years in children undergoing proximal atraumatic restorative treatment in primary molars (hazard ratio: 0.80; 95% CI: 0.66–0.97; one trial; 559 participants; very low-quality evidence). One trial reported limited data showing that rubber dam usage during fissure sealing might shorten the treatment time. None of the included studies mentioned adverse effects, reported the direct cost of the treatment, or reported the level of patient acceptance/satisfaction. There was also no evidence evaluating the effects of rubber dam usage on the quality of the restorations. The authors found some very low-quality evidence, from single studies, suggesting that rubber dam usage in dental direct restorative treatments may lead to a lower restoration failure rate, compared with the failure rate for cotton roll usage.
Significance/direction	Favours rubber dam isolation over cotton roll isolation.
Heterogeneity	The authors do not comment on heterogeneity. Heterogeneity was not an issue, as there was only one study assessing each outcome.
Comments	GRADE was used by the review authors. All trials scored high for risk of bias for one or more parameters. Less than 75% of the trials were judged to have adequate blinding of outcome assessment. The sample size for one outcome was less than 200. The quality of the systematic review was judged as high using AMSTAR 2. The HRB graded the evidence in this review as moderate based on the criteria in our protocol. However, we describe it as low as the analyses were based on one trial only. The review authors graded the evidence as very low because there was only one trial in each analysis.

Cavitated caries

Direct restoration material

Arbildo-Vega *et al.* (2020)

Parameter	Extraction
First author and year of publication	Arbildo-Vega <i>et al.</i> (2020) ¹⁵⁸
Objectives	Evaluated the clinical performance (based on 11 parameters) of bulk-fill direct resin composites used in direct restorations in human teeth and compared them with conventional direct resin composites.
Participants	Mixed dentition, cavitated caries, direct restoration materials Across the 16 included studies, the number of patients ranged from 22 to 86, with a follow-up time of between 6 months and 10 years. Ten studies reported that the mean age of the patients was between 7.4 and 55.3 years. Three studies reported that the patients were children aged under 18 years. In the eight studies that reported gender, 47% of participants were male. The total number of treated patients and restored teeth was 764 and 1,915, respectively. In five studies, Class I and Class II restorations were performed, three studies reported on Class I restorations, six studies covered Class II restorations, and two studies reported on non-carious cervical lesion restorations. Among the types of teeth restored, restorations were performed in the permanent incisors, canines, premolars, and molars. In two studies, restorations were performed in primary molars. Regarding the evaluation criteria used for the clinical evaluation of the restorations, all of the studies used the modified parameters of the United States Public Health Service (USPHS) criteria. Six studies reported that the etch-and-rinse method was used and 12 studies used the self-etch method. Five studies mentioned using a rubber dam for moisture control during the clinical restorative procedure. Other included studies used cotton rolls and suction for isolation.
Setting/context	The study countries were Brazil, Denmark, Germany, Saudi Arabia, Sweden, and Turkey. The clinical settings were not reported.
Description of interventions/phenomena of interest	According to the authors, "Currently, bulk-fill resin composites are the materials of choice for indirect dental restorations. They possess lower post-gel shrinkage and higher reactivity to light polymerization than most conventional composites as a result of their increased translucency, improving the light penetration and the depth of cure. The above-mentioned features allow for placement of 4–5-mm-thick increments of bulk-fill material, shortening the clinical procedure and facilitating handling. Due to their different clinical uses, bulk-fill composites can be categorized as either base or full-body bulk-fill resin composites. Base bulk-fill composites have low viscosity, allowing for their placement and adaptation in deep cavities. However, their lower filler content, which results in lower wear resistance, requires the base of the bulk-fill to be covered with a conventional composite (two-step bulk-fill technique). Full-body bulk-fill composites, however, have a higher filler load, making them highly viscous and resistant to wear. As such, these paste-like bulk-fill materials can be placed in the cavity without any coverage (bulk-fill technique). Bulk-fill composites were reported to promote less polymerization shrinkage stress than conventional microhybrid composite during and after the light-curing process in Class II posterior resin composite restorations".^{158 (p2)} In addition, the authors stated that "The included studies mostly used universal adhesives in self-etching mode when placing bulk-fill resins. These adhesives are gaining popularity among clinicians, allowing for simplified procedures, however their dentin bonding potential can be enhanced by modifying the application method".^{158 (p15)}
Databases and sources searched	The authors searched five electronic databases: the Cochrane Central Register of Controlled Trials (CENTRAL), Embase, MEDLINE via PubMed, Scopus, and Web of Science. The search of the literature was performed without any date limits and

Parameter	Extraction
	was done up until May 2020. Search limits were not reported. There were no supplementary sources searched. The preparation of a protocol was not reported. Extraction and screening were completed in duplicate. The title and abstracts of all the articles identified by the electronic search were read and evaluated by four authors. Disagreements between the reviewers were resolved by consensus among all the authors. Funding: This research received no external funding. Conflicts of interest: The authors declared no conflicts of interest.
Date range (years) of included studies	The included randomised controlled studies were published between 2010 and 2020: four studies were published in 2020, two studies were published in 2019, two studies were published in 2018, five studies were published in 2017, one study was published in 2016, and two studies were published in 2010.
Number of primary studies included in the systematic review	The authors included 16 randomised controlled studies: 14 were split-mouth trials and 2 were parallel trials. The sources of funding for the included primary studies were not reported.
Types of studies included	Only randomised controlled studies were eligible for inclusion. The authors did not provide a list of excluded studies, but did provide their reasons for exclusion.
Country of origin of included studies	The study countries were: Brazil (three studies), Germany (two studies), Saudi Arabia (one study), Sweden (one study), and Turkey (eight studies). One other study was undertaken across facilities in Denmark and Sweden.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	Only one of the 16 included studies was judged to have a low risk of bias; one study was judged to have a high risk of bias and 14 studies were judged to have an unclear risk of bias. All of the 16 included studies were at low risk of bias for randomisation and 12 (75%) studies were at low risk of bias for outcome assessment. The authors report that "randomization and allocation concealment are critical to the design of randomized clinical trials to avoid selection bias. Most of the included studies did not provide a complete description of these steps." Publication bias was not measured or discussed.
Method of analysis	The authors reported that "The data from each study were placed and analysed in the RevMan 5.3 program using a relative risk (RR) measure and with a 95% confidence interval (CI)". ^{158 (p4)}
Outcome assessed	Analysis of the clinical performance of conventional resins and bulk resins in restorations was based on the following 11 parameters: absence of fractures; absence of discolouration or marginal staining; adequate marginal adaptation; absence of post-operative sensitivity; absence of secondary caries; adequate colour stability and translucency; proper surface texture; proper anatomical form; adequate tooth integrity (no wear); adequate restoration integrity; and proper occlusion. The other two clinical parameters – absence of inflammation and adequate point of contact – were not analysed, since each of them was reported by only one included study. The follow-up periods observed in this study ranged from 6 months to 10 years. • Fifteen studies reported an absence of post-operative sensitivity and an absence of secondary caries • 13 studies reported proper surface texture and proper anatomical form • 1 study reported on each of the absence of inflammation and adequate point of contact parameters. Clinical performance (based on 11 parameters): Akman 2020; Balkaya 2020; Çolak 2017; van Dijken and Pallesen 2017; Yazici 2017; van Dijken and Pallesen 2016; Arhun 2010; Manhart 2010; Correia 2020; Frascino 2020; Al-Sheikh 2019; Canali 2019; Heck 2018; Oter 2018; Atabek 2017; Bayraktar 2017.
Results/findings	The authors reported that "The clinical parameters (modified USPHS criteria) evaluating the clinical effectiveness of conventional resins and bulk resins in restorations were determined in all studies, revealing that there were no significant differences between the two types of resins, regardless of the type of

Parameter	Extraction
	restoration, type of tooth restored, or technique used". ^{158 (p13)} However there are some borderline significant results in the post-operative sensitivity subgroup analysis and these findings are presented below. They continued, "The subgroup analysis was performed based on the cavity form (Class I/II and non-carious cervical lesions), type of dentition (primary or permanent), and tooth restoration technique (incremental or bulk or two-step bulk). The analyses showed that in the aspect of absence of fractures, absence of discoloration or marginal staining, adequate marginal adaptation, absence of secondary caries, adequate color stability and translucency, proper surface texture, proper anatomical form of the restoration, adequate integrity of the tooth without the presence of wear, adequate restoration integrity, and proper occlusion, there were no significant differences between conventional resins and bulk resins. The data were found to be homogeneous and around the line of no effect". ^{158 (p13)} With respect to the absence of post-operative sensitivity, the analyses revealed that there were no significant differences when comparing a conventional resin with a bulk-fill resin covered with a conventional resin (two-step bulk-fill technique). However, regarding the type of tooth restored, and technique used there was borderline significant difference between conventional resins and bulk-fill resins in all types of restorations combined (RR: 1.02; 95% CI: 1.00–1.05; $p=0.05$; I²: 0%; 1,185 participants; 13 trials). The results showed reduced or no post-operative sensitivity for the subgroup non-carious cervical lesions restored with composite resins rather than bulk-fill resins (RR: 1.11; 95% CI: 0.99–1.23; $p=0.06$; I²: 0%; 224 participants 3 trials). A favourable and borderline significant effect of absence of post-operative sensitivity was also seen for cavities treated in permanent dentition (RR: 1.03; 95% CI: 1.00–1.06; $p=0.04$; I²: 0%; 913 participants; 11 trials) and with incremental technique for composite resins (RR: 1.02; 95% CI: 1.00–1.05; $p=0.05$; I²: 0%; 1115 participants; 12 trials). The authors stated that "In the present investigation, the null hypothesis was not rejected. The clinical effectiveness of bulk-fill resin is similar to conventional resin, regardless of the type of restoration (Class I, II, or non-carious cervical lesions), the type of tooth restored (primary or permanent teeth), or the restoration technique used (incremental, bulk, or bulk two-step)". ^{158 (p14)} The authors went on to state that, "Given that there are no reported clinical differences between restorations made of conventional resin materials and bulk-fill resin materials (in two-step or bulk techniques), these results seem promising, as most clinicians prefer to work with easy-to-use, clinically reliable bulk-fill resin materials, the placement of which occupies less chair-time in the dental office". ^{158 (p16)}
Significance/direction	The results indicated that there is no difference between restorations with conventional resins and those with bulk-fill resins regardless of the type of restoration, type of tooth restored, and restoration technique used.
Heterogeneity	The authors do not measure or report on heterogeneity.
Comments	According to the authors in their discussion, "This meta-analysis showed that there were no significant differences between conventional and bulk-fill resin compounds in terms of the type of restoration, the type of tooth restored, and the technique used. The results of this systematic review and meta-analysis are similar to those of Veloso <i>et al.</i> 2019 and Boaro <i>et al.</i> 2019. Both studies reported that the clinical performance of conventional and bulk-fill resin compounds in direct posterior tooth restorations was similar, within a follow-up period of 12 to 72 months and up to 10 years, respectively". ^{158 (p15)} The authors note the following limitations: "The current study has some limitations, such as the design of the clinical trial and the follow-up period, which could influence the results of the clinical trial...The clinical trials included in this study used different bulk-fill restorative materials with different etching techniques, which made it more difficult to compare them. All of the studies included in this review used the modified USPHS criteria, however there were some differences between each one, resulting in a lack of standardization...randomization and allocation concealment are critical to the design of randomized clinical trials to avoid selection bias. Most of the included

Parameter	Extraction
	studies did not provide a complete description of these steps...For all of these reasons, the authors recommend that the results of this review should be interpreted with caution. Additional randomized clinical trials with better designs are needed". ^{158 (p16)}

Kielbassa *et al.* (2016 and 2017)

Parameter	Extraction
First author and year of publication	Kielbassa <i>et al.</i> (2016 and 2017) ^{159,160}
Objectives	Compared the clinical performance of high-viscosity glass ionomer cement covered with a resinous coating with the use of amalgam (no studies), resin composite, or other glass ionomer cements in Class I and Class II restorations of posterior primary or permanent teeth. Critically appraised the methodologies of the various studies.
Participants	Mixed, dentition, cavitated caries, direct restoration materials Population: Posterior (premolar or molar) primary or permanent teeth in children and adults. The cavities included were Class I and Class II. Only three trials had a quality assessment completed, and the Health Research Board (HRB) presents the characteristics and results of these three studies. The age of the participants was not provided. The three trials comprised 784 participants and 1,395 teeth with Class I or II cavities. Age and gender are not reported. The follow-up period ranged from 36 to 48 months.
Setting/context	The study countries were not reported.
Description of interventions/phenomena of interest	According to Kielbassa <i>et al.</i> , "recently, high-viscosity glass-ionomer cement (hvGIC) processed with a resinous coating (RC) has been introduced, and has been marketed as a restorative material in load-bearing Class I cavities (and in Class II cavities with limited size), thus serving as a possible alternative to amalgam filling." ^{160 (p9)} Comparator: Amalgam (no studies), resin composite, or other glass ionomer cements
Databases and sources searched	The authors searched four sources (PubMed, Embase, Scopus, and Cochrane Library). No search dates were provided. In addition, the reference lists of included and other relevant papers were searched. The authors did not report preparing a protocol. Two reviewers screened the literature. It is not clear who extracted the data. The source of funding for the study is not reported and conflicts of interest are declared for one author only.
Date range (years) of included studies	The three included trials were published in 2014, 2015, and 2016.
Number of primary studies included in the systematic review	Twenty-six articles based on eight clinical trials or retrospective studies were included. Only three trials had a quality assessment completed, and the HRB presents the characteristics and results of these three studies. The three trials were published in 2014, 2015, and 2016. Two of the included studies were industry funded, and the funding status of the other trial was unclear.
Types of studies included	Clinical trials and cohort studies were eligible for inclusion The list of excluded studies is not reported.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The authors used the Oxford Centre for Evidence-Based Medicine's tool to assess risk of bias.
Appraisal rating	The risk of bias for the three included trials was judged as low for one study, unclear for one study, and high for one study. Two of the three trials had adequate randomisation and one had adequate blinding for outcome assessor. The authors say that the quality of the randomised controlled trials needs improvement, but they do not elaborate on this statement. The focus in the included primary studies appears to be to be permanent or primary posterior teeth.
Method of analysis	The authors reported that they were advised not to do a meta-analysis because there were only three fully reported randomised controlled trials, and two of these were single centre with small sample sizes.
Outcome assessed	Outcome: Clinical performance in the medium or long term

Parameter	Extraction
	Minimum follow-up time: six months Primary outcomes: Colour match and success at three or four years Time frame: six months to six years Klinke 2016; Gurgan 2015; Diem 2014
Results/findings	In a narrative analysis, the authors reported that two of the three included studies reported high survival of Class I restorations and good colour matching using either glass ionomer cement or resin-modified glass ionomer cement. On the other hand, the third study reported a high proportion of unsatisfactory multi-surface Class II restorations. The three trials reported no differences in survival between the intervention and control groups. According to Kielbassa <i>et al.</i>, "Within the respective indications and cavity geometries, the high-viscosity glass ionomer cement with a resinous coating in Class I restorations of posterior primary or permanent teeth would seem possible; this could merge the phase-down of mercury and the objectives of minimally invasive treatment to some extent, and might be a restorative alternative for patients with Class I cavities suffering from allergies to or not willing to afford other sophisticated or expensive techniques, such as composite resin."¹⁶⁰ (p16) However, the evidence from this review is very low quality with a high risk of bias, and is therefore inadequate evidence upon which to judge the performance of high-viscosity glass ionomer cement-resin composites as a restorative intervention.
Significance/direction	No difference.
Heterogeneity	Not discussed.
Comments	GRADE was not used by the review authors. Two of the three trials were judged to have a high or unclear risk of bias. Two (66%) of the three trials had adequate randomisation and one (33%) had adequate blinding for outcome assessor. The quality of the review was rated as critically low using AMSTAR 2 as the authors made no comment on heterogeneity and did not discuss the effects of high or unclear risk of bias on the analysis. The HRB grades the quality of the evidence as low.

Restoration support material

Elkady *et al.* 2020

Parameter	Extraction
First author and year of publication	Elkady <i>et al.</i> (2020) ¹⁶¹
Objectives	Evaluated the effect of chlorhexidine as a cavity pretreatment or mix-in on the survival of atraumatic restorative treatments in primary or permanent teeth with occlusal or occlusoproximal cavities.
Participants	Mixed dentition, cavitated caries, restoration support material Four randomised controlled trials, involving 261 patients with a mean age of 3.84–14.6 years who had received a total of 467 atraumatic restorative treatments, were included. All studies focused on cavitated lesions in primary or permanent teeth, with a minimum cavity size allowing access with a small hand excavator. Two studies included occlusal or occlusoproximal cavities, while the other two studies included only occlusal cavities. Chlorhexidine was used as a glass ionomer cement mix-in in three studies, while another study used it as a cavity pretreatment.
Setting/context	Three studies were conducted in Egypt and one in Brazil. The study settings were primary school, secondary school, and outreach clinic.
Description of interventions/phenomena of interest	The authors stated that "Contemporary ART [atraumatic restorative treatment] includes selective carious tissue removal and hence builds on the concept of restoring the ecological balance within a cavity by sealing residual lesions and bacteria. To support this effect, cavity pretreatment or the use of antibacterial substances as a mix-in into restorative materials used during ART have been suggested, with chlorhexidine being the most prominent substance proposed and used. Chlorhexidine is also suggested to inhibit matrix metalloproteinase and thereby reduce the degradation of resin-dentin hybrid layers and to increase bond

Parameter	Extraction
	strengths of dental adhesives to dentin. It has been employed on its own for cavity pretreatment (by rinsing the cavity) or mixed into a range of restoratives like composites or GICs [glass ionomer cements] for a proposed long-term beneficial effect. Notably, such mix-in into restoration materials has been found to potentially affect the physical properties of the materials.”¹⁶¹ (p2)
Databases and sources searched	Four databases – MEDLINE via PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL)– were searched. The search was conducted up to 5 May 2020. No language or time limitations were set. The authors screened ClinicalTrials.gov for ongoing studies, and they reviewed the reference lists of included studies and related reviews for potentially eligible studies. The authors submitted their protocol for registration, but it was not authorised by the International Prospective Register of Systematic Reviews (PROSPERO). Extraction and screening were completed in duplicate. Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. Conflicts of interest: The authors reported no conflicts of interest.
Date range (years) of included studies	The included studies were published in 2009, 2017, 2018, and 2019.
Number of primary studies included in the systematic review	Four randomised controlled trials were included. Three studies used a parallel-arm design, while one used a split-mouth approach. Two studies were individually randomised trials and the other two studies were cluster-randomised trials (with the individual as cluster, i.e. more than one restoration per patient). The sources of funding for primary studies were not reported.
Types of studies included	The review authors decided to include randomised controlled trials only. The review authors provided a list of excluded studies and justified their exclusion from the review.
Country of origin of included studies	The study countries were Brazil (one study) and Egypt (three studies).
Appraisal instruments used	The revised version of the Cochrane Collaboration’s risk of bias tool for randomised trials was used to assess the included trials.
Appraisal rating	All included trials had an unclear risk of bias. Two (50%) of the four studies was at low risk of bias for randomisation, and all four studies were at low risk of bias for outcome assessment. The authors reported that “Overall, we conclude that data supporting or refuting the use of CHX [chlorhexidine] in ART [atraumatic restorative treatment] are scarce and the included studies of limited robustness. This is also indicated by the risk of bias assessment, which found the studies at unclear risk of bias.”¹⁶¹ (p7) The authors stated that “Given the limited number of included studies, no further assessment of small-study or publication bias (e.g. funnel plot assessment, Egger test) were conducted.”¹⁶¹ (p5)
Method of analysis	A random-effects meta-analysis was conducted, with odds ratios (OR) and 95% confidence intervals (CIs) as effect estimates. Heterogeneity was measured using the I ² inconsistency index. Three studies, involving a total of 167 restorations in the chlorhexidine group and 188 restorations in the control group that had a 1-year follow-up, were submitted to meta-analysis.
Outcome assessed	For all reported follow-up periods, the survival of restorations was measured for both the test and control groups. For meta-analysis, the follow-up period most frequently found across studies (which was one year) was used. Survival: Farag 2009; Duque 2017; Kabil 2017; Mobarak 2019.
Results/findings	Three randomised controlled trials (involving a total of 167 restorations in the chlorhexidine group and 188 restorations in the control group) were entered into the meta-analysis, which included only the three studies reporting on restoration survival after one year. There were no significant differences between the groups and heterogeneity was low (OR: 0.79; 95% CI: 0.26–2.40; <i>p</i>=0.68, I²: 3%; 355 restorations; three trials). Using a sensitivity analysis, the comparative survival after different follow-up periods was assessed, without significant differences between groups. According to the review authors, “We did not find a significant difference in the survival of restorations placed in the experimental (CHX [chlorhexidine]) versus

Parameter	Extraction
	the control (no CHX) group. Overall, the evidence supporting the usage of CHX in ART [atraumatic restorative treatment] is very limited; in our meta-analysis, we could include only three studies, mainly from Egypt and mainly in children or adolescents. Two of them showed possible benefit of CHX at the 1-year recall interval; however, these studies recorded very few events at this point of time (which was also why they also did not find a significant difference)".^{161 (p7)} The authors went on to say that "The strength of the evidence emerging from our study was estimated as low. This was due to downgrading associated with limitations in the studies design and imprecision".^{161 (p7)} The authors reported that, "Overall, we conclude that data supporting or refuting the use of CHX [chlorhexidine] in ART [atraumatic restorative treatment] are scarce and the included studies of limited robustness. This is also indicated by the risk of bias assessment, which found the studies at unclear risk of bias by and large. Overall, we cannot recommend the additional step of cavity pretreatment of mix-in of CHX into restoratives associated with ART (especially considering that this step comes with additional effort and costs)".^{161 (p7)} There were no significant differences between chlorhexidine compared with controls at three months (2 trials), six months (2 trials), nine months (1 trial) one year (3 trials), 1.5 years (1 trial), two years (1 trial) and five years (1 trial). The quality of the evidence was low.
Significance/direction	There were no significant differences between chlorhexidine compared with controls.
Heterogeneity	Heterogeneity was low at one year and high at three months.
Comments	Grading of Recommendations, Assessment, Development and Evaluations (GRADE) was used. The authors noted that "The strength of the evidence emerging from our study was estimated as low. This was due to downgrading associated with limitations in the studies design and imprecision".^{161 (p7)} The authors note that, "as a limitation, only a few studies were available for analysis; mainly from one country and in a non-generalizable population (children and adolescents), with short follow-up times, small sample sizes and few events. Any findings from these studies are prone to erroneous conclusions, and our meta-analysis may be underpowered to demonstrate significant benefit. Larger studies with longer follow-up and studies investigating CHX [chlorhexidine] application in ART [atraumatic restorative treatment] in adults or elderly [patients] are warranted. Third, we pooled two very different applications of CHX, as cavity pretreatment and as mix-in into GI [glass ionomer], into our study, mainly as both serve a similar goal. Given the studies all pointing into the same direction (at least after longer follow-up), we assume the impact of this combined assessment to be low. Statistical heterogeneity was low, too, which supports this notion. Last, our review has not been registered, as despite repeated efforts, no registration on PROSPERO was possible. An ethics-approved protocol is available, though".^{161 (p7)} Furthermore, they stated that, "Given the limited number of included studies, no further assessment of small-study or publication bias (e.g. funnel plot assessment, Egger test) were conducted".^{161 (p5)}

Da Rosa *et al.* (2019)

Parameter	Extraction
First author and year of publication	Da Rosa <i>et al.</i> (2019) ¹⁶²
Objectives	Evaluated the role of calcium hydroxide liner in the treatment of deep carious lesions in primary or permanent teeth with respect to restoration failure.
Participants	Mixed dentition, cavitated caries, restoration support material All participants had to have deep carious lesions treated with and without a calcium hydroxide liner. Participants in the 15 studies evaluating primary teeth ranged in age from 3 to 12 years, while those in the 2 studies evaluating permanent teeth ranged in age from 11 to 35 years.

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	According to Da Rosa <i>et al.</i> , "Considering all the studies in primary teeth (without considering studies with the same subjects evaluated), a total of 1,036 teeth in 567 subjects between 3 and 12 years old were evaluated. The follow-up times varied from 3 to 60 months". ^{162 (p591)}
Setting/context	The study countries and clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: Calcium hydroxide liners. Comparator: Alternatives to calcium hydroxide liners. The authors described the intervention as follows: "In both selective or stepwise removal of carious tissue, calcium hydroxide (CH) continues to be the lining material most commonly used over the carious tissue left in place, because of its alkalinity, biocompatibility and capacity of inducing pulp-dentine remineralization and decreasing bacterial infection. The purpose of using a liner is to promote the formation of a dentine bridge and tertiary dentine to protect pulp tissue from thermal and electrical stimuli, or chemical agents leached from adhesive systems".^{162 (p589)} Their description of the comparator was as follows: "Only two studies evaluated stepwise removal of caries, while the others evaluated selective removal of carious tissue. CH [calcium hydroxide] was compared with an inert material (wax or gutta-percha) in four studies. Seven studies compared CH with adhesive systems, of which four studies compared CH with total-etch materials and four compared it with self-etch adhesives. In the majority of included studies, a resin composite was used as the restorative material".^{162 (p591)}
Databases and sources searched	Two independent reviewers carried out the literature search in eight databases – MEDLINE via PubMed, LILACS, IBECs, Web of Science, Brazilian Library in Dentistry (BBO), Scopus, Scielo, and the Cochrane Library – up to 27 February 2018. Only studies published in the English language were included. The references of the articles included were also manually checked in order to identify additional relevant studies. A protocol was prepared and registered in PROSPERO. Extraction and screening were completed in duplicate. The review was supported by Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul and was financed in part by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES). The authors stated explicitly that there were no conflicts of interest in connection with this article.
Date range (years) of included studies	The included studies were published between 2002 and 2017.
Number of primary studies included in the systematic review	The authors stated that "A total of 17 studies fulfilled all the selection criteria and were included in the qualitative analysis. Among these, 15 studies were performed in primary teeth and two studies in permanent teeth. Six randomised controlled trials in primary teeth were included in the meta-analysis".^{162 (p591)} Fourteen of the studies that evaluated calcium hydroxide liners in primary teeth were randomised controlled trials, while one was a retrospective study. The two studies that evaluated calcium hydroxide liners in permanent teeth were randomised controlled trials. The included studies were published between 2002 and 2017. Study funding details were not reported for the primary studies.
Types of studies included	Prospective or retrospective clinical trials were eligible for inclusion. A list of studies excluded at the full-text stage was not provided in the review.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	Sixteen of the included 17 studies were at high risk of bias. Sixteen (94%) of the 17 included studies were at low risk of bias for randomisation, and 7 (41%) of the 17 included studies were at low risk of bias for outcome assessment. Regarding the risk of bias and how it affected the analysis and quality of the evidence, the authors stated that "the included studies had low risk relative to selection bias (sequence generation, allocation concealment), reporting bias (selective reporting), incomplete outcome data and other biases. High risk of bias was observed for performance (blinding of participants) and detection bias

Parameter	Extraction
	(blinding of operators) in the majority of included studies. Regarding quality of evidence assessed by GRADE, low quality of evidence was considered when the failure in primary teeth with CH [calcium hydroxide] liner versus inert material and with CH liner versus adhesive systems were compared, due to limitations, imprecision and inconsistency of the included studies. Moderate level of evidence was considered when CH liner was compared with glass ionomer cement. In addition, when the failures in permanent teeth were analysed, a very low level of evidence was considered, due to the inclusion of only a few available studies, which also presented methodological limitations, imprecision and inconsistency, in addition to short-term evaluations".^{162 (p597)} Publication bias was considered as part of the GRADE assessment.
Method of analysis	According to Da Rosa <i>et al.</i>, "The analyses were performed with Review Manager Software version 5.2 considering the clinical and radiographic success rate of teeth treated with or without CH [calcium hydroxide] liner with data collected from randomized clinical trials with at least 12 months of follow-up. Global analysis comparing CH with adhesive systems (total-etch and self-etch) and with glass-ionomer cements was performed. Subgroup analysis considering 12, 24 and 50 months of follow-up was also performed. In the global analysis, teeth lost due to exfoliations or dropout patients were not included. Additionally, a sensitivity analysis was performed, considering exfoliations or dropouts as success or failures. Pooled-effect estimates were obtained by comparing the risk difference in each study with a 95% confidence interval (CI). A fixed-effects model was used, and heterogeneity was assessed by using Cochran's Q test and inconsistency I^2 statistics, with values higher than 50% being considered indicative of substantial heterogeneity".^{162 (p590)}
Outcome assessed	The outcomes assessed were failure in primary teeth and failure in permanent teeth. The required outcomes had to be obtained by clinical, radiographic, or laboratory evaluations. Restoration failure: Primary teeth: Bressani 2013; Buyukgural and Cehreli 2008; Casagrande 2008; Casagrande 2009; Casagrande 2010; Dalpian 2012; Dalpian 2014; Duque 2009; Falster 2002; Franzon 2007; Franzon 2009; Marchi 2006; Marchi 2008; Marchi 2016. Permanent teeth: Corralo and Maltz 2013; Pereira 2017.
Results/findings	The authors stated that "A meta-analysis was performed with six RCTs [randomised controlled trials] in primary teeth. Risk difference represents the amount of... risk, which decreased or increased when there was exposure compared with the risk without exposure. A positive risk difference value means increased risk due to the exposure, which was observed throughout the meta-analysis for the CH [calcium hydroxide] liner group. Furthermore, this meta-analysis revealed a non-significant risk difference for clinical success [pulp health status] of deep carious lesions treatment with or without CH liner. The overall risk difference for CH versus adhesive systems was 0.06 [95% CI: 0.01 to 0.13], meaning that CH and adhesive systems had similar clinical success in the treatment of deep carious lesions after selective removal of carious tissue ($p=0.11$). Moreover, the overall risk difference for CH versus GIC [glass ionomer cement] was 0.10 [95% CI: 0.01 to 0.22], with no significant differences between groups ($p=0.08$). When CH liner was compared with only self-etch adhesives, the overall risk difference was 0.01 [95% CI: 0.04 to 0.04], with no significant differences between groups ($p=0.88$; Chi-squared test, $p=0.75$; $I^2=0\%$). Moreover, no difference was found when CH liner was compared with only total-etch adhesives ($p=0.39$; Chi-squared test, $p=0.05$; $I^2=66\%$), with an overall risk difference of 0.07 [95% CI: 0.09 to 0.22]. Subgroup analysis at 12, 24 and 50 months of follow-up also revealed CH and control groups had... similar clinical success rates considering healthy pulp status ($p>0.05$). The sensitivity analysis considering exfoliations or dropouts as success showed the overall risk difference was 0.04 [95% CI: 0.01 to 0.09], with similar clinical success between groups ($p=0.12$; Chi-squared test, $p=0.35$; $I^2=10\%$). Moreover, the sensitivity analysis considering exfoliations or dropouts as failures showed the overall risk difference was 0.04 [95% CI: 0.02 to 0.10], with similar clinical success rates between groups ($p=0.16$; Chi-squared test, $p=0.11$; $I^2=40\%$".^{162 (p593–597)}

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	According to the authors, “The hypothesis tested was accepted since no included study demonstrated a beneficial effect of the use of CH liner in the clinical success of deep caries lesion treatments. Therefore, the treatment of deep caries lesions was not considered a material-dependent technique, with no essential role associated with the CH lining material”.^{162 (p598)} The authors’ overall conclusions were that “Although CH [calcium hydroxide] liner is commonly used by clinicians in deep carious lesion treatments, the available literature demonstrated that this material has no beneficial influence on the clinical success of selective or stepwise removal of carious tissue. For primary teeth, the level of evidence was moderate when CH liner was compared with GIC [glass ionomer cement], and low when it was compared with inert materials or adhesive systems. For permanent teeth, evidence of very low quality indicated that CH liner would have no effect on clinical success of deep caries lesion treatments. Further long-term and well-designed RCTs [randomised controlled trials] are needed to confirm whether the clinical success achieved with CH liner and control materials remains similar over time”.^{162 (p601)}
Significance/direction	Results listed by outcome above
Heterogeneity	Regarding heterogeneity, the authors stated that “heterogeneity was assessed by using Cochran’s Q test and inconsistency I ² statistics, with values higher than 50% being considered indicative of substantial heterogeneity”. ^{162 (p590)}
Comments	GRADE was used by the review authors The authors reported that “Regarding quality of evidence assessed by GRADE, low quality of evidence was considered, when the failure in primary teeth with CH [calcium hydroxide] liner versus inert material and with CH liner versus adhesive systems were compared, due to limitations, imprecision and inconsistency of the included studies. Moderate level of evidence was considered when CH liner was compared with GIC. In addition, when the failures in permanent teeth were analysed, a very low level of evidence was considered, due to the inclusion of only a few available studies, which also presented methodological limitations, imprecision and inconsistency, in addition to short-term evaluations.”^{162 (p597)} According to the authors, “In general, there seemed to be insufficient clinical evidence to support the recommendations for using CH [calcium hydroxide] liner. For primary teeth, the level of evidence obtained was moderate when CH liner was compared with GIC [glass ionomer cement], and low when the use of a liner was compared with inert materials or adhesive systems. While for permanent teeth only studies evaluating CH liner with GIC in the short-term could be included, evidence considered of very low quality indicated that CH liner would have no effect on clinical success of deep caries lesion treatments for these teeth. The quality of the studies included and the evidence obtained emphasizes the need for further well-designed, randomized and controlled clinical trials evaluating the effect of using CH liner in the treatment of deep caries lesions in the long term, both in primary and permanent teeth”.^{162 (p601)}

Göstemeyer and Schwendicke (2016)

Parameter	Extraction
First author and year of publication	Göstemeyer and Schwendicke (2016)¹⁶³
Objectives	Evaluated the risk of retention loss and failure of adhesively placed resin-based restorations after degradation inhibitory cavity pretreatment with chlorhexidine, ethanol wet-bonding, or quaternary ammonium compounds compared with no treatment, placebo, or alternative pretreatments.
Participants	Mixed dentition, cavitated caries, direct restoration techniques Population: Human teeth receiving adhesively placed resin-based restoration Ten randomised controlled trials, published between 2005 and 2015, involving 209 adults and children and 709 teeth, were included. Three studies included children only; in two of these studies, they were aged between 8 and 12 years and had primary teeth restored, while in the third study the children’s median age was 15 years and they had permanent premolar teeth restored. Seven studies included adults, and their ages ranged from 21 to 79 years.

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Setting/context	Study settings were not reported. The study countries were Brazil, Iran, Mexico, and Turkey.
Description of interventions/phenomena of interest	Humans receiving adhesively placed resin-based restorations, with a minimum of two treatment groups comparing degradation inhibitory cavity pretreatment with no such treatment, placebo treatment, or alternative pretreatments, were included. Treatment groups should only differ with regard to pretreatment; other provided treatments (moisture control, carious tissue removal, bonding strategy, restoration) should be identical. Not performing any pretreatment was regarded as a control group or standard care. Pretreatment was seen as the experimental group. The authors did not specify what kind of pretreatment was used for degradation inhibition. However, the articles included identified the following pretreatments: chlorhexidine (seven trials), ethanol wet-bonding (two trials), and quaternary ammonium compounds (one trial).
Databases and sources searched	Three electronic databases (Embase, MEDLINE, and Cochrane Central Register of Controlled Trials (CENTRAL)) were searched using a search strategy (keywords provided) which was adapted for each database. No restrictions regarding language or publication date were applied. The end date for the search was not provided. Studies were cross-referenced via bibliographies of identified full texts. The authors do not mention preparing a full protocol prior to completing the review. Titles and abstracts of identified studies were screened independently by two reviewers for inclusion. Duplicate data extraction was performed independently by two reviewers using a piloted spreadsheet. The source of funding for the review or conflicts of interest were not stated.
Date range (years) of included studies	Ten randomised controlled trials, published between 2005 and 2015, were included.
Number of primary studies included in the systematic review	Ten randomised controlled trials, published between 2005 and 2015. The funding sources were extracted but not reported.
Types of studies included	Studies that compared two or more restorative materials in the restoration of carious lesions on root surfaces were included. All randomised controlled trials and non-randomised controlled trials were eligible for inclusion. The reasons for selecting these study designs were not explained. Studies excluded during full-text screening were listed with their reason for exclusion.
Country of origin of included studies	The study countries were Brazil, Iran, Mexico, and Turkey.
Appraisal instruments used	The risk of bias was evaluated using the Cochrane Collaboration's risk of bias instrument.
Appraisal rating	Nine of the ten included trials were judged to have a high risk of bias and the remaining trial was judged to have a low risk of bias. Only one of the ten trials was judged adequate for randomisation, and five were judged adequate for blinding of outcome ascertainment. There was publication bias for risk of retention loss that may favour no intervention, and limited publication bias for risk of failure that would not change the direction of the findings.
Method of analysis	Meta- and trial-sequential-analyses were performed for both outcomes: retention loss and failure. No quality threshold with regard to risk of bias was used to decide inclusion in quantitative analyses. Continuity correction of +1 was used for trials with zero events. Heterogeneity was assessed using both Cochran's Q test and I ² statistics. Depending on heterogeneity, fixed- or random-effects meta-analysis was performed (I ² : 35% or above random-effects model). Odds ratios and 95% CIs were calculated. Four analyses were performed: (1) per-protocol analysis (i.e. assessment of participants based on the intervention they received and their availability for follow-up to end of study period) accounts for possible bias introduced by attrition and protocol deviations; (2) intention-to-treat analysis (i.e. assessment of participants as randomised regardless of whether they received the intervention or were available for follow-up), for which it was assumed that all missing participants experienced an event; and (3) and (4) scenario analyses following the intention-to-treat analysis principle. Here, attrition was handled differently in the experimental and control groups. In the best-case analysis, it was assumed that dropouts in the control group, but not those in the experimental group, were associated with events. In the worst-case scenario, this was reversed. Scenario analyses explore the uncertainty stemming from missing data via the

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	most extreme imputations. Meta-analysis was performed with the Comprehensive Meta-Analysis programme. Given the low number of trials and their uniform design, no further subgroup or meta-regression analyses were performed. Data were not adjusted to account for possible clustering of teeth in studies using split-mouth design, etc., as it was assumed that the effects of such clustering would be limited. The quality of evidence for each outcome effect estimate was graded according to GRADE using GRADE Profiler. Conventional meta-analysis uses Z-values to compare two interventions, with $Z=0.0$ indicating no difference between intervention groups. If the Z-value exceeds ± 1.96, a difference is traditionally assumed to be statistically significant ($p < 0.05$, two-sided test). As for repeated updates of meta-analyses, a new Z-value is calculated for each update. In trial sequential analysis, this series of Z-values is plotted against the accumulated number of patients, events, or information. This cumulative Z-curve is then assessed regarding its relation to the conventional significance boundaries ($Z = \pm 1.96$), the required information size, and the trial sequential monitoring boundaries for benefit, harm, or futility. The required information size was calculated based on type I error risk of $\alpha = 0.05$, a type II error risk of $\beta = 0.20$ (equivalent to a power of 0.80), and the control event proportion. Relative risk reduction was based on an a priori defined worthwhile interventional effect of 20%. It should be noted that smaller intervention effects might well be relevant. This, however, would increase the required information size even further. The required information size was further adjusted for the diversity in the meta-analysis (diversity-adjusted required information size. The Lan-DeMets version of the O'Brien–Fleming function was used for calculating the trial sequential monitoring boundaries. Results of cumulative Z-value crossing the conventional boundary of significance ($Z = \pm 1.96$) but not the trial sequential monitoring boundaries for benefit or harm were defined as spuriously significant. Firm evidence was assumed to be reached when the Z-curve crossed the trial sequential monitoring boundaries for benefit or harm before the diversity-adjusted required information size (DARIS) was reached. Firm evidence of futility was confirmed by the Z-curve crossing the trial sequential monitoring boundaries for futility. TSA 0.9 was used].
Outcome assessed	Risk of retention loss, risk of failure Follow-up: 6–36 months (not predetermined) Outcome by primary studies: Risk of retention loss: De Araujo 2013; Dutra-Correa 2013; Sartori 2013; Brackett 2007; Carrilho 2007; Helbling 2005; Montagner 2015; Türkün 2005; Mortazavi 2012; Ricci 2010 Risk of failure: De Araujo 2013; Dutra-Correa 2013; Sartori 2013; Helbling 2005; Montagner 2015; Türkün 2005; Mortazavi 2012.
Results/findings	Risk of retention loss was not significantly decreased after pretreatment based on per-protocol (odds ratio: 1.37; 95% CI: 0.68–2.77; I^2: 0%; 10 trials) or intention-to-treat analysis (odds ratio: 1.25; 95% CI: 0.76–2.04; I^2: 0%; 10 trials). Risk of restoration failure was not significantly decreased after pretreatment based on per-protocol (odds ratio: 0.86; 95% CI: 0.56–1.34; I^2: 0%; 7 trials) or intention-to-treat analysis (odds ratio: 1.22; 95% CI: 0.83–1.80; I^2: 0%; 7 trials). Scenario analyses found that great uncertainty was introduced by participant attrition at follow-up. According to trial sequential analysis, no firm evidence was reached. The authors concluded: “In conclusion, there is insufficient evidence to recommend or refute hybrid layer degradation inhibitory cavity pretreatment prior adhesively placing resin-based restorations. Based on this review and the included studies, dentists could pretreat cavities prior adhesively placing restorations (for example as part of rewetting the cavity, or introduced to an adhesive), while evidence supporting this strategy is lacking. The impact of further effects (e.g. disinfection, pulp-irritation) of pretreatment remains unclear”.¹⁶³ (p20) They go on to state that, “Given the high risk of bias and the limited quantity of evidence, our findings were graded as being supported by very weak [very low quality] evidence only. Therefore, degradation inhibitory cavity pretreatment

Parameter	Extraction
	prior adhesively placing resin-based restorations can neither be recommended nor refuted.” ¹⁶³ (p19)
Significance/direction	Results listed by outcome. No difference.
Heterogeneity	No statistical heterogeneity.
Comments	GRADE was used by the review authors. Nine of the 10 included trials were judged to have a high risk of bias. Only one (10%) of the 10 trials was judged adequate for randomisation, and five (50%) were judged adequate for blinding of outcome ascertainment. The sample size was below 200. The quality of the review was rated as low using AMSTAR 2 as the authors could not control for the effects of high or unclear risk of bias on the analysis. The HRB grades the quality of the evidence as low while the review authors rated the quality of the evidence as low.

Schwendicke *et al.* (2015b)

Parameter	Extraction
First author and year of publication	Schwendicke <i>et al.</i> (2015b) ¹⁶⁵
Objectives	Compared the antibacterial effects of different cavity liners with each other, a placebo, or no liner. There was no age limit and any type of teeth could be included.
Participants	Mixed dentition, cavitated caries, restoration support materials Population: There was no age limit and any type of teeth could be included. Eleven randomised controlled trials and three non-randomised trials published between 1998 and 2013, with a total of 457 participants and 500 treated carious lesions, were included in this review; two studies used the same control group and were combined for the analysis. The age of the patients ranged from 4 to 67 years. Gender was not reported. Study countries and settings were not reported.
Setting/context	Study countries and settings were not reported.
Description of interventions/phenomena of interest	According to Schwendicke <i>et al.</i> , “as liners are thought to induce the development of reactionary dentine, reduce post-operative pulpal inflammation, or isolate the pulp from chemical irritants like hydroxyethyl methacrylate, they are commonly used for pulp protection...A second reason why the use of liners has been advocated was their remineralizing effects, especially when selective (incomplete) or stepwise excavation was performed prior to restoration...Last, lining materials are used as they might reduce bacterial numbers, i.e. acting as cavity disinfection. This has been especially postulated for the most widely used material, calcium hydroxide, whose alkaline pH is supposed to exert strong antibacterial effects.” ¹⁶⁵ (p1298) Treatments were categorised as: calcium hydroxide, mineral trioxide aggregate, antibiotic/disinfectant, calcium phosphates, zinc oxide eugenol, black copper cement, and glass ionomer cement liners. Comparator: Antibacterial effects of different liners against each other, or against no liner
Databases and sources searched	Three electronic databases (MEDLINE via PubMed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL)) were searched on 23 September 2014. Grey literature was searched electronically (OpenGrey), and ongoing trials screened using ClinicalTrials.gov. No restrictions on language or publication date were applied. The bibliographies of included articles were also searched. The completion of a protocol was not mentioned in the article. Screening and extraction were completed in duplicate. The authors did not report any conflicts of interest. The source of funding for the review was not provided.
Date range (years) of included studies	Eleven randomised controlled trials and 3 non-randomised trials, published between 1998 and 2013, were included.
Number of primary studies included in the systematic review	Eleven randomised controlled trials and 3 non-randomised trials published between 1998 and 2013, with a total of 457 participants and 500 treated carious lesions, were included in this review; two studies used the same control group

Parameter	Extraction
	and were combined for the analysis. The sources of funding for included studies were extracted but not reported.
Types of studies included	While both randomised and non-randomised trials could be included, only studies which treatments allocated independent of the cavity depth and the baseline bacterial load were eligible for inclusion in order to avoid selection bias by indication. The references and reasons for excluding the 29 excluded studies were provided.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess the risk of bias in primary studies.
Appraisal rating	Based on the Cochrane Collaboration's risk of bias instrument, all included trials were assessed as being at high (13) or unclear (1) risk of bias. The authors reported that six of the 14 included trials had adequate randomisation and all had outcome measurement that was independent of intervention. A funnel plot analysis was performed to assess small study effects or publication bias of pairwise estimates. Trim-and-fill was used to evaluate the effects of such bias. Funnel plot analysis did not indicate a risk of publication bias.
Method of analysis	Networks constructed by plotting different treatments (as nodes) and comparisons (as edges) were inspected for geometry and asymmetry. Random-effects pairwise meta-analyses were performed using Stata, with odds ratio or standardised mean difference as effect sizes. Network meta-analyses were performed using Bayesian random-effects models and a Markov chain Monte Carlo simulation. Heterogeneity within pairwise comparisons was assessed quantitatively using I^2 statistics. Loop inconsistency, i.e. the difference between direct and indirect estimates for three treatments within a loop, was evaluated by the inconsistency factor for the loop.
Outcome assessed	Outcome: The primary outcome was the number of positive bacterial dentine samples remaining in a cavity. Superiority was defined as a treatment yielding significantly fewer positive samples than the comparator. The secondary outcome was the reduction in the number of bacteria remaining in the cavity, with colony-forming units as effect measure. Superiority was defined as a treatment inducing a significantly greater bacterial reduction than the comparator. Time frame: Median follow-up (time between lining and re-entry) was 3 months (range: 1 day to 24 months) (not predefined) Outcome by primary studies: Positive bacterial samples: Bressani (2013); Corallo (2013); Duque (2009); Hoshino (1989); King (1965); Fairbourn (1980); Leung (1980); Neelakantan (2012); Pinheiro (2005); Wicht (2004). Bacterial reduction by lining and/or sealing: Fairbourn (1980); Foley (2003); Leung (1980); Pinheiro (2005); Pinto (2006); Wicht (2004).
Results/findings	Pairwise comparisons found no significant difference between any of the groups in achieving sterility of the cavity floor, with only three comparisons including more than one study. Cavities without liners had 1.5 times the odds of yielding positive samples than cavities lined with calcium hydroxide, but the CIs indicated that this was not significant (odds ratio: 1.50; 95% CI: 0.90–2.51; I^2 : 0%; 5 trials). This probability did not significantly differ in cavities lined with calcium phosphates compared with antibiotic or disinfecting liners (odds ratio: 1.23; 95% CI: 0.01–257; I^2 : 83%; 2 trials), cavities lined with antibiotic liners compared with no active liner (odds ratio: 0.92 95% CI: 0.34–2.48; I^2 : 0%; 2 trials), or cavities lined with zinc oxide eugenol compared with calcium hydroxide (odds ratio: 1.20 95% CI: 0.61–2.33; 1 trial). Except for one comparison, heterogeneity was high. The funnel plot analysis did not indicate a risk of publication bias. Based on the network meta-analysis of the 11 trials included, mineral trioxide lining yielded the greatest probability of achieving sterile cavities after a lining/sealing period (73%), followed by an antibiotic/disinfectant (8%), and zinc oxide eugenol (7%). Only six studies assessed bacterial reduction after lining/sealing, and zinc oxide eugenol was found to have the highest probability of achieving a bacterial reduction. Mineral trioxide was not included in the second

Parameter	Extraction
	analysis. In both analyses, not providing any lining was found to have low antibacterial effects. The bacterial reduction after a certain lining or sealing period was reported by six studies, with 209 cavities or cavity sites being analysed. The available data indicated that not using any lining (or only placebo lining) seems less likely to reduce the bacterial load in the cavity than lining with calcium hydroxide (standardised mean difference: -6.05; 95% CI: -28.89 to 14.78; I²: 99%; 2 trials), but this difference is not significant, the CIs are very wide, and heterogeneity is very high. The difference between glass ionomer cement compared with black copper cement was statistically significantly lower (standardised mean difference: -14.06; 95% CI: -17.81 to -10.31; 1 trial), as was the difference between antibiotic or disinfectant liners and glass ionomer, or zinc oxide eugenol and calcium hydroxide. The funnel plot analysis did not indicate publication bias. Based on these data, another network was constructed, connecting six treatments using a linear structure, the latter being the product of paucity of data rather than a potential evolution of tested treatments. Using network meta-analysis, zinc oxide eugenol was found to have the highest probability of achieving a bacterial reduction, while no lining was ranked lowest. According to Schwendicke <i>et al.</i>, "the underlying data for these findings are sparse; the ranking should thus be interpreted with caution, as indicated by the absence of statistically significant differences in both pairwise and network meta-analyses estimates."¹⁶⁵ (p1303) Heterogeneity and risk of bias were measured and presented, but not discussed.
Significance/direction	Results listed by outcome.
Heterogeneity	Heterogeneity and risk of bias were measured and presented, but not discussed.
Comments	GRADE was not used by the review authors. Both randomised controlled trials and non-randomised trials were included in the review. All included trials were assessed as being at high or unclear risk of bias. The authors reported that six (43%) of the 14 included trials had adequate randomisation and all had outcome measurement that was independent of intervention. The quality of the review was rated as critically low using AMSTAR 2 as the authors included both randomised and non-randomised trials in the analysis, and did not discuss the effects of high or unclear risk of bias or heterogeneity on the analysis. The HRB grades the quality of the evidence as low.

Pereira-Cenci *et al.* (2013)

Parameter	Extraction
First author and year of publication	Pereira-Cenci <i>et al.</i> (2013) ¹⁶⁴ (Cochrane Review) Empty review
Objectives	Compared antibacterial agents incorporated into composite restorations with composite restorations containing no antibacterial agents for the prevention of negative clinical outcomes.
Participants	Mixed dentition, cavitated caries, and materials to support main restoration materials Population: Adults and adolescents in any age group with restorations in the permanent dentition, and children with restorations in the primary dentition No trials matched the inclusion criteria for this review.
Setting/context	No trials matched the inclusion criteria for this review.
Description of interventions/phenomena of interest	According to Pereira-Cenci <i>et al.</i> , "composite restorations consist of two major components: a resin composite for filling and the bonding systems to be applied to the cavity before the placement of filling materials. The incorporation of antibacterial substances in these two components would have different roles relating to the prevention of the harmful effects caused by bacteria within the biofilm covering the tooth/restoration interface. The antibacterial effects of composites for filling would be mainly relevant to inhibition of plaque accumulation on the surface of the materials and tooth around the restoration. In contrast, for bonding systems, their antibacterial effects are discussed in terms of

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	disinfection of the cavity as well as inactivation of bacteria which could invade the adhesive interface due to microleakage." ¹⁶⁴ (p3)
	Comparator: Composite restorations containing no antibacterial agents
Databases and sources searched	The authors searched four electronic databases: the Cochrane Oral Health Group Trials Register (to 23 July 2013), the Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library 2013, Issue 6), MEDLINE via Ovid (1946 to 23 July 2013), and Embase via Ovid (1980 to 23 July 2013). They also searched ClinicalTrials.gov, the ISRCTN registry (www.controlled-trials.com), and the World Health Organization's (WHO's) International Clinical Trials Registry Platform for ongoing trials. No restrictions were placed on the language or date of publication when searching the electronic databases. Hand-searching done as part of Cochrane's worldwide hand-searching programme. All the references lists of the included studies were checked manually to identify any additional studies. Two review authors conducted screening of studies independently. No data extraction was required. The authors prepared a protocol. There are no financial conflicts of interest, and the review authors declare that they do not have any associations with any parties who may have vested interests in the results of this review. The review was funded by the National Institute for Health Research, UK.
Date range (years) of included studies	No trials matched the inclusion criteria for this review.
Number of primary studies included in the systematic review	No trials matched the inclusion criteria for this review. Participants of interest included adults and adolescents in any age group with restorations in the permanent dentition, and children with restorations in the primary dentition.
Types of studies included	The inclusion criteria specified randomised controlled trials. The authors provide a table of excluded studies and the reasons for exclusion.
Country of origin of included studies	No trials matched the inclusion criteria for this review.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was to be used.
Appraisal rating	No trials matched the inclusion criteria for this review.
Method of analysis	The standard Cochrane analysis was planned.
Outcome assessed	Longevity of restorations (failure or success); post-operative sensitivity, marginal adaptation, anatomic form, and other clinical outcomes (tooth vitality and pulpitis); patient satisfaction No trials matched the inclusion criteria for this review.
Results/findings	The main finding from this review is that there is insufficient and inadequate evidence upon which to compare the performance of antibacterial agents incorporated into composite restorations with composite restorations containing no antibacterial agents for the prevention of dental caries. According to Pereira-Cenci <i>et al.</i>, "No studies were included in this review, as we were unable to find any trials directly comparing antibacterial containing composites to other active interventions or controls."¹⁶⁴ (p6)
Significance/direction	No trials matched the inclusion criteria for this review.
Heterogeneity	No trials matched the inclusion criteria for this review.
Comments	The authors intended to use GRADE. No evidence, as no trials met the inclusion criteria for this review.

Restoration material and support material

Schwendicke *et al.* (2016)

Parameter	Extraction
First author and year of publication	Schwendicke <i>et al.</i> (2016) ²⁵
Objectives	Compared the survival of combinations of adhesive and restorative materials placed in one of two types of cavitated lesions (cervical cavitated lesions or load-bearing posterior cavitated lesions) with each other in permanent and primary teeth. The lesions may or may not be due to caries.

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Participants	Mixed dentition, cavitated caries, direct restorations Population: Adults and children with cervical cavitated lesions and load-bearing posterior cavitated lesions in permanent and primary teeth. Seventy-two randomised controlled trials, published between 2005 and 2015, were included. A total of 11,070 restorations (5,330 cervical and 5,740 load bearing) were placed in 3,633 patients in the included 72 trials. Thirty-six trials investigated restoration of cervical lesions (all in permanent teeth), and 36 investigated restoration of load-bearing lesions (8 in primary teeth and 28 in permanent teeth). Age and gender were not reported. The follow-up period ranged from 12 months to 13 years.
Setting/context	Sixty-nine studies were set in second-tier dental clinics, and three were set in primary-level dental clinics. The study countries were not reported.
Description of interventions/phenomena of interest	Restorative and adhesive materials were categorised as follows: Restorative materials: (1) conventional composite resin (nanofilled, microfilled, and hybrid). These were distinguished from those composites clearly marketed as different, including (2) ormocer, (3) bulk fill (flowable and packable), and (4) siloranes. Moreover, (5) compomer, (6) amalgam, and (7) glass ionomer cements or resin-modified glass ionomer cements were assessed. If restoration material combinations had been used (as for some bulk fills, with bulk material being covered by a conventional composite resin), the material in the bulk fill component was used for classification. Adhesive materials: (1) Four- or three-step etch-and-rinse, (2) two-step etch-and-rinse, (3) two-step self-etch, (4) one-step self-etch, and (5) no adhesive used. Such classification of adhesive materials has been used before by Heintze <i>et al.</i> (2015). Comparator: Each other
Databases and sources searched	The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (via PubMed), and Embase (via Ovid) were searched on 2 March 2015 for relevant publications. The search strategy is presented in an appendix. The search was limited to studies published from 2005 onward in order to include current adhesive and restorative materials. The search was not restricted by language. The references of full-text articles were examined to identify additional studies. Two reviewers independently screened titles and abstracts for eligibility and extracted data. The authors do not report preparing a protocol. This study was funded by a grant of the German Research Foundation and a grant from the Ministry of Science and Technology in Taiwan. The authors declare no potential conflicts of interest.
Date Range (years) of included studies	Seventy-two randomised controlled trials, published between 2005 and 2015, were included.
Number of primary studies included in the systematic review	Seventy-two randomised controlled trials, published between 2005 and 2015, were included. A total of 11,070 restorations (5,330 cervical and 5,740 load bearing) were placed in 3,633 patients in the included 72 trials. Thirty-six trials investigated restoration of cervical lesions (all in permanent teeth), and 36 investigated restoration of load-bearing lesions (8 in primary teeth and 28 in permanent teeth). The sources of funding for primary studies were not reported.
Types of studies included	The systematic review included randomised controlled trials only. Excluded studies were listed with their reasons for exclusion.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included studies.
Appraisal rating	Of the 72 included randomised controlled trials, 71 were judged to have a high risk of bias and one to have a low risk of bias. Twenty-nine of the 72 studies were judged adequate for randomisation and 41 had adequate blinding of outcome assessment. Sixteen studies were excluded from meta-analysis. Publication bias was assessed by funnel plots and some comparisons were prone to publication bias. Inspection of funnel plots found possible publication bias towards self-etch adhesives and resin-modified glass ionomer cement, as well as towards ormocers and siloranes.
Method of analysis	The systematic review included randomised controlled trials only. The findings were synthesised using network meta-analysis, which allows the investigator to

Parameter	Extraction
	rank the interventions from best to worst and use both direct and indirect evidence. Network meta-analysis was performed separately for cervical and load-bearing cavitated lesions in either primary or permanent teeth. Networks of interventions were constructed by plotting different treatments (as nodes) and comparisons (as edges) and were inspected for geometry and asymmetry. Random-effects pairwise meta-analysis was performed with Stata. Network meta-analyses were performed with Bayesian random-effects models and a Markov chain Monte Carlo simulation. Median odds ratios and their 95% credible intervals were reported. Credible intervals are the range of estimated parameters after exclusion of extreme values. Different material combinations were ranked according to their probability of having the lowest versus highest odds, and the average rank was calculated. The surface under the cumulative ranking line was plotted and the area under the curve calculated. Inconsistency was assessed. In addition, annual failure rates were calculated and used to evaluate the impact of pretreatment and lining.
Outcome assessed	The primary outcome was survival; that is, restorations not needing any restorative reintervention (replacement, repair) due to loss, fracture, secondary caries, or other clinical issue. Superiority was defined as a material combination requiring significantly fewer restorative retreatments (i.e. having significantly higher survival rates and fewer failures per total sample size) than the comparator. The unit of analysis for meta-analysis was patients. The follow-up period ranged from 12 months to 13 years. Outcome by primary studies: Annual failure rates <i>Primary load bearing:</i> Alves dos Santos 2010; Andersson-Wenckert 2006; Casagrande 2013; Cehreli 2006; Daou 2009a; Daou 2009b; Pascon 2006; Zulfikaroglu 2008. <i>Permanent load bearing:</i> Baracco 2013; Beck 2014; Boeckler 2012; Bottenberg 2009; Brackett 2007; Celik 2014; Delbons 2015; Deliperi 2012; Efes 2006a; Efes 2006b; Efes 2013; Fagundes 2009; Frankenberger 2014; Goncalves 2013; Mahmoud 2008; Mahmoud 2014a Mahmoud 2014b; Manhart 2010; Monteiro 2010; Perdigao 2009; Schirrmeister 2009; Schmidt 2014; Shi 2010; van Dijken 2013b; van Dijken 2014a; van Dijken 2014b; van Dijken 2015; Yazici 2014. <i>Cervical lesions:</i> Adeleke 2012; Aw 2005; Brackett 2010; Burgess 2013; Burrow 2007; Celik 2007; Dalton Bittencourt 2005; Dondi Dall'Orologio 2014; Dutra-Correa 2013; Eliguzeloglu Dalkilic 2012; Ermis 2012; Franco 2006; Häfer 2015; Jyothi 2011; Kim 2009; Koubi 2006; Kubo 2006; Logueicio 2007; Moosavi 2013; Paula 2015; Perdigao 2012a; Perdigao 2012b; Pollington 2008; Qin 2013; Söderholm 2013; Stojanac 2013; Tuncer 2013; Türkün 2005; Türkün 2008; van Dijken 2007; van Dijken 2008; van Dijken 2010; van Dijken 2012; van Dijken 2013a; van Landuyt 2014; Zhou 2009.
Results/findings	In cervical lesions, nine different material combinations had been used. Pairwise meta-analysis found that resin-modified glass ionomer cements were significantly less prone to failure than conventional resin composites placed with two-step etch-and-rinse adhesives (odds ratio: 5.23; 95% CIs: 2.07–13.21; I^2: 0%; 5 trials). The latter adhesives were also found to be significantly inferior to composites placed with three-step etch-and-rinse adhesives, which were less likely to fail (odds ratio: 0.67; 95% CIs: 0.45–0.98; I^2: 7.5%; 7 trials), and to be borderline significantly inferior (odds ratio: 1.36; 95% CIs: 0.96–1.93; I^2: 9.6%; 8 trials) to composites placed with two-step self-etch adhesives. This was reflected in the network meta-analysis, with resin-modified glass ionomer cements having the highest probability of being ranked first (i.e. having the lowest risk of failure). The strategies with the poorest ranks were compomers and conventional resin composites placed with two-step etch-and-rinse adhesives. Heterogeneity was low in all meta-analyses of cervical lesion restorations and adhesives. If mean surface under the cumulative ranking line values were calculated for different bonding strategies regardless of the restoration material used, resin-modified glass ionomer cements were ranked highest (98 out of a maximum of 100), followed by two-step self-etch adhesives (67) and three-step etch-and-rinse adhesives (62); one-step self-etch (46) and two-step etch-and-rinse adhesives (21)

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	showed the lowest surface under the cumulative ranking line values. Mean annual failure rates varied between 1.8% (resin-modified glass ionomer cement) and 21% (two-step etch-and-rinse adhesives with compomers). Ranking according to annual failure rates was largely in line with network meta-analysis findings. The most frequently stated reasons for failure were fracture and retention loss. In most groups, mean annual failure rates were lower when lesions were additionally prepared prior to restoration. In load-bearing posterior cavitated lesions in permanent teeth, nine different material combinations had been employed. Network meta-analysis found conventional resin composites placed with two-step etch-and-rinse adhesives to have the highest probability of being the best material combination, but these findings were not statistically significant. Using the same bonding material combined with bulk fills or applying conventional resin composites with three-step etch-and-rinse adhesives also showed ranking values. Combinations involving siloranes or ormocers were at the lower end of the ranking. When mean surface under the cumulative ranking line values of restoration materials were assessed regardless of the bonding strategies used, conventional resin composites showed higher values (62 out of 100) than bulk fills (53), ormocers (40), or siloranes (26). The same analysis of bonding system performance regardless of restoration material found high ambiguity (two-step etch-and-rinse adhesives: 62 out of a maximum of 100; three-step etch-and-rinse adhesives: 59; one-step self-etch: 45; two-step self-etch: 41). The pairwise comparisons were based on few studies, with 13 based on one trial and 7 based on two trials. Where more than two trials were in the analysis, there was low to moderate statistical heterogeneity. Mean annual failure rates varied between 0.6% (two-step etch-and-rinse adhesives with conventional resin composites) and 4.2% (one-step self-etch with conventional resin composites). Ranking according to annual failure rates found conventional resin composites to be the best material, except when placed with one-step self-etch adhesives. Alternatives (bulk fill, siloranes, and ormocer composites) did not obviously differ with regard to annual failure rate (1.6–2.3%). Fracture and retention loss were the most frequent reasons for failure. Annual failure rates were generally higher when liners were placed prior to restoration. In load-bearing cavitated lesions in primary teeth, nine different material combinations had been employed. Conventional resin composites placed with two-step etch-and-rinse adhesives were used most often. Pairwise pooled effect estimates indicated significant advantages of conventional resin composites placed with two-step etch-and-rinse adhesives over amalgam restorations (odds ratio: 0.20; 95% CIs: 0.05–0.74; one trial), while no other significant differences were found. Network meta-analysis found conventional resin composites placed with one-step self-etch adhesives had the highest probability of being the best material combination based on only two studies. Fifteen treatment groups were supported by only one study and three by two studies. Statistical heterogeneity was low for two pairwise comparisons and substantial for one comparison. Otherwise, surface under the cumulative ranking line values indicated high uncertainty, as differences among material combinations were limited. When mean surface under the cumulative ranking line values of restoration materials were assessed regardless of the bonding strategies used, conventional resin composites showed higher probability values (69 out of 100) than resin-modified glass ionomer cements (50), compomers (45), siloranes (39), and amalgams (21). From the nine formed loops, two showed evidence of statistical inconsistency. Inspection of funnel plots did not indicate publication bias. Mean annual failure rates ranged between 0.0% (one-step self-etch adhesives conventional used with resin composites) and 15.8% (one-step self-etch adhesives used with compomer). The most frequently stated reason for failure was endodontic. In most groups, lesions had been lined; lined lesions showed lower mean annual failure rates. The authors concluded that, “Based on our findings, certain recommendations can be made. For cervical lesions, RMGICs [resin-modified glass ionomer cements] or, if aesthetics is an issue, conventional resin composites or compomers placed via 2SE [two-step self-etch adhesives] or 3ER [three-step etch-and-rins] adhesives might be preferred. Adhesives combining primer and bonding (2ER [two-step etch-and-rinse], 1SE [one-step self-etch adhesives]) seem inferior

Parameter	Extraction
	for this indication. For load-bearing lesions, conventional or bulk-fill composites seem suitable (though bulk fills had not all been placed in bulk but in increments in included studies, which possibly artificially improved this material class' performance). Further uncertainty remains towards the best adhesive strategy. In permanent teeth, etch-and-rinse adhesives might be preferable; for primary teeth, self-etch systems might be suitable, too, but only a few studies investigated this situation. Given that most trials are short term and show high risk of bias, caution is required when interpreting our findings." ²⁵ (p621)
Significance/direction	Results listed by outcome.
Heterogeneity	Heterogeneity was low in all meta-analyses of cervical lesion restorations and adhesives. Where more than two trials were in the analysis, there was low to moderate statistical heterogeneity.
Comments	GRADE was not used by the review authors. Most of the trials had a high risk of bias. Twenty-nine (40%) of the 72 studies were judged adequate for randomisation and 41 (57%) had adequate blinding of outcome assessment. The quality of the systematic review was judged as low using AMSTAR 2 as the authors could not control for the high risk of bias in the analysis of the studies. Considering these limitations, the quality of evidence is low for all outcomes.

Restoration processes or techniques

Cardoso *et al.* (2020)

Parameter	Extraction
First author and year of publication	Cardoso <i>et al.</i> (2020) ¹⁶⁶
Objectives	Evaluated the efficiency (time for treatment, caries removal, anaesthesia, and colony-forming units count) of alternative methods (chemomechanical methods, laser, and air- and/or sono-abrasion) for caries removal, compared with the conventional mechanical method (rotary or hand instruments), for removing dental caries from primary and permanent decayed teeth. Studies on atraumatic restorative treatments were excluded.
Participants	Mixed dentition, cavitated caries, restoration technique Primary and permanent decayed teeth with dentine lesions in humans More than 1,600 patients with primary dental caries were treated in the included studies. The treated patients' age ranged from 3 to 84 years, with an overall mean of 10 years. One study did not specify the included patients' age range, mentioning only that they were aged over 18 years. Gender was not reported.
Setting/context	The clinical settings and study countries were not reported.
Description of interventions/phenomena of interest	Intervention: Alternative methods (chemomechanical methods, laser, and air- and/or sono-abrasion) The authors reported that "Different therapeutic approaches regarding dental cavities have been discussed and reconsidered in order to be as conservative as possible and to preserve tooth structure by only removing the irreversibly damaged dental tissues. This leads to increased tooth longevity and prevents the repetitive restorative cycle. Although mechanical methods for caries removal are widely accepted quick techniques, various alternative therapeutic approaches have been demonstrated to be promising, such as chemomechanical methods, lasers, or air- and/or sono-abrasion. Chemomechanical caries removal systems are solutions which act on the principle of carious tissue softening to facilitate their removal and application of sodium hypochlorite (NaOCl) or enzyme-based agents. After use, the gel often changes color and becomes turbid or produces bubbles, making the identification of the occurring reaction, completion, or absence easier (meaning that there is no remaining decayed tissue); then, the softened tissue is removed by non-cutting tip instruments. The enzyme-based materials can be associated with anti-inflammatory properties, which can lead to better treatment experiences and less induced pain. Agents with hypochlorite are also associated with less anaesthesia being necessary, since

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	the sodium hypochlorite acts within the already damaged collagen fibrils. Examples of sodium hypochlorite-based agents are GK-101E (and CariSolv; examples of enzyme-based agents are Carie-care, Papacarie, and Brix 3000. Laser ablation systems for caries removal use laser wavelengths that achieve a major interaction with either the mineral or water content or both in the decayed tissues (unless there is plasma-mediated ablation by ultrashort pulses). In the most common systems for caries removal, the primary mechanism of action is the water heat at the surface and the subsurface which causes its expansion, and the tissue is exploded out from the surface. The most commonly used laser systems for caries removal are the Er:YAG (Erbium-doped Yttrium Aluminium Garnet) laser and the Er,Cr: YSGG (Erbium, Chromium-doped Yttrium, Scandium, Gallium, and Garnet) laser. Air-abrasion systems for caries removal are a technique based on the blasting of the tooth surface with high-velocity particles carried in a stream of air, removing tissue from the cavity. Furthermore, sono-abrasion systems for caries removal use high-frequency sonic air-scalers with modified abrasive tips; different-shaped tips help prepare the intended cavity outlines and remove carious dentin. Conventional cavity preparation and caries removal methods use mechanical means, mostly burs, and are associated with pain and fear, especially for children. Although the pain can be managed through local anesthesia, fear of the needle, noise, and vibration of mechanical preparation remains a cause of discomfort for the patient. Moreover, these techniques present the risk of easily removing healthy dental tissues or damaging the pulp through temperature rise, which may be the origin of discomfort (thermal stimulation).^{166 (p3407)} Comparator: Conventional mechanical method (rotary or hand instruments) and, later in the paper, alternative methods are compared with each other. Studies on atraumatic restorative treatments were excluded.
Databases and sources searched	Four electronic databases were searched up to 5 August 2020: the Cochrane Library, Embase, MEDLINE via PubMed, and Web of Science. ClinicalTrials.gov was searched for unpublished trials. No restrictions on language or date of publication during the electronic database screening were applied. The search strategies were presented in a table in the article. The reference lists of the relevant articles were manually searched to locate additional studies. The protocol was registered with PROSPERO. Duplicate screening were completed. Details on who completed data extraction were non provided. The review received no external funding and the authors declared that they had no conflicts of interest.
Date range (years) of included studies	Thirty-seven controlled trials published between 2000 and 2020 were included in this review.
Number of primary studies included in the systematic review	Thirty-seven controlled trials published between 2000 and 2020 were included in this review. Eighteen studies evaluated chemomechanical methods compared with control; 13 studies evaluated laser compared with control; one study evaluated air- and/or sono-abrasion systems compared with control; three studies evaluated CariSolv compared with Papacarie compared with control; one study evaluated CariSolv compared with Papacarie compared with Er:YAG laser compared with control; and one study evaluated sodium hypochlorite gel compared with Brix 3000 compared with control. The funding sources of primary studies were not reported.
Types of studies included	Controlled trials were eligible for inclusion. The list of studies excluded at full-text screening was not provided, but their reasons for exclusion were reported.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	One study was judged to have a high risk of bias and 36 studies to have an unclear risk of bias. Fifteen of the 37 included studies were judged to have adequate randomisation and 10 had adequate blinding of outcome assessment. Publication bias was not measured. The authors reported that "Regarding the quality assessment of all included studies, the performance bias was common since the characteristics of the caries removal systems at use are easily distinguished from each other (conventional compared with alternative systems). In general, the studies were found to present insufficient information on their methodology. On other biases, previous

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	experiences were considered because alternative methods for caries removal are not the standard first-line treatment, and patients were certainly treated in previous sessions with rotary instruments. Traumatic events may have occurred, influencing the reported treatment experience with different methods. Additionally, the patient's state of mind influences their behaviour and reported experience, and it may bias the results because of its subjective nature or the comparison of patients with different exposures where the diverse backgrounds of each patient will bias the results."¹⁶⁶ (p3407) The authors reported that "A sensitive search of multiple databases was conducted to identify the potential studies to be included in this review, where no restrictions on language were applied. An attempt to contact some study authors was made for missing information, however, without success. We recognize that the missing data and the included studies' bias reduces the robustness of the analysis performed. Still, there was consistency in the workflow, and the reasons behind the conclusions are reported."¹⁶⁶ (p3405)
Method of analysis	The approach to analysis was not described in the methods.
Outcome assessed	Outcomes: Time for treatment, caries removal, anaesthesia (need, pain and pain perception), colony-forming units count, and restoration performance The was no predetermined time frame for outcome assessment. <i>Chemomechanical compared with control (18 studies)</i> Time taken for caries removal: Unable to determine exact references. Fourteen studies reported that treatment times were longer for intervention treatment than for conventional treatment. 12. Aneundi 2012; 26. Lozano-Chourio 2006; 27. Goyal 2015; 29. Subramaniam 2008; 30. Mizuno 2011; 33. Matsumoto 2013; 34. Motta 2013; 35. Rajakumar 2013; 36. Hegde 2014; 37. Motta 2014; 38. Motta 2014; 43. Ismail 2019; 45. Khalek 2017; 48. Soni 2014; 50. Sontakke 2019; 51. Fure 2000; 53. Pandit 2007; 59. Bottega 2018. Caries removal: Unable to determine exact references. Six studies reported caries removal-related outcomes comparing chemomechanical caries removal with another intervention. The size of the cavity was larger with rotary instruments compared with chemomechanical removal. CariSolv produced significantly smaller free carious lesions in one out of three studies, and Papacarie in one out of one study. Regarding efficacy of caries removal considering the several different criteria, there was no statistical difference between outcomes for caries removal with rotary instruments and Carie-care in one out of one study and CariSolv in two out of two studies. Anaesthesia: 26. Lozano-Chourio 2006 34. Motta 2013; 37. Motta 2014; 38. Motta 2014 51. Fure 2000. In all five studies, patients treated with conventional methods requested anaesthesia more often. Colony-forming units count: 12. Aneundi 2012; 27. Goyal 2015; 29. Subramaniam 2008; 38. Motta 2014; 43. Ismail 2019. Five studies counted colony-forming units. Two studies reported similar reductions in colony-forming units after conventional treatments and treatment with CariSolv and Papacarie, whereas three studies reported higher reductions following treatment with CariSolv and Papacarie. Restoration performance: 30. Mizuno 2011; 33. Matsumoto 2013; 36. Hegde 2014; 37. Motta 2014; 51. Fure 2000; 59. Bottega 2018. There were no statistically significant differences for the success of restorations between caries removal methods used in the six studies. Patients' pain perception: 12. Aneundi 2012; 26. Lozano-Chourio 2006; 27. Goyal 2015; 33. Matsumoto 2013; 34. Motta 2013; 35. Rajakumar 2013; 36. Hegde 2014; 43. Ismail 2019; 45. Khalek 2017; 48. Soni 2014; 50. Sontakke 2019; 51. Fure 2000; 53. Pandit 2007; 59. Bottega 2018. Fourteen studies assessed the patients' pain perception or behaviour during the intervention. Patients receiving alternative approaches for carious lesion removal showed statistically significantly better treatment experiences and fewer signs of discomfort or pain during the consultation in 10 studies. One study reported a more negative experience with the intervention than with the control. <i>Laser compared with control (12 studies)</i>

Parameter	Extraction
	Time for treatment: 10. Sarmadi 2018; 28. Liu 2006; 31. Eren 2013; 32. Hjertton 2012; 42. Valério 2015. The time for treatment was significantly longer in laser treatments than the conventional treatments in four out of five studies. Caries removal: 46. DenBesten 2000; 47. DenBesten 2001. Two studies reported that less energy was required for caries removal during laser treatment compared with conventional treatments. Anaesthesia: 10. Sarmadi 2018; 46. DenBesten 2000. In two studies, less anaesthesia was required for caries removal during laser treatment compared with those treated with conventional methods. Restoration performance: 10. Sarmadi 2018; 40. Zhegova 2014; 42. Valério 2015 44. Polizeli 2019; 52. Hadley 2000. The five studies assessing restoration performance during follow-up periods reported no significant differences between the two caries removal methods examined. Patients' pain perception: 10. Sarmadi 2018; 28. Liu 2006; 32. Hjertton 2012; 39. Zhegova 2014; 40. Zhegova 2014; 42. Valério 2015 44. Polizeli 2019; 46. DenBesten 2000; 47. DenBesten 2001; 52. Hadley 2000; 57. Belcheva 2014; 58. Belcheva 2014. Seven out of 12 studies assessing pain reported that laser treatment provided a significantly better treatment experience than conventional treatment, and there were fewer signs of discomfort or pain during the consultation. In one study, the smell and taste complaints were significantly higher in the patients receiving treatment with the Er:YAG laser compared to conventional treatment. <i>Air- and/or sono-abrasion (VS) systems compared with control (1 study):</i> Chomyszyn-Gajewska 2006. Treatment time: Treatment with VS was significantly longer than conventional treatment in one study. Patients' pain perception/behaviour: Treatment with VS induced significantly less pain than conventional treatment. <i>CariSolv compared with Papacarie compared with control:</i> 15. Ammari 2014; 41. Hegde 2016; 54. Kochhar 2011. Treatment time: 15. Ammari 2014; 41. Hegde 2016; 54. Kochhar 2011. In three studies, CariSolv and Papacarie showed longer treatment times compared with conventional treatment. However, Papacarie was faster than CariSolv in one study and significantly quicker than CariSolv in one of the studies. Caries removal: 41. Hegde 2016; 54. Kochhar 2011. In one of the included studies, Papacarie was significantly more efficient than CariSolv within the criteria used. In another study, there were fewer remaining caries in the Papacarie group than in the patients treated with Carisolv. Colony-forming units count: 15. Ammari 2014. In one of the included studies, both conventional and alternative methods significantly reduced dentine bacterial count, with no differences identified between approaches. Patients' pain perception/behaviour: 41. Hegde 2016; 54. Kochhar 2011. In two of the included studies, Papacarie induced significantly less pain and offered a more comfortable treatment approach, making it the most accepted treatment. <i>CariSolv compared with Papacarie compared with Er:YAG laser compared with control (1 study):</i> Bohari 2012. Treatment time: Treatment with the Er:YAG laser was significantly faster than treatment with CariSolv and Papacarie. Treatment with Papacarie was slightly quicker than CariSolv. Caries removal (remaining caries, cavity dimensions, or other): The included study performed measurements with DIAGNOdent, where the laser-treated teeth showed the highest percentage of change after treatment, which was significantly higher than that measured in teeth treated with CariSolv or with Papacarie. It is not clear whether the change is positive or negative, but the HRB assumed a negative percentage deterioration in the tooth performance.

Parameter	Extraction
	<i>Sodium hypochlorite gel compared with Brix 3000 compared with control (1 study): 49. Alkhouli 2020.</i> Treatment time: Treatment times with the sodium hypochlorite gel and Brix 3000 were significantly longer than those of conventional methods.
Results/findings	Narrative findings are presented with each outcome above. The alternative methods had longer treatment times compared with the conventional methods. Both conventional and alternative approaches reduced cariogenic flora within the cavities. Alternative methods for caries removal showed a tendency to produce more comfortable treatment experiences and had reduced requests for anaesthesia. Although every method decreased self-reported pain in patients when compared with conventional mechanical treatment, the chemomechanical treatments were statistically significantly better than the other alternative methods (Er:YAG and Er,Cr:YSGG laser systems). The vector system also presented with significantly less induced pain. However, smell and taste were found to be factors for increased anxiety. The longevity and survival of restorations performed by each method did not significantly differ from each other. Papacarie was the most studied chemomechanical treatment and presented efficiency for caries removal and high patient acceptance. The authors concluded that "The restorations performed by each method did not significantly differ from each other in terms of longevity and survival. Alternative methods for caries removal tend to prolong treatment time and cause fewer requests for anesthesia during treatment; however, dentition, cavity extension, and pulpal response before treatment and patient-related factors should be considered when establishing the treatment plan. Both conventional and alternative approaches are efficient in reducing cariogenic flora from the cavities. The marginal integrity of restorations did not differ significantly between methods for caries removal. Patients reported more pleasant treatment experiences with alternative treatment approaches and higher percentages for acceptance and preference in future treatments for alternative methods were registered. Chemomechanical solutions seem to be the best option for minimally invasive treatments, with good control of their application and action, as well as good treatment experiences for patients. Papacarie was the most studied solution in this treatment modality and presented efficiency for caries removal and high patient acceptance." ¹⁶⁶ (p3406–3407)
Significance/direction	Results listed by outcome; intervention effectiveness appears equal while patients reported better experiences when using alternative interventions.
Heterogeneity	No statistical heterogeneity was reported, as a meta-analysis was not completed.
Comments	GRADE was not used by the review authors. This systematic review included a mix of randomised and non-randomised trials with an unclear or high risk of bias for all trials. Less than one-half of the trials had adequate randomisation and less than one-third had adequate blinding for ascertainment of outcome. There was no description of the analysis methods and meta-analysis was not employed. Heterogeneity was not mentioned in the article. The review is a summarisation using a vote counting approach rather than a synthesis of findings. The quality of the systematic review was judged as low using AMSTAR 2 as the review authors were not able to control for risk of bias in the analysis. Considering these limitations, the quality of evidence is very low for all outcomes.

Zhang *et al.* (2020)

Parameter	Extraction
First author and year of publication	Zhang <i>et al.</i> (2020) ¹⁶⁷
Objectives	Evaluated the extent of microleakage from tooth cavities in humans prepared by Er,Cr:YSGG lasers compared with microleakage from cavities prepared by traditional burs, and the effectiveness of acid etching on the adhesive potential of self-etch and etch-and-rinse adhesives after laser preparation compared with no etching.
Participants	Permanent or primary dentition, cavitated lesions, restoration technique

Parameter	Extraction
	Tooth cavities in humans prepared for restoration Thirteen randomised and quasi-randomised trials, published between 2001 and 2018, with 1243 teeth were included in this review. Eight studies included permanent teeth and five included primary teeth. There were a number of different classes of cavity covered in the study: nine studies covered Class V cavities, two studies covered Class II cavities, one study covered Class III cavities, and one study did not report the cavity type. The main restoration material used was a form of resin, although one study used resin-modified glass ionomer cement. All the studies that used resin restorations used either self-etch or etch-and-rinse adhesives. Age and gender were not reported.
Setting/context	The clinical settings were not reported. The study countries were Brazil, Germany, Iran, Spain, and Turkey.
Description of interventions/phenomena of interest	Intervention: The authors reported that “The member of erbium laser family, Erbium, Chromium:Yttrium Scandium Gallium Garnet (Er,Cr:YSGG) has gained the approval for caries removal and cavity preparation by the Food and Drug Administration [3]. Compared with traditional burs, Erbium, Chromium:Yttrium Scandium Gallium Garnet (Er,Cr:YSGG) laser does not contact the tooth directly and has less vibration, noise, pressure, and thermal damage during cavity preparation. Moreover, previous studies have reported a significant alteration in surface topography of the cavity after laser preparation, which might improve adhesion and the restorative procedure. Several researchers have measured the microleakage of cavities prepared by lasers and reported favorable results, while other studies have reported the opposite results. Additionally, some researchers have recommended the use of acid etching in combination with self-etch and etch-and-rinse adhesives following laser preparation.”¹⁶⁷ (p1–2) Comparator: Conventional drills or traditional burs, and enamel etching compared with no etching when using the Er,Cr:YSGG laser
Databases and sources searched	Three electronic databases were searched up to July 2019: PubMed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL). EBSCO was also searched but the names of the databases searched in EBSCO were not reported. The search strategy had no language restrictions and is provided in the text. To avoid missing eligible studies, the reference lists of all the selected full-text studies were also screened. The authors did not report preparing a protocol. Duplicate screening and extraction were completed. The authors declared that they have no competing interests and no funding was sought for the review.
Date range (years) of included studies	Thirteen randomised and quasi-randomised trials, published between 2001 and 2018, with 1243 teeth were included in this review.
Number of primary studies included in the systematic review	Thirteen randomised and quasi-randomised trials, published between 2001 and 2018, with 1243 teeth were included in this review. Eight studies included permanent teeth and five included primary teeth. There were a number of different classes of cavity covered in the study: nine studies covered Class V cavities, two studies covered Class II cavities, one study covered Class III cavities, and one study did not report the cavity type. While the main restoration material used was a form of resin, one study used resin-modified glass ionomer cement. The sources of funding for primary studies were not reported.
Types of studies included	Randomised controlled trials and quasi-randomised trials were eligible. A list of studies excluded at full-text screening was not provided, but their reasons for exclusion were reported.
Country of origin of included studies	The study countries were Brazil, Germany, Iran, Spain, and Turkey.
Appraisal instruments used	The Cochrane Collaboration’s risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	All 13 studies were judged to have an unclear risk of bias. One (8%) of the 13 studies was judged to have adequate randomisation and 7 (54%) had adequate blinding of outcome assessment. Publication bias was not measured. The authors reported that “The quality of the included studies was not favorable, possibly decreasing the reliability of conclusions drawn in the present study.”¹⁶⁷ (p4)
Method of analysis	Statistical analysis was performed using RevMan 5.3 software provided by the Cochrane Collaboration. Risk ratio was used along with 95% CIs for dichotomous

Parameter	Extraction
	data, while the mean difference was used with 95% CIs for continuous data. In addition, the Z-test was used. The I^2 Inconsistency Index on the level of $\alpha=0.10$ was used to evaluate statistical heterogeneity. When there was significant statistical heterogeneity ($I^2 > 50\%$), a random-effects model was used to analyse the data. If I^2 was $\leq 50\%$, a fixed-effects model was used. The statistical significance for the hypothesis testing was set at $\alpha < 0.05$ (two-tailed Z-tests). When the data could not be pooled in the meta-analysis, they were summarised qualitatively.
Outcome assessed	Outcomes: Microleakage from cavities prepared by a specific laser compared with microleakage from cavities prepared using a traditional bur: Malekafzali 2017; Subramaniam 2016; Ergin 2018; Shahabi 2008 or 2010; Fattah 2013; Shafiei 2015; Shafiei 2014; Yazici 2012; Gutknecht 2001; Trelles 2012; Marotti 2010 (not in meta-analysis: Rossi 2008; Geraldo-Martins 2013). Acid etching in combination with self-etch following laser preparation compared with no etching following laser preparation: Shafiei 2015; Shafiei 2014. Acid etching in combination with etch-and-rinse adhesives following laser preparation compared with no etching following laser preparation: Shahabi 2008 or 2010; Gutknecht 2001.
Results/findings	Meta-analysis using a random-effects model indicated that the incidence of microleakage was not statistically significantly higher when employing a traditional bur compared with the Er,Cr:YSGG laser both on the dentine and the whole marginal line (relative risk: 1.03; 95% CI: 0.85–1.25; $p=0.74$; I^2: 80%; 1,243 teeth; 11 trials; dentine margin: relative risk: 1.26; 95% CIs: 0.67–2.38; $p=0.47$; I^2: 88%; 424 teeth; 6 trials; whole marginal line: relative risk: 1.27; 95% CIs: 0.44–3.67; $p=0.66$; I^2: 85%; 395 teeth; 5 trials). In addition, the results of the enamel margin subgroup revealed a non-significant increase in microleakage in the Er,Cr:YSGG laser group (relative risk: 0.87; 95% CIs: 0.60–1.27; $p=0.47$; I^2: 84%; 424 teeth; 6 trials). Two studies did not report specific microleakage scores or indexes and were excluded from the meta-analyses. One excluded study reported no difference in microleakage and the other reported that the Er,Cr:YSGG group had a higher incidence of microleakage compared with the traditional bur group. There was significant (or substantial) statistical heterogeneity among the studies in the meta-analyses. It was reported that prior acid etching improved the adhesive potential of self-etching adhesives and significantly decreased microleakage after laser preparations (relative risk: 2.69; 95% CI: 1.74–4.15; $p<0.00001$; I^2: 0%; 112 teeth; 2 trials). The significant difference was detected both in the enamel and dentine margin subgroups (enamel margin: relative risk: 3.0, 95% CI range: 1.54–5.83; $p=0.001$; I^2: 0%; 56 participants; 2 trials; dentine margin: relative risk: 2.44; 95% CI range: 1.38–4.34; $p=0.002$; I^2: 0%; 56 teeth; 2 trials). Prior acid etching did not improve the adhesive potential of the etch-and-rinse adhesives or incidence of microleakage when compared with no etching (relative risk: 1.18; 95% CI: 0.63–2.22; $p=0.60$; I^2: 81%; 50 teeth; 2 trials). The result revealed substantial statistical heterogeneity among the studies.
Significance/direction	Varied by outcome.
Heterogeneity	The authors reported that “it should be noted that there was significant heterogeneity among the included studies, and the conclusions reached in the present study should be interpreted cautiously.” ^{167 (p7)}
Comments	GRADE was not used by the review authors. This systematic review included a mix of randomised and quasi-randomised trials with an unclear risk of bias for all 13 trials. One (8%) of the 13 studies was judged to have adequate randomisation and 7 (54%) had adequate blinding of outcome assessment. Meta-analysis was employed to analyse these low-quality studies. Heterogeneity was high for all the main outcomes and sample sizes were small for secondary outcomes. The quality of the systematic review was judged as critically low using AMSTAR 2 as the review authors were not able to control for risk of bias in the analysis and did not discuss heterogeneity. Considering these limitations, the quality of evidence is very low for all outcomes.

Li *et al.* (2019)

Parameter	Extraction
First author and year of publication	Li <i>et al.</i> (2019) ¹⁶⁸
Objectives	Evaluated the clinical efficacy (operation time, pain, and long-term outcomes) of the Er:YAG laser for caries removal and cavity preparation in children compared with that of the conventional mechanical method.
Participants	Mixed dentition, cavitated caries, restoration technique The study included children diagnosed with dental decay (in primary teeth or permanent teeth). Participants in the included studies ranged in age from 3 to 16 years. Primary teeth were the exclusive focus in four trials, permanent teeth were the exclusive focus in one trial, and both primary and permanent teeth were examined in two trials.
Setting/context	The study countries or clinical settings were not reported.
Description of interventions/phenomena of interest	Interventions: The use of Er:YAG laser for caries removal and cavity preparation Control interventions: The use of traditional mechanical method for caries removal and cavity preparation The authors defined the intervention as follows: “The Er:YAG laser (erbium:yttrium aluminum garnet) was introduced into dentistry for the ablation of dental hard tissue and was approved for caries removal and cavity preparation in 1997 by the US Food and Drug Administration. The Er:YAG laser is a solid-state laser with a wavelength of 2940 nm [nanometers], which coincides with the peak of water absorption. The laser can selectively cut infected enamel and dentin with precision and efficiency. Furthermore, the laser reduces the unpleasant sound and does not produce vibration or pressure during the caries removal process or cavity preparation; as a result, laser treatment is preferred by most patients, especially children”. ^{168 (p273)}
Databases and sources searched	The authors searched nine databases – PubMed, MEDLINE, the Cochrane Library, Ovid, ScienceDirect, Chinese National Knowledge Infrastructure (CNKI), Chinese Biological Medicine (CBM), VIP information/ Chinese Scientific Journals database, and Wanfang Data – with publication date limits of 1997 to July 2017. Other search limits were not reported. There were no other sources reported as searched for additional materials. The authors did not report preparing and registering a protocol. Extraction and screening were completed in duplicate. The sources of funding for the review were not reported. The authors declare that they have no conflict of interest.
Date range (years) of included studies	The included studies were published from 1997 to 2017.
Number of primary studies included in the systematic review	Seven randomised controlled trials (five split-mouth trials and two practice-based trials), published from 1997 to July 2017, were included. The sources of funding for primary studies were not reported.
Types of studies included	Randomised controlled trials were eligible for inclusion. A list of studies excluded at the full-text stage was not provided in the review. However, the reasons for exclusion were provided in the main text.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	According to Li <i>et al.</i> , “The reviewers assessed the quality of all the included research using the modified Jadad scale. In the modified Jadad scale, the maximum quality score is 7 points, and a quality score ≥ 4 is considered high quality for randomized controlled trials. A score < 4 is considered to be low quality”. ^{168 (p274)}
Appraisal rating	The authors stated that “The quality of all included research studies was assessed using the modified Jadad scale. In this meta-analysis, four studies scored > 4 and were considered to be high quality, and three studies scored < 4 and were considered low quality”. ^{168 (p275)} According to the authors, four of the seven studies had adequate randomisation. Risk of bias regarding outcome assessment was not reported. In this meta-analysis, there were four high quality studies among the seven fully evaluated studies. Regarding publication bias, the authors stated that “The results of the Begger’s test indicated there was no publication bias in any of the research included in this meta-analysis”. ^{168 (p276)}

Parameter	Extraction
Method of analysis	According to Li <i>et al.</i>, "This study used STATA version 10.0 software to conduct the meta-analysis. A Cochran's Q test was conducted to assess the heterogeneity of each study. The heterogeneity results were used to determine if the Mantel–Haenszel fixed-effects model ($p \geq 0.1$) or the DerSimonian Laird random-effects model ($p < 0.1$) was used for the calculation of pooled standardised mean difference (SMD) or relative risk (RR) and 95% confidence interval (95% CI). Begger's test was used to assess publication bias with a $p < 0.1$ indicating statistical significance. All p-values were two-sided. The meta-analysis was performed with the longest follow-up period of each index".^{168 (p274)}
Outcome assessed	The outcomes assessed were: procedure time, pain, complete restoration retention rates, marginal discolouration, marginal adaptation, and secondary caries. Clinical efficacy: Liu 2006; Valerio 2016; GV 2015 (not in bibliography); Lv 2015; Xu 2015 ; Wei 2016 ; Zhang 2013.
Results/findings	The authors reported that "The procedure time was assessed in five RCTs [randomised controlled trials], and the Cochran's Q test analysis showed heterogeneity among these studies (Chi-squared test=70.50, $p < 0.001$, $I^2=94.3\%$). The meta-analysis result using a random-effects model indicated that the time required by the Er:YAG laser was longer (SMD [standardised mean difference]: 1.945, 95% CI: 0.942 to 2.948, $p < 0.001$) than that of the conventional mechanical method".^{168 (p275)} They continued, "The pain score was assessed in five RCTs [randomised controlled trials], and the Cochran's Q test showed that there was [substantial] heterogeneity Chi-squared test =45.02, $p < 0.001$, $I^2=93.3\%$). The meta-analysis result of our random-effects model suggested that the pain caused by the Er:YAG laser was less (SMD: -1.013, 95% CI: -1.829 to -0.791, $p < 0.001$) than the pain reported from the conventional mechanical method".^{168 (p275)} According to the authors, "The complete retention result was assessed in four RCTs [randomised controlled trials], and the Cochran's Q test showed there was no [or some] heterogeneity (Chi-squared test =1.410, $p = 0.495$, $I^2=41.8\%$). The meta-analysis result of a fixed-effects model showed that there were no significant differences (RR [relative risk]=1.011, 95% CI: 0.937 to 1.091, $p = 0.783$) for the complete retention of restoration using the Er:YAG laser and conventional mechanical method".^{168 (p275)} Li <i>et al.</i> reported that "The marginal discoloration result was assessed in three RCTs [randomised controlled trials], and a Cochran's Q test showed there was no heterogeneity (Chi-squared test =0.280, $p = 0.594$, $I^2=0.00\%$). The meta-analysis result of the fixed-effects model showed that there were no significant differences (RR: 1.638, 95% CI: 0.224 to 11.986, $p = 0.627$) in the marginal discoloration of restoration for the Er:YAG laser and conventional mechanical methods".^{168 (p275)} The authors stated, "The marginal adaptation result was assessed in three RCTs [randomised controlled trials], and the Cochran's Q test showed there was no heterogeneity (Chi-squared test =0.160, $p = 0.692$, $I^2=0.00\%$). The meta-analysis result of the fixed-effects model showed that there were no significant differences (RR=1.480, 95% CI: 0.257 to 8.515, $p = 0.661$) in the marginal adaptation of restoration for the Er:YAG laser and conventional mechanical method".^{168 (p276)} However, the authors also noted that "There were insufficient data to perform a meta-analysis of secondary caries results".^{168 (p276)} According to Li <i>et al.</i>, "In this meta-analysis, there were four high-quality studies among the seven fully evaluated studies. Studies were designed using a split-mouth comparison, and all procedures were performed by a single physician to reduce the error variance and improve the statistical power. The results of the Begger's test indicated that there was no publication bias in any of the research included in this meta-analysis. Furthermore, we selected the appropriate analysis model based on previous Cochran's Q test heterogeneity assessment results. Therefore, this meta-analysis is reliable".^{168 (p276)}
Significance/direction	"Overall, the authors concluded that: (1) The operation time of the Er:YAG laser treatment is longer than the conventional mechanical method (2) The pain produced by the Er:YAG laser is reduced compared with the conventional mechanical method, and

Parameter	Extraction
	(3) There are no statistical differences in complete restoration, retention, marginal discolouration, and marginal adaptation between the Er:YAG laser and conventional mechanical method." ^{168 (p279)}
Heterogeneity	The authors provided the following statement regarding heterogeneity: "A Cochran's Q test was conducted to assess the heterogeneity of each study. The heterogeneity results were used to determine if the Mantel-Haenszel fixed-effects model ($p \geq 0.1$) or the DerSimonian Laird random-effects model ($p < 0.1$) was used for the calculation of pooled standard mean difference or relative risk and 95% confidence interval". ^{168 (p274)}
Comments	According to the authors, "This meta-analysis is the first systematic evaluation of the effectiveness of the Er:YAG laser for caries removal and cavity preparation in children". ^{168 (p276)}

Cianetti *et al.* (2017)

Parameter	Extraction
First author and year of publication	Cianetti <i>et al.</i> (2017) ¹⁶⁹
Objectives	Evaluated the effectiveness (treatment time, need for anaesthesia, clinical performance and pulpal complications) and degree of acceptance (pain, discomfort, and fear) by children and adolescents of the use of Sonic and ultrasonic devices with oscillating tips compared with conventional rotating drills to remove carious tissue from primary or permanent teeth.
Participants	Mixed dentition, cavitated caries, restoration technique Children and adolescents with caries. Studies carried out on patients affected by specific oral or systemic diseases were excluded. Both deciduous and permanent teeth were included, with only restored and non-vital teeth excluded. The two clinical controlled trials had a split-mouth design and involved a total of 103 children, whose ages ranged from 2 to 12 years. The study in Poland involved 31 children, 62 teeth, and 62 caries; the children's ages ranged from 7 to 11 years. The study in China involved 72 children, 186 teeth, and 186 caries; the children's ages ranged from 3 to 12 years.
Setting/context	The study in China involved children attending the Peking University Department of Paediatric Dentistry. The study in Poland involved children attending the Department of Paediatric Dentistry, Cracow University [of Technology].
Description of interventions/phenomena of interest	Intervention: Sonic and ultrasonic devices to remove caries and to prepare cavities for fillings. Comparator: Conventional high-speed and/or low-speed rotating instruments. The authors noted that "Sonic and ultrasonic devices belong to an alternative group of so-called 'micro-traumatic' tools to remove caries that include several other alternative devices/approaches to rotating instruments. The most noteworthy are atraumatic restorative techniques, chemomechanical removal of caries, lasers, air abrasion and polymer rotary burs. Oscillating devices, therefore, are potentially useful tools [for treating] caries with a 'psychological microinvasive approach' reducing the recourse to more complicated pharmacological procedures, such as conscious sedation or general anaesthesia. It is well reported that psychological condition impacts children's and adolescents' oral health status, by conditioning their dental service attendance as well as their compliance with treatment. Hence, sonic and ultrasonic ablation devices can be attractive alternative tools to overcome concerns regarding dental anxiety." ^{169 (p2)}
Databases and sources searched	The authors searched four databases (MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL), the Cochrane Library, and Web of Science) up to October 2017. No language limitations were placed on the search results. Moreover, studies reported in reference lists of obtained articles (reviews and/or studies) and specified in reference lists of the most relevant textbooks in this field were screened in order to find additional relevant studies. If multiple publications of a single trial were available, only the first publication was considered, except in cases where additional data were reported, such as delayed outcome results. The completion of a protocol was not mentioned in the article.

Parameter	Extraction
	Extraction and screening were completed in duplicate. Agreement of selection and quality appraisal procedures between the reviewers was almost perfect ($\kappa > 0.94$). Funding: This study was funded by the Italian National Centre for Disease Prevention and Control – Ministry of Health). The sponsor was not involved in the format of the study; the collection, analysis, or interpretation of the data; or the writing of the article and the decision to submit it for publication. The authors were independent from the study sponsors. No conflicts of interest were declared by the authors.
Date range (years) of included studies	The included studies were published in 2004 and 2010 and without language limitations.
Number of primary studies included in the systematic review	Only two non-randomised controlled clinical trials, published in 2004 and 2010, were included in the review. The systematic review asked for information on source of funding for the primary studies, but none was declared
Types of studies included	Randomised controlled trials and controlled clinical trials were eligible for inclusion. Excluded studies with reasons for their exclusion are listed in an online supplementary appendix.
Country of origin of included studies	The studies were carried out in China and Poland.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	Both of the included studies were at high risk of bias. Both studies were at high risk of bias for randomisation and at unclear risk of bias for outcome assessment. Cianetti <i>et al.</i> stated that "By default, the two included trials were not randomised and were considered at high risk of selection bias. In addition, none of the studies reported whether the outcome assessor was blinded and were judged unclear in terms of detection bias. No concern was identified in terms of attrition bias as well as selective reporting bias. Basic characteristics of the patient population were similar between the groups".^{169 (p4)} Publication bias assessment was not relevant, as only two studies were summarised.
Method of analysis	According to the authors, "Where possible, for dichotomous outcomes we calculated risk ratios with 95% CI for each trial; for continuous data, we calculated mean difference. In the case of studies of split-mouth design, we planned to calculate log risk ratio and standard error separately for each outcome. We planned to combined data from split-mouth studies with data from parallel-group trials using the method suggested by Elbourne <i>et al.</i> , employing the generic inverse-variance method available in Review Manager V.5. Due to heterogeneity of the data, it was not possible to conduct any meta-analysis." ^{169 (p3)}
Outcome assessed	The planned outcomes were: Primary outcomes – episodes of pain and discomfort during and after treatment; dental fear; and removal of caries as confirmed by clinical, radiological, or other validated assessment tools. Secondary outcomes – durability of restoration (marginal integrity), recurrent caries, pulpal necrosis, patients' acceptance of treatment, patients' preferences, need for anaesthesia, dental practitioner's assessment, duration of treatment, costs of intervention, and adverse events. The actual outcomes assessed were dental caries removal, dental anxiety, pain, discomfort, patients' preference, duration of treatment, and durability of restoration. Effectiveness and degree of acceptance: Chomyszyn-Gajewska 2006; Li 2010.
Results/findings	Dental caries removal According to the authors, "This outcome was reported only by Li <i>et al.</i> In this study, no cases of residual caries were described in either intervention group. Analysis did not show... any difference between the sonic and standard drill (one study, 93 treated caries in each group, risk ratio: 1.00 (95% CI: 0.98 to 1.02))".^{169 (p5-6)} Dental anxiety

Parameter	Extraction
	The authors reported that “This outcome was reported in one study...the dental anxiety was measured together with patient cooperation forming the following single outcome: dental anxiety and patient’s cooperation. The percentage of children showing dental anxiety and negative cooperation with the dentist was lower when an ultrasonic tip (n=39/93; 42%) was used than when a traditional drill was used (n=51/93; 55%) but the difference was not statistically significant (RR 0.78 (95% CI: 0.58 to 1.03)).”^{169 (p6)} Pain Cianetti <i>et al.</i> stated that “This outcome was considered in one study. When the Verbal Hochman Scale was employed, 14 out of 31 participants (45%) treated with an ultrasonic tip and abrasive suspension reported pain compared with 22 participants (71%) treated with a traditional drill (risk ratio: 0.64 (95% CI: 0.41 to 1.00); $p=0.05$). Similarly, when the Visual Facial Expression Scale was used, 16 paediatric patients (50%) treated with a traditional drill reported pain or discomfort compared with 25 patients (22%) treated with an ultrasonic tip and abrasive suspension (risk ratio: 0.64 (95% CI: 0.44 to 0.94); $p=0.02$).”^{169 (p6)} Discomfort The review noted that “Only one study reported on this outcome. Patient discomfort during dental treatment was usually due to sight, noise or vibration related to use of ablating instruments. In the intervention group (ultrasonic tip), children experienced moderate or high uncomfortable sensation (for values within the latest two levels of the Five Faces Rating Scale) in 10 out of overall 93 [patients] (11%) during treatment. Conversely, in the control group (traditional rotating drill) children felt a comfortable or slightly uncomfortable experience only in 25 out of 93 (27%) of the cases. A statistically significant difference was found between these two compared instruments in terms of discomfort, with a better performance in favour of an ultrasonic tip (risk ratio: 0.40 (95% CI: 0.20 to 0.79); $p=0.008$).”^{169 (p6)} Patients’ preference According to Cianetti <i>et al.</i>, “Of the two included studies, only one study demonstrated an overwhelmingly higher percentage of paediatric patients (88.2%) who preferred to be treated with ultrasonic devices for future dental care. Conversely, only a lower percentage of study participants (11.8%) chose the traditional rotating drill. In the other study, no data on this outcome were reported.”^{169 (p6)} Duration of treatment Cianetti <i>et al.</i> stated, “In one study, the traditional drill was statistically significantly faster at ablation compared with the ultrasonic tip (average time: 3.5 minutes, SD [standard deviation] ± 2.3 minutes compared with 4 minutes, SD ± 2.5 minutes; $p<0.05$). Likewise, the other study demonstrated that in terms of length of time to prepare cavities, rotating drills were significantly faster (3.9 minutes during treatment for dentinal caries just beyond the amelo-dentinal junction; 5.5 minutes during treatment for dentinal caries advancing for at least half the depth of the dentine) compared with ultrasonic tips (9 to 16.8 minutes) ($p<0.0002$).”^{169 (p6)} Durability of restoration The authors stated that “Of the two studies, only one considered the durability of restoration. They found that all 93 dental fillings in both intervention and control groups were retained in their cavities at 1 week, 3 months or 6 months. Moreover, in this study also, the dental sensitivity was considered a sign of filling integrity over time. One out of 93 filled teeth in the intervention group versus 4 out of 93 restored teeth in the control group reported sensitivity at 6 months after initial visit.”^{169 (p6)} According to the authors, “The use of oscillating devices for caries removal is becoming more common among dental practitioners. Unfortunately, the high expectations regarding the use of oscillating devices to remove caries were not completely supported by data from published clinical studies. Only a few methodologically low-quality clinical studies described the effectiveness of oscillating devices to manage caries. Therefore, the potential positive features of oscillating tips, in terms of caries removal and ultraconservative preparation of

Parameter	Extraction
	cavities, in addition to low pain, decreased discomfort and reduced anxiety induction, remain clinically unproven.” ¹⁶⁹ (p6–7)
Significance/direction	The authors stated that “The lack of available literature with a high methodological quality prevented us from answering the main question of this systematic review. The effectiveness of sonic and ultrasonic tips for managing pain and dental fear in children and adolescents who required caries removal remains, therefore, unproven and further research is required.” ¹⁶⁹ (p7)
Heterogeneity	The authors provided the following comment on heterogeneity: “Due to heterogeneity of the data, it was not possible to conduct any meta-analysis.” ¹⁶⁹ (p3)
Comments	GRADE was used by the review authors. The authors reported that “Only a few methodologically low-quality clinical studies described the effectiveness of oscillating devices to manage caries. Therefore, the potential positive features of oscillating tips, in terms of caries removal and ultraconservative preparation of cavities, in addition to low pain, decreased discomfort and reduced anxiety induction, remain clinically unproven.” p6

Dorri *et al.* (2017)

Parameter	Extraction
First author and year of publication	Dorri <i>et al.</i> (2017) ³⁰ (Cochrane Review)
Objectives	Compared atraumatic restorative treatment with conventional treatment (the drill and fill approach) for managing dental carious lesions in the primary and permanent teeth of children and adults.
Participants	Mixed dentition, cavitated caries, restoration technique Population: Primary and permanent teeth of children and adults Fifteen randomised controlled trials in 22 articles published between 2003 and 2016, with 3,760 participants, were included in this Cochrane Review. The mean age of the participants was 25.4 years (ranging from 3 to 101 years). Forty-eight per cent of participants were male. Eleven studies evaluated the effects of atraumatic restorative treatment on primary teeth only, and four on permanent teeth only.
Setting/context	The study setting was dental clinics or hospitals for seven studies, schools for two studies, and nursing homes for two studies. Four studies did not report the setting. Studies were completed in Brazil, China, Colombia, Indonesia, Ireland, Suriname, Tanzania, and Turkey. There was one international multicentre trial.
Description of interventions/phenomena of interest	Atraumatic restorative treatment “is a minimally invasive approach, which involves removal of decayed tissue using hand instruments alone, usually without use of anesthesia and electrically driven equipment, and restoration of the dental cavity with an adhesive material such as glass ionomer cement, composite resins, resin-modified glass ionomer cement, or compomers.” ³⁰ (p6) Comparator: Conventional treatment (drill) using the same material. Conventional methods (drill and fill) involve the use of electric drills to clear away decayed areas of the tooth before filling. A local anaesthetic (painkiller) is normally injected in order to prevent pain during the procedure.
Databases and sources searched	The authors searched six databases: Cochrane Oral Health Group Trials Register (to 22 February 2017), the Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library, 2017, Issue 1), MEDLINE via Ovid (1946 to 22 February 2017), Embase via Ovid (1980 to 22 February 2017), Latin American and Caribbean Health Sciences Literature database (LILACS) via BIREME Virtual Health Library (1982 to 22 February 2017), and Brazilian Library in Dentistry (BBO) via BIREME Virtual Health Library (1986 to 22 February 2017). ClinicalTrials.gov and the WHO’s International Clinical Trials Registry Platform were searched for ongoing trials. No restrictions were placed on the language or date of publication when searching the electronic databases. All search strategies were provided in an appendix. The authors examined the reference lists of relevant trials to identify studies not identified in the previous searches. The authors completed a protocol. Screening and extraction were completed in duplicate.

Parameter	Extraction
	None of the authors had conflicts of interest. The authors received funding from several public funding sources.
Date range (years) of included studies	Fifteen randomised controlled trials in 22 articles published between 2003 and 2016 were included.
Number of primary studies included in the systematic review	Fifteen randomised controlled trials in 22 articles published between 2003 and 2016, with 3,760 participants, were included in this Cochrane Review. Eleven studies evaluated the effects of atraumatic restorative treatment on primary teeth only, and 4 on permanent teeth only. Five studies were individually randomised parallel-group studies, six were cluster-randomised parallel-group studies, and four were randomised studies that used a split-mouth design. Four primary studies received industry support to carry out the research or had other conflicts of interests.
Types of studies included	The authors excluded 27 studies and provided details and reasons for exclusion.
Country of origin of included studies	Studies were completed in Brazil, China, Colombia, Indonesia, Ireland, Suriname, Tanzania, and Turkey. There was one international multicentre trial.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included trials.
Appraisal rating	All 15 included trials were judged to be at high risk of bias due to performance, attrition, and selective reporting bias based on the Cochrane Collaboration's risk of bias instrument. Nine of the 15 trials were judged to have adequate randomisation, and 8 had adequate blinding of the outcome assessors. The authors did a comprehensive search and planned to quantitatively assess publication bias, but said that they did not have enough trials, and instead considered this in their GRADE assessment.
Method of analysis	The authors pooled only studies that used the same restorative materials in both comparator groups, as different restorative materials require different cavity designs and have different properties that may affect the study outcomes. The analysis includes data only of those whose results are known, using as a denominator the total number of participants for whom data were recorded for the particular outcome. The authors expected differences in effect estimates between studies in terms of the number of cavities or surfaces treated per participant and also the duration of follow-up. Therefore, the authors applied a random-effects model for any meta-analyses. They pooled parallel and split-mouth data using the generic inverse variance. They did not pool data if heterogeneity was over 75%. This was mainly because indicating an average value for the intervention effect when there is significant inconsistency in the direction of effect may be misleading. The authors anticipated variation in the timing of end points across the studies, both in terms of participant-reported pain and clinical restoration failure. They included in the meta-analysis the longest follow-up reported for each study. Where studies had multiple intervention or comparator trial arms, they combined summary statistics from all groups where appropriate. They excluded any intervention arms without atraumatic restorative treatment from the meta-analysis. The data were analysed using RevMan 5 software. In the event that there were insufficient clinically homogeneous trials for any specific intervention or insufficient study data that could be pooled, a narrative synthesis was presented. Subgroup and sensitivity analyses were planned.
Outcome assessed	Outcome by primary study: Restoration failure at 6 months or more: Cruz 2016; Da Mata 2015; De Menezes 2009; Eden 2006; Estupiñan-Day 2006; Lin 2003; Ling 2003; Lo 2006; Luz 2012; Miranda 2005; Roeleveld 2006; Schriks 2003; Van den Dungen 2004; Van de Hoef 2007; Yu 2004. Restoration failure at 12–24 months: Lin 2003; Roeleveld 2006; Van den Dungen 2004; Van de Hoef 2007; Yu 2004. Pain during and around procedure: De Menezes 2009. Adverse events (no evidence). Secondary caries (not usable as not analysed by trial arm). Participant experience (no difference in anxiety): Eden 2006. Costs (no evidence).
Results/findings	Meta-analysis was used for the main analysis. Subgroup and sensitivity analyses were done where numbers of primary studies permitted.

Parameter	Extraction
	For the main comparison of atraumatic restorative treatment, the authors compared conventional treatment using the same material. All but two studies used high-viscosity glass ionomer as the restorative material; one of these studies used a composite material, while the other used resin-modified glass ionomer cement. Atraumatic restorative treatment (as opposed to conventional treatment placing high-viscosity glass ionomer cement) may increase the risk of restoration failure in the primary dentition over a follow-up period ranging from 12 to 24 months (random effects: odds ratio: 1.60; 95% CI range: 1.13–2.27, I²: 0%; 5 studies; 643 participants analysed; low-quality evidence). The authors' confidence in this effect estimate is limited due to serious concerns over the risk of performance and attrition bias. For the comparison, atraumatic restorative treatment may reduce pain experienced by children during the procedure compared with conventional treatment, although there was no difference in pain experienced (fixed-effects: mean difference: –0.65; 95% CI range: 1.38–0.07; not statistically significant; 40 participants analysed; 1 study; very low-quality evidence). Comparisons of atraumatic restorative treatment with conventional treatment for placing composite or resin-modified glass ionomer cement were downgraded to low quality due to indirectness, imprecision, and high risk of performance and attrition bias. Given the very low quality of the evidence from single studies, the review authors were uncertain about the restoration failure of atraumatic restorative treatment compared with conventional treatment using composite over a 24-month follow-up period (random effects: odds ratio: 1.11; 95% CI range: 0.54–2.29; 1 study; not statistically significant; 57 participants; very low-quality evidence) and with atraumatic restorative treatment when placing resin-modified glass ionomer cement in the permanent teeth of older adults with root carious lesions over a 6-month follow-up period (random effects: odds ratio: 2.71; 95% CI range: 0.94–7.81; 1 study; 64 participants; very low-quality evidence). The main finding from this review suggests that there is low-quality or very low-quality evidence upon which to compare the performance of atraumatic restorative treatment with that of the conventional technique when placing restorations in the permanent teeth of children or adults. According to Dorri <i>et al.</i>, “given the very low-quality of the evidence from single studies, we are uncertain about the restoration failure of atraumatic restorative treatment compared with conventional treatment using composite over a 24-month follow-up period and atraumatic restorative treatment using resin-modified glass ionomer cement in the permanent teeth of older adults with root carious lesions over a six-month follow-up period.”³⁰ (p24)
Significance/direction	Results listed by outcome
Heterogeneity	The results indicate that heterogeneity was not an issue.
Comments	GRADE was used by the review authors The authors acknowledged the high risk of bias in all studies and the very small sample sizes. Nine (60%) of the 15 trials were judged to have adequate randomisation, and 8 (53%) had adequate blinding of the outcome assessors. The quality of the systematic review was judged as low using AMSTAR 2, as the authors could not control for risk of bias in their meta-analysis. The HRB grade the quality of evidence is as low for all outcomes. The authors assessment of the quality of evidence corresponds with the HRB's assessment for some outcomes and is lower for other outcomes.

Tao *et al.* (2017)

Parameter	Extraction
First author and year of publication	Tao <i>et al.</i> (2017) ¹⁷⁰
Objectives	Evaluated the comparative clinical success (restoration loss, pulpal vitality, and post-operative sensitivity) and efficacy (procedure time, requirement for

Parameter	Extraction
	anaesthesia and acceptability) of erbium laser, compared with traditional drilling, in individuals with carious lesions.
Participants	Mixed dentition, cavitated caries, restoration technique The studies included 1,442 participants and examined 1,646 teeth with dental caries. The 1,442 participants' ages ranged from 3 to 68 years and 45% were male. According to the authors, "This sample size was sufficient to obtain robust conclusions."¹⁷⁰ (p331)
Setting/context	The study countries were Bulgaria (two studies), China (two studies), Germany (two studies), India (one study), Taiwan (one study), Turkey (two studies), the United Kingdom (UK) (one study), and the USA (three studies). The clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: Erbium laser equipment for caries removal: both Er:YAG and Er,Cr:YSGG laser systems were included because they have similar working principles. Both of their wavelengths coincide with the maximum absorption by water molecules and [by] hydroxyl group in enamel and dentine. Comparator: Traditional drilling. The intervention was described by the authors as follows: "Since the early days of laser use in dentistry by Goldman <i>et al.</i>, there are different types of lasers used to remove caries, such as ruby; CO₂ [carbon dioxide]; neodymium-doped yttrium aluminum garnet (Nd:YAG); argon fluoride (ArF) excimer; erbium, chromium, yttrium-scandium-gallium-garnet (Er,Cr:YSGG); and erbium yttrium aluminum-garnet (Er:YAG) lasers. The most popular one is the Er:YAG laser, which was authorized for use on human teeth by the [US] Food and Drug Administration in 1997. The Er:YAG laser wavelength (2940 nm) coincides with the peak of water absorption and hydroxyl radicals of hydroxyapatite. Effective ablation of the carious tissue occurs via microexplosions from the evaporation of the water contained in the mineralized tissue."¹⁷⁰ (p325) According to the authors, "Erbium laser equipment versus traditional drilling for caries removal was selected in our meta-analysis. Both Er:YAG and Er,Cr:YSGG laser systems were included because they have similar working principles. Both of their wavelengths coincide with the maximum absorption by water molecules and [by] hydroxyl group in enamel and dentin."¹⁷⁰ (p325) The authors described the comparator as follows: "Traditional drilling treatment removes caries through bur rotation, which generates a lot of heat and vibration. These can act on the nerve fibers of dentin to cause pain. But most of the energy of the erbium laser is absorbed by water and converted to kinetic energy, reducing pain. Moreover, it possesses a shallow force of penetration due to its non-contact caries removal mode and high biocompatibility because water is used as the energy mediator."¹⁷⁰ (p332)
Databases and sources searched	Four databases (MEDLINE via PubMed, the Cochrane Library, Embase, and Chinese National Knowledge Infrastructure CNKI) were searched from the earliest available data indexing to December 2016. No other search limits were reported. Reference lists of relevant studies were examined manually to identify additional eligible articles. The authors did not report preparing or registering a protocol. Extraction and screening were completed in duplicate. This work was supported by the Chinese National Science & Technology Pillar Program during the 12th Five-year Plan Period of China and the Science & Technology People-benefit Application Demonstration Project of Chengdu. The authors stated that they have no actual or potential conflicts of interest.
Date range (years) of included studies	The randomised controlled trials, quasi-randomised controlled trials, or controlled clinical trials of parallel design were published between 1997 and 2015.
Number of primary studies included in the systematic review	Fourteen studies, published from 1997 to 2015, were included in this review. According to the authors, "Data used in this meta-analysis were all from randomised controlled trials, quasi-randomised controlled trials, or controlled clinical trials of parallel design that compared the effects of erbium laser technology with traditional drilling/rotary instruments for caries removal."¹⁷⁰ (p325) The sources of funding of primary studies were not reported.
Types of studies included	Randomised controlled trials, quasi-randomised controlled trials, or controlled clinical trials of parallel design were included according to the text in the abstract.

Parameter	Extraction
	A list of studies excluded at full-text stage was not reported, but reasons for exclusion were provided.
Country of origin of included studies	The study countries were Bulgaria (two studies), China (two studies), Germany (two studies), India (one study), Taiwan (one study), Turkey (two studies), the UK (one study), and the USA (three studies).
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	One of the 14 studies was at a high risk of bias, two studies were at a low risk of bias, and the other 11 studies were at an unclear risk of bias according to the Cochrane Collaboration's assessment. Only two (14%) of the 14 studies were at low risk of bias for randomisation, whereas 12 (86%) of the 14 studies were at low risk of bias for outcome assessment. The authors conducted a sensitivity analysis for studies with large sample size and low risk of bias by eliminating trials with small sample size or high risk of bias. The results of the sensitivity analysis was consistent with the main meta-analysis results using all 14 studies. The authors report that "This review was limited by both the data quantity and data type available till December 2016".¹⁷⁰ (p331) Publication bias was not measured or discussed.
Method of analysis	Statistical analysis According to Tao <i>et al.</i>, "We used inverse variance weighted random-effects analysis with 95% confidence intervals (CIs) to estimate association for all the studies included. The random-effects models were used to measure the effect sizes because there was heterogeneity in the treatment efficacy. Random-effects meta-analysis was performed to acquire estimates of outcomes, and we presented the outcomes as mean differences (continuous outcomes, including time for cavity preparation) or risk ratios (RRs, dichotomous outcomes, including local anesthesia requirement, restoration loss, pulpal vitality, and post-operative sensitivity) with 95% CIs. We assessed heterogeneity using I^2 statistical index, and $I^2 > 50\%$ represented a high heterogeneity. $p < 0.05$ was regarded as statistically significant, apart from the heterogeneity test where $p < 0.1$ was considered statistically significant."¹⁷⁰ (p326–327) Sensitivity analysis The authors stated that "To assess the robustness of our meta-analysis results, sensitivity analysis was performed: (1) high-quality studies versus low-quality studies and (2) studies with small sample size versus studies with large sample size."¹⁷⁰ (p327)
Outcome assessed	Outcomes were evaluated during treatment or at follow-up visits as follows: (1) time for cavity preparation, (2) local anaesthesia requirement, (3) subjective acceptance by patients, (4) restoration loss, (5) pulpal vitality, and (6) post-operative sensitivity. Clinical success and efficacy: Zhegova 2015; Belcheva 2014; Zhang 2013; Eren 2013; Bohari 2012; Yazici 2010; Dommisch 2008; Liu 2006; DenBesten 2001; Hadley 2000; Evans 2000; Keller 1998; Pelagalli 1997; He 2013.
Results/findings	Time for cavity preparation (minutes) Tao <i>et al.</i> stated that "Six of the 14 studies reported time for cavity preparation. All of the 6 studies reported a shorter preparation time using conventional rotary instruments than erbium laser equipment. Heterogeneity of the 6 studies was indicated to be significant ($p < 0.01$, $I^2 = 98\%$). Meta-analysis demonstrated a significantly shorter time for cavity preparation using conventional rotary instruments than erbium laser equipment (mean difference: 3.48, 95% CI: 1.90–5.06, $p < 0.0001$)."¹⁷⁰ (p327) Local anaesthesia requirement According to the authors, "Four studies compared patients' requirement of local anesthesia using 2 kinds of treatment. No evidence of significant heterogeneity was found within these 4 studies ($p = 0.30$, $I^2 = 18\%$). A significant difference between the 2 kinds of treatment was noted. Fewer persons in the laser group experienced pain during cavity preparation and asked for the use of local anesthesia (risk ratio: 0.28, 95% CI: 0.13–0.62, $p = 0.002$)."¹⁷⁰ (p327–329) Subjective acceptance by patients

Parameter	Extraction
	The authors reported that “Two trials investigated subjective acceptance by patients of these 2 kinds of treatments. Belcheva <i>et al.</i> demonstrated that erbium YAG laser had a better level of subjective acceptance among patients compared with conventional rotary instruments for caries removal. Vibration, sight, and sound, which were the most common annoyance factors for patients during conventional cavity preparation, were eliminated using laser technology. However, one study reported that smell and taste during laser preparation were increased compared with drilling (prevalence of vibration in bur/laser group: 86.7%, 2.2%; prevalence of sight in bur/laser group: 40%, 20%; prevalence of sound in bur/laser group: 62.2%, 15.6%; prevalence of smell in bur/laser group: 17.8%, 66.7%; and prevalence of taste in bur/laser group: 22.2%, 42.2%). One study also reported that laser technology showed a better level of subjective acceptance compared with traditional drilling among patients older than 10 years. Significantly less vibration was felt during laser preparation than with drilling, but treatment time was significantly longer in the laser group. Smell, taste, and sound showed no significant difference between the 2 groups in this study. Meta-analysis could not be performed comparing subjective acceptance of patients in 2 kinds of treatment because data available in both studies were limited.”^{170 (p329)} Restoration loss According to Tao <i>et al.</i>, “Six of the included 14 studies reported restoration loss. Follow-up time in the six studies was 3 months, 6 months, 1 year, 2 years, 3 months, and 2 years, respectively. Heterogeneity could not be observed among the 6 studies ($p=0.73$, $I^2=0\%$). There was no significant difference between the 2 treatment groups considering restoration loss (risk ratio: 0.90, 95% CI: 0.21–3.84, $p=0.89$.”^{170 (p329)} Pulpal vitality The authors stated that “Four trials assessed pulpal vitality. Follow-up time in the four studies was 3 months, 6 months, 1 year, and 1 year, respectively. One study tested pupal vitality immediately after the treatment. Heterogeneity of these four studies was not significant ($p=0.97$, $I^2=0\%$). Meta-analysis did not show a statistically significant difference between the 2 kinds of treatment comparing pulpal vitality (risk ratio: 0.46, 95% CI: 0.09–2.40, $p=0.35$).”^{170 (p329)} Post-operative sensitivity According to the authors, “Four studies evaluated post-operative sensitivity. Follow-up time in the studies was 3 months, 1 year, 2 years, and 2 years, respectively. No significant heterogeneity was found ($p=0.7$, $I^2=0\%$). Meta-analysis demonstrated no significant difference between the 2 treatment groups with regard to post-operative sensitivity (risk ratio: 0.80, 95% CI: 0.17–3.88, $p=0.78$).”^{170 (p330)} Sensitivity analysis The authors reported: “We conducted sensitivity analysis for studies with large sample size and low risk of bias. When eliminating trials with small sample size or high risk of bias, all results were consistent to the meta-analysis results using all 14 studies.”^{170 (p330)} According to the authors, “The sensitivity analysis outcomes indicated that our meta-analysis results were of high quality.”^{170 (p331)} Authors’ overall conclusions The authors found that “Erbium laser technology is a safe and effective caries removal method in clinical practice. According to our findings, it can significantly reduce pain but requires a longer treatment time. Dentists are encouraged to consider using laser technology to remove caries, especially when treating children, patients with deep caries, and patients with anxiety. However, we still look forward to more well-designed studies to confirm our results.”^{170 p332}
Significance/direction	The authors found that “Erbium laser technology showed an increased time when removing caries compared with drilling (mean difference: 3.48, 95% CI: 1.90–5.06, $p<0.0001$). However, erbium laser technology reduced the requirement for local anesthesia (risk ratio: 0.28, 95% CI: 0.13–0.62, $p=0.002$). Erbium laser technology was also not significantly different to traditional drilling with regard to restoration loss, pulpal vitality, and post-operative sensitivity.”^{170 (p324)}
Heterogeneity	Regarding heterogeneity, the authors noted that “Cavity preparation time was longer using erbium laser technology than using rotary instruments according to

Parameter	Extraction
	our review. The high-speed bur ablation speed is approximately 10 times that of the laser, and in dentin, the laser ablation speed is approximately the same as a slow rotating bur, which can explain our results. Nevertheless, the outcome of time for preparation indicated high heterogeneity. Many factors can affect the time for caries removal, such as patients' age, carious site, carious area, carious stage, and different energy settings for the laser equipment. We tried to conduct subgroup analyses according to different factors, but high heterogeneity still existed, which confirmed that there was more than 1 factor affecting treatment time in each study included. The included studies recruited both children and adults, but treatment time for children is usually longer than for adults because of their limited self-control abilities and lower tolerance of pain. The carious site, area, and stage are also crucial parameters for caries removal time. Different energy settings for laser equipment were suggested to cause different treatment time. These are all possible sources of high heterogeneity in our outcome of time for cavity preparation. ¹⁷⁰ (p331–332)
Comments	GRADE was not used by the review authors.

Montedori *et al.* (2016)

Parameter	Extraction
First author and year of publication	Montedori <i>et al.</i> (2016) ¹⁷¹ (Cochrane Review)
Objectives	Compared laser-based methods with conventional mechanical methods for removing dental caries in deciduous and permanent teeth with respect to pain, anaesthesia, durability of restoration, pulp damage.
Participants	Mixed dentition, cavitated caries, restoration technique to remove carious tissue Dental caries in deciduous and permanent teeth Nine randomised controlled trials, involving 662 participants with an age range of 3.5–84 years, were included in this review. The proportion of male participants ranged between 22% and 63% in the individual trials. Four trials involved children and adolescents, four trials involved only adults (permanent teeth), and one trial involved children, adolescents, and adults.
Setting/context	The studies (where known) were set in both primary (one dental clinic) and secondary care facilities (seven university clinics and one paediatric hospital). The studies were completed in Bulgaria, Germany, Taiwan, Turkey, the United Kingdom (UK), and the USA.
Description of interventions/phenomena of interest	According to Montedori <i>et al.</i> , "laser is an acronym standing for light amplification by stimulated emission of radiation. Laser is a device emitting a high coherence light beam with waves at single frequency (very narrow spectrum)." ¹⁷¹ (p7) Laser-based methods were used to remove caries. The conventional mechanical methods for removing dental caries are: a handpiece with a bur, the chemomechanical system, the sono-abrasion system, and the air-abrasion system.
Databases and sources searched	The authors searched seven electronic databases: Cochrane Oral Health Group Trials Register (searched 22 June 2016), the Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 5) in the Cochrane Library (searched 22 June 2016), MEDLINE via Ovid (1946 to 22 June 2016), Embase via Ovid (1980 to 22 June 2016), ProQuest Dissertations & Theses Global (1980 to 22 June 2016), Zetoc (limited to conference proceedings) (1993 to 22 June 2016), and Web of Science (limited to conference proceedings) (1990 to 22 June 2016). They checked the reference lists of relevant articles to identify additional studies. They searched ClinicalTrials.gov and the WHO's International Clinical Trials Registry Platform for ongoing trials. There were no language restrictions. The authors present a series of search strategies in their appendices. The authors completed a study protocol. Screening and extraction were completed in duplicate. The authors reported no conflicts of interest. The review was funded by the University of Perugia, Italy; Regional Health Authority of Umbria, Italy; Cochrane Oral Health Group Global Alliance, UK; and the National Institute for Health Research, UK.

Parameter	Extraction
Date range (years) of included studies	The authors included nine randomised controlled trials published between 1998 and 2014.
Number of primary studies included in the systematic review	The authors included nine randomised controlled trials published between 1998 and 2014. Nine randomised controlled trials involving 662 participants with an age range of 3.5–84 years were included in this review. Five studies declared that they received financial support for their trials from device manufacturers of laser. No mention of funding was reported for the remaining four trials.
Types of studies included	The authors specified that they would include randomised and cluster-randomised controlled trials only. The 11 excluded trials and their reasons for exclusion were provided.
Country of origin of included studies	The studies were completed in Bulgaria, Germany, Taiwan, Turkey, the UK, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess risk of bias.
Appraisal rating	Overall, the individual trials had small sample sizes, and the majority were judged to have an unclear or high risk of bias based on the Cochrane Collaboration's risk of bias instrument. Six (66%) of the nine included trials were judged to have adequate randomisation and three (33%) trials were reported to have adequate blinding for assessing outcome. Publication bias was mentioned as part of the quality of evidence, but its influence is not discussed.
Method of analysis	Where feasible, the authors calculated risk ratios with 95% CIs for all prespecified, dichotomous outcomes for each trial outcome. They calculated mean difference for continuous data. They assessed heterogeneity using the chi-square test and the I ² Inconsistency Index. They carried out meta-analysis using Review Manager software according to Cochrane statistical guidelines. The authors combined relative risks for dichotomous data, and mean differences for continuous data, using random-effects models. They combined data from split-mouth studies with data from parallel group trials using the method suggested by Elbourne, employing the generic inverse-variance method in Review Manager 5. They undertook subgroup analysis for type of participants (children, adults) but not for type of tooth (deciduous, permanent) or type of intervention (laser and its beam characteristics).
Outcome assessed	Outcomes by primary studies: Confirmed caries removal: DenBesten 2001; Hadley 2000. Pain during and after treatment: Belcheva 2014; Liu 2006; Zhang 2013. Need for anaesthesia: Keller 1998; Liu 2006; Zhang 2013; DenBesten 2001. Marginal integrity: Hadley 2000; Yazici 2010; Zhang 2013. Durability of restoration: Hadley 2000; Harris 2000; Yazici 2010; Zhang 2013. Recurrent caries: Hadley 2000; Yazici 2010. Pulp damage: DenBesten 2001; Hadley 2000; Harris 2000; Keller 1998.
Results/findings	The primary outcomes were evaluated in a limited number of trials using pairwise random-effects meta-analyses. The removal of caries was evaluated in four trials (but only two reported quantitative data), and episodes of pain in five studies. There was insufficient evidence to suggest that either lasers or drills were better at caries removal (risk ratio (relative risk): 1.00; 95% CI: 0.99–1.01; I ² : 0%; 2 trials; 256 treated caries; low-quality evidence). The incidence of moderate or high pain was greater in the drill group compared with the laser group using the 6-face rating scale (relative risk: 0.40; 95% CI range: 0.28–0.57; I ² : 50%; 2 trials; 143 participants; low-quality evidence). The need for anaesthesia was significantly higher in the drill group than in the laser group (relative risk: 0.25; 95% CI: 0.10–0.65; I ² : 0%; 3 trials; 217 children/adolescents; low-quality evidence); the same trend was observed for adults. In terms of marginal integrity of restoration, there was no evidence of a difference between laser and drill comparisons evaluated at six months (relative risk: 1.00; 95% CI: 0.21–4.78; I ² : 0%; 3 trials; very low-quality evidence), one year (relative risk: 1.59; 95% CI: 0.34–7.38; I ² : 0%; 2 trials; very low-quality evidence), or two years (relative risk: 1.00; 95% CI: 0.21–4.74; 1 trial; I ² : 0%; very low-quality evidence). There was no evidence of a difference for durability of restoration between laser therapy or drill at 6-month follow-up (relative risk: 2.40; 95% CI: 0.65–8.77; I ² : 0%; 4 trials; very low-quality evidence), at

Parameter	Extraction
	one year (relative risk: 1.40; 95% CI: 0.29–6.78; I²: 0%; 2 trials; very low-quality evidence), or at 2-year follow-up (relative risk: 0.50; 95% CI: 0.02–14.60; one trial; very low-quality evidence). Only two trials investigated the recurrence of caries, but no events occurred during the 6-month follow-up period. There was insufficient evidence of a difference between laser or drill in terms of pulpal inflammation or necrosis at 1 week (relative risk: 1.51; 95% CI: 0.26–8.75; I²: 0%; 3 trials; very low-quality evidence) and at 6 months (relative risk: 0.99; 95% CI: 0.10–9.41; I²: 0%; two trials; very low-quality evidence). According to Montedori <i>et al.</i>, “despite some encouraging results, the applicability of lasers in current clinical practice is uncertain.”¹⁷¹ (p24) They went on to state that “Despite the inclusion of a fair number of studies in this systematic evaluation, only two studies with limited sample size assessed and provided data for the outcome removal of caries. The evidence was too limited to either claim or refute a difference between laser and drill treatment for caries removal (low-quality evidence). Four studies that evaluated pain showed that laser treatment may have some advantage in terms of limiting pain in children, adolescents and adults. However, the quality of the evidence was low.”¹⁷¹ (p25)
Significance/direction	Results listed by outcome
Heterogeneity	Heterogeneity was low to moderate.
Comments	GRADE was used by the review authors. The HRB agrees with the authors’ low to very low GRADE scores due to the inclusion of both randomised and quasi-randomised trials, the high or unclear risk of bias in the majority of studies (Six (66%) of the nine included trials were judged to have adequate randomisation and three (33%) trials were reported to have adequate blinding for assessing outcome), and the small or very small sample sizes and very wide CIs. The quality of the systematic review was judged as low using AMSTAR 2, as the authors could not control for risk of bias in their meta-analysis.

Hamama *et al.* (2015)

Parameter	Extraction
First author and year of publication	Hamama <i>et al.</i> (2015) ¹⁷²
Objectives	Compared the time required for chemomechanical (sodium hypochlorite-based agent, known as Carisolv, and enzyme-based agent, known as Papacarie) caries removal with the other conventional caries removal methods in primary and permanent teeth.
Participants	Mixed dentition, cavitated caries, caries removal technique Population: Primary and permanent teeth (molars) The 19 included randomised clinical trials were published between 2003 and 2012. The number of participants included in these trials was not provided. However, 1,909 teeth were included. The teeth, where described, were classified as primary (14 trials) or permanent (five trials) molars. Age and gender were not reported. Only seven trials reported follow-up subsequent to the procedure, and follow-up times ranged from one week to 24 months; four trials had follow-ups at six months.
Setting/context	The geographical regions covered by the studies were: Asia (Egypt, India, Pakistan), Europe, North America (the USA), and South America. Settings were not reported.
Description of interventions/phenomena of interest	For all the selected randomised clinical trials, either a sodium hypochlorite-based chemomechanical caries removal agent (modified CariSolv gel; 5% sodium hypochlorite) has been used, and/or an enzyme-based chemomechanical caries removal agent (either the papain-based Papacarie or the trypsin-based Biosolv) was used. The two chemomechanical caries removal methods were compared with conventional hand excavation, atraumatic restorative technique, and/or rotary caries removal methods.
Databases and sources searched	At least three databases were searched: Scopus, PubMed, and Cochrane Library from 2000 onwards. EBSCOhost was also searched although the exact databases were not reported. The search keywords are provided. The authors hand-

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	searched at least three non-electronic journals. There were time and language restrictions. The time restrictions were explained. The authors prepared an unpublished protocol for their systematic review. The studies were screened in triplicate. It is not clear how many reviewers extracted or checked the data. The authors reported no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article. The source of funding for the review is not provided.
Date range (years) of included studies	The 19 randomised clinical trials were published between 2003 and 2012.
Number of primary studies included in the systematic review	The 19 randomised clinical trials were published between 2003 and 2012. The teeth, where described, were classified as primary (14 trials) or permanent (five trials) molars. Only seven trials reported follow-up subsequent to the procedure, and follow-up times ranged from one week to 24 months; four trials had follow-ups at 6 months. The sources of funding for primary studies were not provided.
Types of studies included	The trials selected for the current systematic review were at least two-arm prospective randomised clinical trials that were written in English. Some (but not all) of the excluded full-text trials are referenced.
Country of origin of included studies	The geographical regions covered by the studies were: Asia (Egypt, India, Pakistan), Europe, North America (the USA), and South America.
Appraisal instruments used	The methodology of each randomised controlled trial was assessed based on the Delphi ideal criteria for quality assessment of randomised clinical trials.
Appraisal rating	The authors reported that "It was found that none of the current reviewed trials fulfilled all the ideal [methodological] requirements of clinical trials."¹⁷² (p177) Thirteen (68%) of the 19 included clinical trials clearly described randomisation of their study population. The blinding of the evaluators to the treatment method was reported in only four trials (21%). The HRB considers these trials to be at high or unclear risk of bias. Publication bias was not measured.
Method of analysis	The majority of the trials evaluated the time taken for caries excavation by chemomechanical (test group) and conventional (control group) caries removal methods. For each caries excavation method, the sample size and the mean caries excavation time (minutes) were extracted from the studies and subjected to a meta-analysis using the Comprehensive Meta-Analysis software, version 2, at the 95% CI. The meta-analysis of this systematic review followed the statistical model of Borenstein, which has been designed for comparing the meta-analysis outcomes of different groups within the same study. The results of the meta-analysis were subjected to a further one-way analysis of variance, followed by the Tukey post hoc multiple comparison test using GraphPad InStat software version 3.10. This additional step was performed to quantify the difference in the excavation time between the conventional and the chemomechanical caries removal methods.
Outcome assessed	Time taken to complete caries removal. Time frame was not predefined. Only seven trials reported follow-up subsequent to the procedure, and follow-up times ranged from one week to 24 months; four trials had follow-ups at six months. Outcomes by primary studies: All trials measured time taken to complete caries removal Conventional rotary drill: Bohari 2012; Kochhar 2011; Singh 2011; Kotb 2009; Peric 2009; Subramaniam 2008; Hosein and Hasan 2008; Pandit 2007; Peters 2006; Lozano-Chourio 2006; Bergmann 2005; Azrak 2004; Kavvadia 2004; Kakaboura 2003. Hand excavation (using atraumatic restoration technique): Bohari 2012; Kochhar 2011; Topaloglu-Ak 2009; Barata 2008; Pandit 2007; Kirzioglu 2007. CariSolv chemomechanical caries removal: Bohari 2012; Kochhar 2011; Peric 2009; Topaloglu-Ak 2009; Subramaniam 2008; Barata 2008; Hosein and Hasan 2008; Pandit 2007; Kirzioglu 2007; Peters 2006; Lozano-Chourio 2006; Bergmann 2005; Fure and Lingstrom 2004 (compared two different strengths to each other); Azrak 2004; Kavvadia 2004; Kakaboura 2003. Papacarie chemomechanical caries removal: Bohari 2012; Kochhar 2011; Singh 2011; Bussadori 2011 (no comparison); Kotb 2009.

Parameter	Extraction
Results/findings	The results of the meta-analysis of the mean caries excavation time are as follows: Conventional rotary drill: 12 trials; average time per excavation: 2.99 minutes (standard deviation: ± 0.001 minutes) Papacarie chemomechanical caries removal: four trials; average time per excavation: 6.36 minutes (standard deviation: ± 0.08 minutes) Hand excavation (using atraumatic restoration technique): four trials; average time per excavation: 6.98 minutes (standard deviation: ± 0.17 minutes) CariSolv chemomechanical caries removal: 13 trials; average time per excavation: 8.12 minutes (standard deviation: ± 0.02 minutes) The authors reported that one-way analysis of variance and the Tukey post hoc test revealed that the shortest estimated mean excavation time was recorded during rotary caries excavation (2.99 minutes), followed by the papain-based (Papacarie) chemomechanical caries removal method (6.36 minutes) and the hand excavation method (6.98 minutes). The longest caries excavation time (8.12 minutes) was recorded for the CariSolv chemomechanical caries removal method. The authors concluded that "It was found that none of the current reviewed trials fulfilled all the ideal [methodological] requirements of clinical trials. Furthermore, the current scientific evidence shows that the NaOCl-based [CariSolv or sodium hypochlorite] chemomechanical caries removal method was more time consuming when compared to enzyme-based (Papacarie) chemomechanical and conventional caries removal methods. Further prospective randomized controlled clinical trials evaluating the long-term follow-up of papain-treated permanent teeth are needed."¹⁷² (p177)
Significance/direction	Favours rotary drill as a time-saving method, followed by Papacarie and atraumatic removal of caries.
Heterogeneity	Heterogeneity was not assessed or discussed.
Comments	GRADE was not used by the review authors. The HRB graded the quality of evidence as very low, as the risk of bias in all studies was either high or unclear, and less than 75% of studies had adequate randomisation or blinding of outcome ascertainment. Heterogeneity was not measured or discussed. The quality of the systematic review was judged as critically low using AMSTAR 2, as the authors could not control for risk of bias in their meta-analysis and did not measure heterogeneity.

Schwendicke *et al.* (2015c)

Parameter	Extraction
First author and year of publication	Schwendicke <i>et al.</i> (2015c) ¹⁷⁴
Objectives	Evaluated and compared the effects (with respect to risk of complications, pain, time required for excavation, and/or number of bacteria remaining) of using different criteria for caries removal in primary and permanent teeth.
Participants	Mixed dentition, cavitated caries, caries removal technique and quantity Population: Natural primary or secondary carious lesions in primary or permanent teeth with excavated caries. Most of the 1,782 patients (2,555 carious lesions) were children or adolescents, although 10 studies investigated adult patients also. Most of the teeth included were primary teeth, but some were permanent. Age and gender were not reported. Most studies did not have any follow-up, but reported outcomes during treatment. For studies reporting risk of complications, median follow-up was 12 months (range: 0–24 months).
Setting/context	The studies' settings or countries were not provided.
Description of interventions/phenomena of interest	Criteria (interventions/controls): The authors compared different criteria used for caries excavation, as defined clinically or by the self-limiting excavation method used: State of dentine Tactile hard: Excavation was terminated when the dentine remaining at the cavity floor or in proximity to the pulp did not stick to probing instruments and did not exert any tug-back, the remaining dentine was assessed as tactile.

Parameter	Extraction
	Tactile softened: Excavation was terminated when the dentine remaining at the cavity floor or in proximity to the pulp was not hard, as defined above, but was leathery, stuck to probing instruments, or exerted tug-back, the remaining dentine was assessed as tactile Non-stainable: Excavation was terminated when the dentine remaining at the cavity floor or in proximity to the pulp was not stainable by a caries-detector dye anymore. Method of caries removal Chemomechanical caries removal (CMCR), i.e. using Carisolv, Caridex, or Papacarie, with the excavation end point being defined by the excavation method: After repeated application of the gel and subsequent manual excavation, the gel eventually did not turn cloudy/turbid anymore, i.e. it stayed clear, indicating to terminate excavation. Polymer bur, i.e. using PolyBur or Smartbur, with the excavation end point being defined by the condition of the bur: An abraded, blunt bur did not allow any further excavation and indicated termination of the excavation. Fluorescence-based feedback systems, for example coupled with an Er:YAG laser, with the excavation end point being defined by the feedback system: If fluorescence dropped below a certain threshold, excavation was terminated.
Databases and sources searched	Three electronic databases (PubMed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL)) were searched between 4 June 2014 and 23 July 2014 for relevant studies. Basic searches were provided in a figure. Cross-referencing from retrieved full-text studies was used to identify further articles. Grey literature was searched via OpenGrey, and ongoing trials identified via ClinicalTrials.gov. The search was limited to studies published in English. The preparation of a protocol was not reported. Title and abstract of identified studies were screened for eligibility by two reviewers. The number of reviewers extracting the data was not provided. One author was funded by a grant from the Ministry of Science and Technology in Taiwan. Other funding sources or conflicts of interest were not stated.
Date range (years) of included studies	Twenty-eight studies published between 1993 and 2014 were included.
Number of primary studies included in the systematic review	Twenty-eight studies published between 1993 and 2014 were included. Nineteen studies were randomised controlled trials and 9 studies were non-randomised controlled trials. Twelve studies reported using a split-mouth design. Most of the 1,782 patients (2,555 carious lesions) were children or adolescents, although 10 studies investigated adult patients also. The funding sources of primary studies were not reported.
Types of studies included	Both randomised controlled trials and non-randomised controlled trials were included in the review. The authors included non-randomised studies to broaden the database for their analyses. The excluded studies with reasons for exclusion were provided in an appendix.
Country of origin of included studies	The studies' settings or countries were not provided.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included studies.
Appraisal rating	Using conventional Cochrane summary judgements, all 28 studies were judged as having a high risk of bias. Excluding blinding of providers and participants, 12 of the 28 studies were judged to have a high risk of bias and 16 to have an unclear risk of bias. Sixteen of the 28 studies had adequate randomisation and 10 had adequate blinding of outcome assessment. All counts were based on the table in the supplementary appendix. Publication bias was measured, and there was significant publication bias for the selection of pain literature. The authors stated that when they excluded studies with high risk of bias, comparisons were more limited, but that "only small differences in the estimates were found, with no changes in direction or statistical significance of the estimates."¹⁷⁴ (p11)
Method of analysis	The authors used dichotomous and continuous data to calculate effect estimates. The unit of analysis was the excavated lesion or lesion site. They did not adjust for the possible effects of clustering. If several treatments in a study used the same criterion category (e.g. CariSolv and Papacarie being performed until the gel

Parameter	Extraction
	stayed clear, or hand and bur excavation performed until only hard dentine remained), the more common one (CariSolv, bur) was used for data synthesis. For microbiological data, the authors used total bacteria counts; if these were not available, counts of cultivable <i>Lactobacilli</i> were used for synthesis. For trials with zero events or mean/standard deviation being zero, constant continuity correction of 1 or 0.01 was performed, respectively. For pairwise comparison, a random-effects model was applied using Comprehensive Meta-Analysis version 2.2.64 with odds ratios and 95% CIs being calculated. Network meta-analysis was performed using Bayesian random-effects models and a Markov chain Monte Carlo simulation via GeMTC 0.619 implemented in R version 3.0.3. To fit the model, the authors used a non-informative uniform prior distribution and assessed convergence based on the Brooks-Gelman-Rubin criteria and inspection of history plots. Simulations were performed with 1,000 tuning iterations and further 5,000 simulations per chain at a thinning interval of 50. The authors calculated posterior median odds ratios or standardised mean differences and 95% credible intervals, which equal the range of estimated parameters after exclusion of extreme values. Different criteria were ranked according to their probability of having the lowest compared with the highest odds or differences. Heterogeneity was assessed quantitatively using the I^2 Inconsistency Index, and funnel plot analysis and the Egger test were performed to assess small study effects or publication bias of pairwise estimates. Trim-and-fill was used to evaluate the effects of publication bias. For sensitivity analyses, the authors compared subgroups of studies with different quality (risk of bias) and teeth of different dentitions using both pairwise and network meta-analysis.
Outcome assessed	Risk of complications, pain, time required for excavation (excluding anaesthetic time), and/or number of bacteria remaining. No predetermined time frames. Risk of complications: Franzon 2014; Fure 2000; Kirzioglu 2007; Lozano-Chourio 2006; Matsumoto 2013; Orhan 2010; Orhan 2008; Peric 2009; Ribeiro 1999; Topaloglu-Ak 2009. Risk of pain: Ericson 1999; Fure 2000; Kirzioglu 2007; Lager 2003; Lozano-Chourio 2006; Matsumoto 2013; Motta 2013; Peric 2009. Time (excluding anaesthetic time): Ericson 1999; Franzon 2014; Fure 2000; Hosein and Hasan 2008; Kakaboura 2003; Kavvadia 2004; Kirzioglu 2007; Kochhar 2011; Kotb 2009; Lozano-Chourio 2006; Matsumoto 2013; Nadanovsky 2001; Peric 2009; Topaloglu-Ak 2009. Bacterial numbers in colony-forming units: El-Tekeya 2012; Kidd 1993a; Kidd 1993b; Lula 2009; Lula 2011; Zakirulla 2011.
Results/findings	The authors reported that the risk of complications was highest when excavating until only non-stainable dentine remained, and lowest when not attempting to remove all softened dentine. The results present odds ratios and 95% credible intervals. All except one are statistically significant. The authors did not detect inconsistency, while global heterogeneity was moderate (I^2: 51%) Tactile hard: OR: 0.42 (95% CI: 0.13/1.23), 0.79 (0.29/1.72), 3.84 (0.46/44.2) Tactile soft: 1.92 (0.43/7.33), 9.11 (1.52/87.0) NS CMCR: 4.94 (0.52/69.3) Non-stainable CMCR is chemomechanical caries removal. NS is not significant Risk of pain significantly decreased if self-limiting chemomechanical excavation or fluorescence-assisted lasers were used instead of excavating until all dentine was hard. The authors did not detect inconsistency, and global heterogeneity was low (I^2: 25%). Tactile hard: OR: 0.16 (95% CI: 0.06/0.31), 0.09 (0.01/0.56) CMCR: 0.52 (0.01/4.92) NS Er:YAG laser When not attempting to remove all softened dentine, the time required for excavation was shortest, while the greatest number of bacteria remained. The authors did not detect inconsistency, while global heterogeneity was substantial (I^2: 93%). All time measures exclude giving anaesthetic where required. Tactile hard: OR: -10.1 (95% CI: -15.2/-4.9), 3.5 (2.0/4.9), -4.2 (-9.6/1.1) NS Tactile soft: 14.2 (8.2/19.3), 5.9 (-1.6/13.2) NS

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	CMCR: -7.7 (-13.2/-2.6) Non-stainable Not attempting to remove all softened dentine resulted in the highest number of bacteria remaining and the highest chance of leaving any cultivable bacteria. However, none of the detected differences were statistically significant. The authors did not detect inconsistency, while global heterogeneity was moderate and substantial (I^2 was 15% and 94%, respectively). Tactile hard: OR: 2.7 (95% CI-1.4/8.2), 0.2 (-5.4/5.6), 0.1 (-5.8/6.1), 0.6 (-3.5/5.5) Tactile soft: - 2.5 (-10/4.0), -2.7 (-11/4.3), -2.0 (-7.2/2.1) CMCR: -0.1 (-8.3/8.3), 0.4 (-6.3/7.8) Polymer bur: 0.6 (-6.5/8.4) Non-stainable all NS Where feasible, relevant sensitivity and subgroup analyses were completed, but these did not change the direction of the findings. The authors stated that "In conclusions and within the limitations of this study and the supporting evidence, not attempting to remove all softened or stainable dentine could reduce the risk of complications. Chemo-mechanical removal seems advantageous with regards to pain, but is time consuming, and was not found beneficial with regards to clinical outcomes. Data regarding other self-limiting excavation methods was insufficient for definitive conclusions."¹⁷⁴ (p13)
Significance/direction	Results listed by outcome
Heterogeneity	Heterogeneity and inconsistency were measured and the results were stated but their implications were not discussed.
Comments	GRADE was not used by the review authors. The HRB graded the quality of evidence as low, as both randomised and non-randomised trials were included in the analysis, the risk of bias in all studies was either high or unclear, and less than 75% of the included studies had adequate randomisation or blinding of outcome ascertainment. Heterogeneity was substantial in two of the outcome analyses. The quality of the systematic review was judged as low using AMSTAR 2, as the authors could not control for risk of bias in their meta-analysis.

Li et al. (2014)

Parameter	Extraction
First author and year of publication	Li et al. (2014) ¹⁷³
Objectives	Evaluated CariSolv for chemomechanical caries removal from primary or permanent teeth, compared with the conventional rotary instrument, for the outcomes complete caries removal rate, the treatment time (in minutes), and the use of local anaesthesia.
Participants	Mixed dentition, cavitated caries, restoration technique The participants had primary or permanent teeth with carious lesions and these teeth had no previous endodontic symptoms. According to the authors, "The patients of three reports were children and adolescents, with ages ranging from 3 to 17 years old, and the other three papers included the adult patients from 18 to 84 years old."¹⁷³ (p438) The carious lesions were located in the crown of the participants' tooth in four papers and in the root of the participants in one paper. One study selected 137 patients aged 3–85 years old whose carious lesions were located in crown, root or a combination of the two sites. Li et al. stated that "the age of the patients in all six studies was inconsistent; patients of some reports were children and adolescents, and other [reports] included adult patients from 18 to 84 years old. The mixed age group will cause the heterogeneity [between studies to be] higher."¹⁷³ (p441) The number of patients in each of the randomised controlled trials ranged from 32 to 137 (with a total of 578 teeth).
Setting/context	The clinical settings and study countries were not reported.
Description of interventions/phenomena of interest	Intervention: The chemomechanical caries removal system, Carisolv. Comparator: Control (rotary drills).

Parameter	Extraction
	According to the authors, “The chemomechanical caries removal system includes air abrasion with aluminium oxide, chemomechanical caries removal, atraumatic restorative therapy and lasers... Some products of CMCR [chemomechanical caries removal] such as Caridex, CariSolv and Papacarie are being used to remove caries tissue at present. This CMCR reagent can cause further degradation of the partially degraded collagen, preserve the deep layers of the dentine and only remove the infected layers. This new method of treatment [laser] has gained high acceptance especially among children and patients with dental anxiety.”¹⁷³ (p432–433) In describing the comparator, Li <i>et al.</i> explained that the “Conventional caries removal method involves the use of a drill on a high-speed handpiece to gain access to the carious lesions and a low-speed handpiece to remove carious dentine.”¹⁷³ (p432)
Databases and sources searched	The authors searched five databases: PubMed, the Cochrane Library (Issue 6, 2013), Embase (1984–2013), Web of Science (1995–2013), and Chinese National Knowledge Infrastructure (CNKI) (1982–2013). No language restriction was imposed on the search results. The reference lists of all articles were examined for identification of further eligible studies. The authors did not report preparing a protocol. Extraction and screening were completed in duplicate. Funding: The study was supported by Scientific Research Foundation of Sichuan University Young Teachers and innovative Research Team of Education Department of Sichuan Province. The authors reported that they did not have any possible conflict of interest.
Date range (years) of included studies	The included studies were published between 1999 and 2009.
Number of primary studies included in the systematic review	Six randomised controlled trials, published in 1999, 2000, 2003, 2005, 2006, and 2009, were included in this review. The sources of funding of primary studies were not reported.
Types of studies included	Completed randomised or quasi-randomised controlled trials (in humans) were eligible for inclusion. A list of excluded studies at full-text was not provided. However, the reasons for exclusion were reported.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	According to the authors, “The methodological quality of each trial was evaluated using the Jadad scale. The scale consists of four items describing randomisation (0–2 points), randomisation concealment (0–2 points), blinding (0–2 points), and dropouts and withdrawals (0–1 point) in the report of an RCT [randomised controlled trial]. A score of 1 is given for each of the points described. A further point is obtained where the method of randomisation, randomisation concealment and/or blinding is given and is appropriate, and a point is deducted where it is inappropriate. The quality scale ranges from 0 to 7 points. Higher scores indicate better reporting. The studies are deemed low quality if the Jadad score is ≤ 3 and high quality if the score is ≥ 4.”¹⁷³ (p434)
Appraisal rating	Based on the Jadad scale, five of the six included studies were rated high quality (i.e. they were deemed to have a low risk of bias). Five of the six studies were at low risk of bias for randomisation. Outcome assessment was not rated on its own using the Jadad scale. However, no four trials scored zero and two trials scored one for blinding indicating that blinding was inadequate in all trials. Li <i>et al.</i> stated that “The quality of the included studies was assessed by the Jadad score. The median Jadad score of the studies included was 5 (range, 4–6).”¹⁷³ (p434) According to the authors, “we used the Jadad score to evaluate the methodological quality of each trial; although all six studies were of high quality, they also had shortcomings...all studies were insufficient or ambiguous in blinding, and one study also had the deficiency of randomisation concealment and dropouts and withdrawals.”¹⁷³ (p441) Publication bias was not measured or discussed.
Method of analysis	The authors reported that “For each study, risk ratios (RRs) along with 95% confidence intervals (CIs) were calculated to estimate the effect of interventions. Meta-analysis was conducted for studies with similar designs, intervention and

Parameter	Extraction
	outcome measures. The significance of discrepancies in the estimates of the treatment outcomes from different studies was assessed by the Cochran Q test the I^2 statistic. Studies with an I^2 statistic of 25–50% are considered to have low heterogeneity, those with an I^2 statistic of 50–75% have moderate heterogeneity, and those with an I^2 statistic of >75% have a high degree of heterogeneity. An I^2 value >50% indicates significant heterogeneity. A fixed-effects model was applied to combine the data in cases in which no variation existed among studies ($p \geq 0.1$, $I^2 < 50\%$). When significant heterogeneity ($p < 0.1$, $I^2 > 50\%$) was detected, a random-effects model was used to reassess the data. If heterogeneity still existed, descriptive statistics were used. All analyses were performed using Revman version 5 software provided by the Cochrane Collaboration.”¹⁷³ (p434)
Outcome assessed	Outcomes: The outcome measurement included the complete caries removal rate (the number of cases with complete caries removal in study and control groups after different treatment), the treatment time (minutes), and the use of local anaesthesia. The completeness of clinical caries removal was judged on the basis of clinical criteria; that is, the explorer should not stick in the dentine, and not give a tug-back sensation. The outcomes assessed included complete caries removal rate, treatment time (in minutes), and use of local anaesthesia. Outcomes complete caries removal rate, the treatment time (in minutes), and the use of local anaesthesia: Lozano-Chourio 2006; Ericson 1999; Fure 2000; Bergmann 2005; Kakaboura 2003; Peric 2009.
Results/findings	Complete caries removal rate The authors reported that “Six studies involving 578 teeth described CCR [complete caries removal] by showing the number of caries-free teeth. Because moderate heterogeneity existed between studies, we used random-effects models to aggregate the data. When data were combined in meta-analysis, the summary risk ratios was 0.98 (95% CI, 0.94–1.03). On the basis of the current available evidence, there was no statistically significant difference in CCR between the CariSolv group and the rotary instruments group in teeth with caries ($p = 0.05$).”¹⁷³ (p438) Treatment time (minutes) According to Li <i>et al.</i>, “All six studies reported data for the treatment time (mean time in minutes $\pm$ SD [standard deviation]) about the CariSolv group and rotary instruments group. The heterogeneity of the CariSolv group versus rotary instruments group for all the studies was analysed. The chi-square value was 48–84, with five degrees of freedom (df) and $p < 0.00001$ in a random-effects model. I^2, another index of the test of heterogeneity, was 90%, suggesting high heterogeneity. We therefore chose the random-effects model to synthesise the data. The overall MD [mean difference] for the CariSolv group versus rotary instruments group was 4.51 [95% CI 3.06–5.79, $p < 0.00001$; I^2: 90%; 565 restorations; 6 trials;]. The treatment time (min) of the CariSolv group was significantly longer than that of the rotary instruments group. We also performed a stratified subgroup analysis by carious lesion and found that no matter where the caries were located in the crown [MD [mean difference] 5.57; 95% CI (4.89–6.60); $p = 0.13$; I^2: 47%; 377 restorations; 4 trials] or root [MD 2.05; 95% CI (0.43–3.67); $p = 0.14$ I^2: 55%; 88 restorations; 2 trials], it comes to the same result.”¹⁷³ (p438–439) Use of local anaesthesia The authors stated that “Six trials (569 teeth) reported the use of local anaesthesia. Overall, CariSolv decreased the RR [risk ratios] for local anaesthesia; the summary RR was 0.21 [95% CI (0.13–0.33; $p < 0.00001$; I^2: 55%; 569 restorations; 6 trials)]. We found a significant difference between the two treatment groups, with fewer patients in the CariSolv group experiencing discomfort and using local anaesthesia ($p = 0.25$). No evidence of significant heterogeneity was noted among these two groups.”¹⁷³ (p439) Overall comments In summary, Li <i>et al.</i> stated that “The present meta-analysis indicated that there was no significant difference between the CariSolv group and the rotary instruments group in CCR [complete caries removal]. However, substantial heterogeneity was observed among these studies, which was not surprising given

Parameter	Extraction
	the differences in characteristics of age distribution of patients, working process and study designs. Our sensitivity analyses suggested that one multi-centre study in which four times more patients have been assigned to the CariSolv treatment group probably contributed to the heterogeneity."¹⁷³ (p440) They continued, "the outcome of the treatment time had a high degree of heterogeneity; one possible reason may be there is lack of consistency about the measurement and analysis of the treatment time. In all six trials, the treatment time of CariSolv was taken from the beginning of CariSolv gel application until the end of the caries removal procedure, but the time of each [coating application] ranged from 20 to 30 seconds."¹⁷³ (p440)
Significance/direction	According to the authors, "In conclusion, this systematic review indicated that Carisolv, as a chemomechanical caries removal system, can reduce the use of local anaesthesia although it had the longer treatment time [compared with the conventional rotary instruments method]. There was no statistically significant difference in CCR [complete caries removal] between these two methods. These conclusions are not definitive based on poor methodological quality and small sample sizes. Further large-scale, high-quality, well-designed RCTs [randomised controlled trials] on this area are required."¹⁷³ (p441)
Heterogeneity	Li <i>et al.</i> stated that "The significance of discrepancies in the estimates of the treatment outcomes from different studies was assessed by Cochran's Q test and the I² statistics. Studies with an I² statistic of 25–50% are considered to have low heterogeneity, those with an I² statistic of 50–75% have moderate heterogeneity, and those with an I² statistic of >75% have a high degree of heterogeneity. An I² value >50% indicates significant heterogeneity. A fixed-effects model was applied to combine the data in cases in which no variation existed among studies ($p \geq 0.1$, $I^2 < 50\%$). When significant heterogeneity ($p < 0.1$, $I^2 > 50\%$) was detected, a random-effects model was used to reassess the data. If heterogeneity still existed, descriptive statistics were used."¹⁷³ (p434) The authors made the following comment on heterogeneity: "moderate to severe heterogeneity could be witnessed among the included studies."¹⁷³ (p441)
Comments	GRADE was not used by the review author.

Schwendicke *et al.* (2013)

Parameter	Extraction
First author and year of publication	Schwendicke <i>et al.</i> (2013) ¹⁷⁵
Objectives	Compared one- or two-step incomplete removal with complete caries removal of primary or permanent teeth with primary carious lesions requiring a restoration with respect to risk of pulpal exposure, post-operative pulpal symptoms, overall failure, and caries progression.
Participants	Mixed dentition, cavitated caries, restoration techniques Population: Primary dentine caries in primary or permanent teeth Nine parallel-group trials and one split-mouth trial, reported in 17 articles published between 1977 and 2012 and representing 1,257 patients and 1,628 teeth, were included. Age and gender were not reported. Most participants were children, with two studies also investigating adults.
Setting/context	The study settings were mostly university-based dental hospitals, with one study using both a university-based dental hospital and community-based dental clinics. The studies were completed in Brazil, Germany, Scandinavia, Scotland, Thailand, Turkey, and the USA.
Description of interventions/phenomena of interest	According to Schwendicke <i>et al.</i>, "Incomplete (one- or two-step excavation, indirect pulp treatment, or capping) and complete caries removal techniques were investigated. If re-entry was performed for cavity floor assessment or microbiological sampling, but no further excavation was attempted, this was not classified as stepwise, but as one-step incomplete caries removal."¹⁷⁵ (p307) Comparator: Complete caries removal techniques
Databases and sources searched	Identification of studies to be considered for inclusion was based on a search strategy for four electronic sources (Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, PubMed, and Embase) between 16 May 2012 and 23 July

Parameter	Extraction
	2012. The start date was 1967. The search was limited to the English and German languages. The search strategies were presented in an appendix. The references from included studies were screened. Unpublished trials were searched electronically (ClinicalTrials.gov). The completion of a protocol was not mentioned in the article. Screening and data extraction were completed in duplicate. The authors declared no potential conflicts of interest with respect to the authorship and/or publication of this article. This study was funded by the authors and their institutions.
Date range (years) of included studies	Nine parallel-group trials and one split-mouth trial, reported in 17 articles published between 1977 and 2012, were included.
Number of primary studies included in the systematic review	Nine parallel-group trials and one split-mouth trial, reported in 17 articles published between 1977 and 2012 and representing 1,257 patients and 1,628 teeth, were included. The sources of funding for primary studies were not reported.
Types of studies included	The inclusion criteria specified randomised or quasi-randomised controlled trials. The 70 excluded studies and their reasons for exclusion were listed.
Country of origin of included studies	The studies were completed in Brazil, Germany, Scandinavia, Scotland, Thailand, Turkey, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included studies.
Appraisal rating	Based on the Cochrane Collaboration's risk of bias instrument, all studies were judged to be at high risk of bias. Five of the 10 included studies were judged adequate for randomisation, and 3 were judged adequate for blinding the outcome assessor. Publication bias was assessed by funnel plots and assumed for papers on failure of restorations. The sources of funding for the included studies were not reported.
Method of analysis	Treatment effects were measured based on reported outcomes. Pulpal exposure, pulpal symptoms, and failure were measured dichotomously. Teeth with exposed pulps were not included in calculations of other risks (post-operative symptoms, failure), since they were not always followed up and usually received further treatment (direct capping, root canal treatment), which could influence treatment outcomes. As a secondary outcome, caries progression was assessed and reported as either relative or absolute progression. Calculations were based on the number of teeth, not patients. Data synthesis was performed according to measured outcomes for subgroups of treatments (e.g. one- or two-step incomplete excavation). To overcome unit-of-analysis errors for pooled data from multi-arm studies, the authors combined suitable groups to create a single pairwise comparison. They used a random-effects model to calculate weighted and summary odds ratios with a 95% CI and forest plots. Heterogeneity was assessed quantitatively by chi-square test and I^2 Inconsistency Index. If $p > 0.2$ or $I^2 < 70\%$, subgroups were also pooled for data.
Outcome assessed	Outcome: Risk of failure, caries progression, pulpal exposure, and pulpal symptoms Time frame: 6 months to 10 years Outcome by primary studies: Risk of failure: Leksell 1996; Mertz-Fairhurst 1998; Bjørndal 2010; Foley 2004; Ribeiro 1999; Orhan 2010; Heinrich 1991; Lula 2009; Phonghanyudh 2012. Caries progression: Leksell 1996; Bjørndal 2010; Orhan 2010; Magnusson and Sundel 1977; Heinrich 1991; Lula 2009; Phonghanyudh 2012. Pulpal exposure: Leksell 1996; Mertz-Fairhurst 1998; Bjørndal 2010; Foley 2004; Ribeiro 1999; Orhan 2010; Magnusson and Sundel, 1977; Heinrich 1991; Lula 2009; Phonghanyudh 2012. Pulpal symptoms: Bjørndal 2010; Ribeiro 1999; Orhan 2010; Heinrich 1991; Lula 2009; Phonghanyudh 2012.
Results/findings	Pairwise random-effects meta-analysis showed significant risk reduction for pulpal exposure (odds ratio: 0.31; 95% CI: 0.19–0.49; I^2: 28%; 7 trials; 990 teeth; moderate-quality evidence downgraded by the HRB to very low; up to 16 months) and a non-significant reduction for pulpal symptoms (odds ratio: 0.58; 95% CI: 0.31–1.10; I^2: 0%; 6 trials; 680 teeth; low-level evidence downgraded by the HRB to very low; up to 16 months) for teeth treated with one- or two-step incomplete

Parameter	Extraction
	excavation. Risk of failure seemed to be similar for both complete and incomplete excavation, but data for this outcome were of limited quality and inconclusive (odds ratio: 0.97; 95% CI: 0.64–1.46; I ² : 0%; 9 trials; 1,011 teeth; very low-level evidence; up to 10 years). Secondary caries data were reported by three studies but the data were described as sparse and inconclusive. Subgroup analyses were completed. Based on the reviewed studies, incomplete caries removal seems advantageous compared with complete excavation, especially in proximity to the pulp. However, evidence levels are currently insufficient for definitive conclusions because of the high risk of bias within studies.
Significance/direction	Results listed by outcome
Heterogeneity	Heterogeneity was low to moderate and is acknowledged by authors.
Comments	GRADE was used by the review authors. The HRB graded the quality of evidence as low, the risk of bias in all studies was high, and less than 75% of studies had adequate randomisation or blinding of outcome ascertainment. The quality of the systematic review was judged as low using AMSTAR 2, as the authors could not control for risk of bias in their meta-analysis. The HRB upgraded the ratings of the review authors for some outcomes.

Appendix J: Data extraction for studies on non-carious lesion management in permanent dentition studies

Factors influencing direct restoration material

de Oliveira Correia *et al.* (2020)

Parameter	Extraction
First author and year of publication	de Oliveira Correia <i>et al.</i> (2020) ¹²¹
Objectives	Evaluated how tooth- and cavity-related properties of non-carious cervical lesions in humans' permanent teeth that already had resin composite restorations affect the retention of such restorations. The restoration retention rate was examined by one or more of the following: 1) arch distribution; 2) tooth location; 3) wear facets; 4) dentine sclerosis; 5) shape; 6) size; 7) depth; 8) occlusogingival distance; and 9) margin location.
Participants	Permanent dentition, non-carious cervical lesions,, determinants of retention Non-carious cervical lesions in humans' permanent teeth that already had resin composite restorations Twenty-four randomised clinical trials published between 1993 and 2019, with 962 participants and 3,129 restorations, were included in this review. The participants' ages ranged from 18 to 84 years.
Setting/context	The clinical settings and study countries were not reported.
Description of interventions/phenomena of interest	Intervention: Tooth- and cavity-related properties Comparator: None
Databases and sources searched	An electronic search was performed in MEDLINE via PubMed, citation databases (Scopus and Web of Science), LILACS, Brazilian Library in Dentistry (BBO), the Cochrane Library, and ongoing trial databases, including ClinicalTrials.gov and ReBEC (the Brazilian Registry of Clinical Trials), up to July 2018. The non-peer-reviewed literature was searched using the using the OpenSIGLE database. Additionally, the reference lists of the included studies were checked to identify possible relevant studies. No restrictions were placed on the publication date or language. The search strategy was appropriately modified for each database and was presented in a table. The authors registered a protocol with PROSPERO. Duplicate screening and extraction were completed. The authors certified that they had no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that was presented in this article. They were

Parameter	Extraction
	funded by a public institution (Coordination for the Improvement of Higher Education Personnel).
Date range (years) of included studies	Twenty-four randomised clinical trials, published between 1993 and 2019, were included in this review.
Number of primary studies included in the systematic review	Twenty-four randomised clinical trials published between 1993 and 2019, with 962 participants and 3,129 restorations, were included in this review. The funding sources for primary studies were not reported.
Types of studies included	Randomised clinical trials with a follow-up period of at least two years were eligible. A list of studies excluded at full-text screening was not provided, but their reasons for exclusion were reported.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	Nine of the 24 included studies were judged to have a high risk of bias, 11 studies had an unclear risk of bias, and 4 studies had a low risk of bias. Nine of the 24 studies were judged to have adequate randomisation and 14 had adequate blinding of outcome assessment. Publication bias was measured. No statistical signs of publication bias (arch distribution: $p=0.693$; tooth location: $p=0.489$; dentine sclerosis: $p=0.174$) were found.
Method of analysis	The approach to analysis was not described in the methods.
Outcome assessed	Outcome by primary study: Restoration retention rate at two years and beyond: 1) arch distribution; Abdalla and Sayed 2008; Aw 2005; C,elik 2007; Fagundes 2014; Hafer 2015; Horsted-Bindslev 1996; Karaman 2012; Kubo 2006; Kubo 2010; Oginni and Adelek 2014; Ozgunaltay and Onen 2002; Tuncer 2013; Tuncer 2017; van Dijken 2013. 2) tooth location: Abdalla and Sayed 2008; Aw 2005; C,elik 2007; Fagundes 2014; Karaman 2012; Kubo 2006; Oginni and Adelek 2014; Tuncer 2013; Tuncer 2017; van Dijken 2013; van Meerbeek 1993. 3) wear facets: Aw 2005; Oginni and Adelek 2014. 4) dentine sclerosis: Aw 2005. Caneppele 2018 (no reference in article); Dall'Orologio 2010; Dall'Orologio and Lorenzi 2014; Loguercio 2015; Sartori 2013; Torres 2014; van Dijken 2004; van Dijken 2005; van Dijken 2010; van Dijken 2013. 5) shape: Aw 2005; Caneppele 2018 (no reference in article); Sartori 2013; 6) size: van Dijken 2010; van Dijken 2013. 7) depth: Aw 2005; Caneppele 2018 (no reference in article); Dall'Orologio 2010; Hafer 2015; Sartori 2013; van Dijken 2010; van Dijken 2013. 8) occlusogingival distance: Aw 2005; Caneppele 2018 (no reference in article). 9) margin location: Dall'Orologio 2010; Dall'Orologio and Lorenzi 2014. The follow-up periods ranged from two to eight years.
Results/findings	The results of the review suggest that the location of the tooth in the dental arch and the presence of wear facets interfere with the retention rate of resin restorations in non-carious cervical lesions. In contrast, other aspects – such as dentine sclerosis, shape, size, depth, occlusogingival distance, and margin location of the cavity – demonstrated no influence on the retention rate. Eleven studies were included that examined the influence of the tooth location in the dental arch. The overall results were: risk ratio: 1.08; 95% CI: 1.00–1.16; 11 trials; moderate evidence downgraded by the HRB to low. The heterogeneity was substantial (I^2: 82%). Anterior tooth location favours the retention rates of resin restoration of non-carious cervical lesions by a factor of 1.08. For wear facets, only two studies were included. The results were: risk ratio: 0.91; 95% CI: 0.83–0.099; I^2: 0%; low-quality evidence. The presence of wear facets was a risk factor for the retention rate of resin composite restorations. For arch distribution (maxillary compared with mandibular), 14 studies were included. The overall results were: risk ratio: 1.01; 95% CI: 0.98–1.05; I^2: 23%; low-quality evidence, suggesting that the arch distribution of the non-carious cervical lesions does not affect the success rate of the resin composite restoration. For dentine sclerosis (compared with without), 11 studies were included. The overall results were: risk ratio: 0.99; 95% CI: 0.93–1.05; I^2: 60%; low-quality

Parameter	Extraction
	evidence, suggesting that dentine sclerosis does not affect the success rate of the resin composite restoration of non-carious cervical lesions. Three studies investigated the shape of the lesion. The overall results were: risk ratio: 1.03; 95% CI: 0.91–1.18; I²: 51%; very low-quality evidence, suggesting that the shape of non-carious cervical lesions does not affect the success rate of resin composite restorations. For the size of lesions, two studies by the same author were included. The size of non-carious cervical lesions does not affect the retention rate of the composite restorations (relative risk: 0.97; 95% CI: 0.88–1.08; I²: 0%; low-quality evidence). For the depth (shallow/moderate compared with deep) of non-carious cervical lesions, seven studies were included, and this characteristic did not seem to affect the retention rate of composite restorations (risk ratio: 0.98; 95% CI: 0.92–1.04; I²: 0%; low-quality evidence). Two studies reported the occlusogingival distance of lesions and its influence on the retention rate of restorations. The results of the meta-analysis for this characteristic showed no effect on the retention rate of restorations (risk ratio: 1.03; 95% CI: 0.93–1.13; I²: 0%; low-quality evidence). For margin location (above/aligned compared with intrasulcus), only two studies were included. High heterogeneity was detected (I²: 83%; $p=0.02$). With a risk ratio of 4.14 (95% CI: 0.17–99.76; low-quality evidence), the margin location of the non-carious cervical lesions did not influence the retention rate of the resin composite restorations. The authors stated that “All studies for each tooth- and cavity-related aspect were included, despite their risk of bias. The impact of this decision was evaluated in a sensitivity analysis, where only studies with low risk of bias were included. No change in the overall significance was shown (data not shown).”¹²¹ (pE131) According to de Oliveira Correia <i>et al.</i>, “The indirect evidence was responsible for downgrading the quality of the evidence by one level for all factors related to NCCLs [non-carious cervical lesions]. For some characteristics (wear facets, shape, size, and occlusogingival distance), the strength of evidence was also downgraded one level due to imprecision (the optimal information size criterion was not met). Moreover, the inconsistency in the data due to high and nonexplained heterogeneity was responsible for downgrading the results for tooth location, dentine sclerosis, shape, depth, and margin location.”¹²¹ (pE133)
Significance/direction	Results listed by outcome
Heterogeneity	The authors stated that “The inconsistency in the data due to high and nonexplained heterogeneity was responsible for downgrading the results for tooth location, dentine sclerosis, shape, depth, and margin location.” ¹²¹ (pE133)
Comments	GRADE was used by the review authors. Most trials scored high or unclear for risk of bias for one or more parameters. Less than 75% of trials were judged to have adequate random sequence generation and blinding of outcome assessment. The authors reported that the analysis had high and unexplained heterogeneity. The quality of the systematic review was judged as moderate. The HRB graded the evidence in this review as low while the review authors graded the evidence as moderate to very low.

Direct restoration material

Bezerra *et al.* (2020)

Parameter	Extraction
First author and year of publication	Bezerra <i>et al.</i> (2020) ¹²²
Objectives	The study evaluated, through a systematic review and meta-analysis, the clinical performance/longevity of composite resin restorations (based on seven parameters) and glass ionomer cements restorations used in adults with non-carious cervical lesions.
Participants	Permanent dentition, non-carious cervical lesions, direct restoration material

Parameter	Extraction
	The number of non-carious cervical lesions restorations in each of the included studies ranged from 48 to 336, with the number of participants ranging from ten to 44 in each study. In addition to the control group and the experimental group, eight studies had other groups that used other materials, such as compomers, polyacid-modified resin, primer with glass ionomer cement, or those using the sandwich technique (glass ionomer cement as a base material composite resin).
Setting/context	The study countries or clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: Use of glass ionomer cement (conventional and/or resin-modified) Comparison: Use of composite resin According to the authors, "Composite resins (CR) are the materials most used in NCCL [non-carious cervical lesion] restoration because they have favorable aesthetic and mechanical properties. In contrast, resins exhibit polymerization shrinkage and a high modulus of elasticity, causing stress due to occlusal forces. In the search for an alternative material to CR, studies have shown an increase in the choice of glass ionomer cements (conventional and/or resin-modified) because they have a modulus of elasticity similar to that of dentin and release fluoride. However, these materials have worse aesthetic properties because they are translucent and have fewer color options. GICs [glass ionomer cements] have less resistance to abrasion, increasing the surface roughness of these materials over time. Furthermore, due to the presence of reduced particles in CR, these materials have a smoother surface when compared to GIC."¹²² (p2)
Databases and sources searched	Four databases were searched (MEDLINE via PubMed, Scopus, Web of Science, and the Cochrane Library). There were no restrictions on the language or date of publication, and articles were searched until March 2020. In order to locate unpublished or ongoing studies, PROSPERO was searched manually, with no restriction on the date of publication. This systematic review and meta-analysis was registered in the PROSPERO database and followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Extraction and screening were completed in duplicate. Funding was provided by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES). Conflicts of interest: The authors declared no conflicts of interest.
Date range (years) of included studies	The included studies were published from 1995 to 2019.
Number of primary studies included in the systematic review	In total, 15 trials were included in this review. Nine of these 15 studies had a split-mouth randomised controlled trial design, one study had a randomised controlled trial parallel design, and five studies were split-mouth non-randomised clinical trials. The included studies were published from 1995 to 2019. The sources of funding for primary studies were not reported.
Types of studies included	The planned study design for inclusion is not clearly stated in the methods, but randomised and non-randomised controlled trials were included. A list of excluded studies with their reason for exclusion was not provided.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	According to the authors, "Only four studies described in detail the method used for random sequence generation and allocation concealment, indicating low risk of bias. The other 11 studies did not describe in sufficient detail the method used for random sequence generation and allocation concealment and are therefore classified as unclear risk of bias. In some studies each patient received at least one restoration of each material evaluated. Some authors reported that the restorative materials were randomly assigned to the lesions, but they did not report the method. The selective reporting and incomplete outcome criteria had a low risk of bias for the 15 studies. Two studies were the only ones classified as 'unclear risk of bias' for the criterion 'Other sources of bias' because they did not inform the brand of the materials used and did not report age, teeth involved or study site. The other studies were classified as 'low risk of bias' for this criterion. Regarding the blinding of participants, professionals and assessors involved in the

Parameter	Extraction
	research, these criteria were not considered key criteria due to the nature of the articles".^{122 (p4)} Four (27%) of the included 15 studies were at low risk of bias for randomisation, and all 15 studies were at low risk of bias for outcome assessment. Bezerra <i>et al.</i> stated that the "included studies presented some unclear risk of bias, which compromises the quality of evidence".^{122 (p12)} Publication bias was not measured or discussed.
Method of analysis	Seven meta-analyses based on 13 of the 15 included studies were performed, considering: (1) the clinical performance of the parameters in common: retention, marginal discolouration, marginal adaptation, secondary caries, colour, anatomic form, and surface texture; and (2) a follow-up time of 12, 24, and 36 months. The prevalence of successful restorations and the total number of restorations per clinical parameter/follow-up time point were used to calculate the risk difference, with a 95% CI and statistical significance of 5%. Random-effects models were used, and heterogeneity was tested using the I² inconsistency index.
Outcome assessed	The outcomes assessed were clinical performance/longevity of restorations including anatomic form, colour, surface texture, secondary caries, marginal discolouration, marginal adaptation, and retention, according to the USPHS/Ryge criteria and FDI World Dental Federation (FDI) criteria. The follow-up time ranged from six months to ten years, and the data transcribed to the data extraction table included only results after 12 months of evaluation. The modified USPHS criteria were the most widely used and were found in 13 studies. Only one study used the FDI criteria and one study did not report the criteria used. In all except four of the studies, there were losses to follow-up during the follow-up period. Clinical performance/longevity: Adeleke, Oginni. 2012; Brackett 2003; Burgess 2004; Celik 2019; De Oliveira 2012; Federlin 1998; Franco 2006; Santiago 2010; Hussainy 2018; Matis 1996; Neo 1996; Onal 2005; Perdig~ao 2012; Popescu 2016; Powell 1995. All meta-analyses grouped only the data available for the clinical parameters in common, with follow-up times of 12, 24, and 36 months.
Results/findings	According to the authors, "In the meta-analysis that analyzed the anatomic form, there was no significant difference between the two materials at any of the follow-up times and consequently in the final analysis. The risk difference (95% CI) for the anatomic form between glass ionomer cement and CR [composite resin] was 0.00 (-0.02 to 0.02) ($p=0.83$)".^{122 (p4)} Bezerra <i>et al.</i> stated that "Evaluation of the parameters color, surface texture, and secondary caries was performed and there was no difference in the behavior of the materials. The color and surface texture heterogeneity varied between 80 and 63%, and the risk difference (95% CI) was -0.02 (-0.08 to 0.04) ($p=0.48$) and -0.02 (-0.06 to 0.02) ($p=0.31$), respectively. For the presence of secondary caries, the risk difference was 0, indicating low heterogeneity and risk difference (95% CI) of 0.00 (-0.01 to 0.01) ($p=0.87$)".^{122 (p4)} They continued: "Regarding marginal discoloration and marginal adaptation, only in the follow-up at 36 months was there a difference between the performance of the materials, with better results obtained from restorations with GIC [glass ionomer cement], most likely due to the studies exhibiting a higher confidence interval at this follow-up time. However, in the final analysis, there was no difference between GIC and CR. The risk difference for marginal discoloration and marginal adaptation in the final analysis was 0.01 (-0.01 to 0.03) ($p=0.23$) and 0.01 (-0.01 to 0.04) ($p=0.34$), respectively, with low heterogeneity (3 and 32%)".^{122 (p4)} The authors stated that, "Regarding retention, GIC [glass ionomer cement] showed significantly better clinical performance than CR [composite resin] at the 36-month follow-up time and in the final analysis. The difference in clinical performance for retention (95% CI) in the final analysis between GIC and CR was 0.07 (0.02-0.12) ($p=0.003$), and the heterogeneity obtained was considered high (76%). This was the only parameter in which one material showed superiority over another".^{122 (p4-10)} According to the authors, "the results showed that the clinical performance of the analyzed materials (CR and GIC) was similar for most of the analyzed parameters

Parameter	Extraction
	(anatomic form, color, marginal discoloration, secondary caries, surface texture and marginal adaptation) in NCCLs [non-carious cervical lesions]. However, for the retention parameter, restorations performed with GIC presented significantly better clinical performance than those performed with CR...The difference in the adhesion mechanisms between the two materials may explain the better performance of GIC for retention than CR". ^{122 (p10)} They also said that "The similarity of the clinical materials tested in the present study indicates that both GIC [glass ionomer cement] and CR exhibit promising results. However, with regard to retention, GIC seems to be the more appropriate material. Results from this systematic review should be interpreted with care, since this summarized evidence included studies developed under different conditions. Some of the outcomes considered for this meta-analysis presented high heterogeneity, which suggests imprecision of the findings from previous studies". ^{122 (p12)}
Significance/direction	According to Bezerra <i>et al.</i> , "Among all the parameters evaluated in this study, the retention rates of resin-modified GIC [glass ionomer cement] were higher than composite resin restorations. The retention rate is the most important evaluation criteria, which is why glass ionomer cements seem to be the most suitable material for restoring NCCLs [non-carious cervical lesions]". ^{122 (p15)}
Heterogeneity	According to the authors, "With regard to heterogeneity, the retention (76%), color (80%) and surface texture (63%) meta-analyses showed high heterogeneity. The meta-analyses did not control the biases of each primary study individually. Therefore, in this case, the high heterogeneity can be attributed to the etiology of the lesions and differences in the teeth, the size of the lesions, the skill of the professional and/or evaluator and the commercial brand used because studies from 1995–2018 were included" ^{122 (p12)}
Comments	Only 2 of the 15 included studies used conventional glass ionomer cement, and thus, the results presented here on the performance of this type of material are more broadly applied to resin-modified glass ionomer cement, likely due to its better aesthetic properties.

Boing *et al.* (2018)

Parameter	Extraction
First author and year of publication	Boing <i>et al.</i> (2018) ²⁶
Objectives	Compared retention and colour match of glass ionomer cement restorations with resin-based composite restorations in non-carious cervical lesions in the permanent teeth of adults.
Participants	Permanent dentition, non-carious cervical lesions, direct restoration material Non-carious cervical lesions in the permanent teeth of adults The mean age of the participants ranged from 47 to 61 years, and the full age range was 18–88 years. The number of participants was approximately 321 and the number of restorations was 1,640. With the exception of two studies, the vast majority of patients were female.
Setting/context	The treatment setting or study countries were not reported.
Description of interventions/phenomena of interest	The intervention was resin-modified glass ionomer cement (RMGIC) or glass ionomer cement to repair non-carious cervical lesions in permanent teeth. According to Boing <i>et al.</i> , "out of the 15 studies analyzed in this systematic review, 10 used resin-modified glass ionomer cement (RMGIC) and only 5 used glass ionomer cement (GIC). RMGICs were developed to overcome some of the problems of early moisture sensitivity and reduced mechanical strength of the GIC...RMGIC/GIC are self-adhesive by forming ionic bonds between the carboxyl groups of polyalkenoic acid and hydroxyapatite and by producing micromechanical interlocking of the polymer with the dentine substrate." ^{26 (p444)} Comparator: Resin-based composite restorations
Databases and sources searched	The authors searched six sources (PubMed, Scopus, Web of Science, LILACS, BBO, and the Cochrane library) up to March 2016. No restrictions to publication date or languages were implemented. Grey literature and trial registries were also

Parameter	Extraction
	explored. The reference lists of all primary studies were searched for additional relevant publications. The search strategy is provided in a table in the article. The screening process for abstracts is not provided. Three authors completed screening for full text and extraction, but it is not clear if one or two authors selected and extracted each paper. A protocol was prepared and registered (not accessible). The source of funding or conflicts of interest for the systematic review were not reported.
Date range (years) of included studies	Nineteen articles published between 1988 and 2014, examining 15 randomised controlled trials, were included in this review.
Number of primary studies included in the systematic review	Nineteen articles published between 1988 and 2014, examining 15 randomised controlled trials, were included in this review. The funding sources of primary studies were not reported.
Types of studies included	The inclusion criteria specified randomised clinical trials. Article references and reasons for exclusion were provided for studies excluded at full-text screening.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess the quality of the included trials.
Appraisal rating	Thirteen trials were judged to have an unclear risk of bias and 2 trials had a high risk of bias. Three of the 15 trials were judged to have adequate random sequence generation and 12 were considered to have adequate blinding of outcome assessors. Publication bias was dealt with through GRADE and the robust search.
Method of analysis	Dichotomised data (loss of retention, surface texture, marginal adaptation, secondary caries, colour match, and marginal discolouration) were collected and pairwise random-effects meta-analyses were completed to obtain a pooled estimate of the overall risk ratio with a 95% CI. Due to the fact that some studies reported the results for different follow-up periods, a separate meta-analysis was performed by grouping the studies with similar follow-up periods. When more than one resin composite, resin-modified glass ionomer cement, or glass ionomer cement material was included in the study, their values were combined to make a single entry. In case of data inconsistencies between reports from different follow-up time points of the same study, data were collected from the most recently published primary study. Only studies classified as having a low or unclear risk of bias were used for meta-analysis. Random-effects models were employed. Heterogeneity was assessed using the Cochran Q test and the I^2 Inconsistency Index. In the presence of substantial heterogeneity ($p < 0.1$, $I^2 > 75\%$), sensitivity analysis was conducted in an attempt to identify the causes of the heterogeneity. All analyses were conducted using the software Review Manager 5.3.
Outcome assessed	Outcome: Retention and colour match. Other outcomes included surface texture, marginal adaptation, marginal discolouration, and secondary caries. Time frame: 1–10 years; more commonly 1, 2, or 3 years Loss of retention (at 1, 2, 3, and 5 years): Adeleke 2012; Brackett 2003, 2002; Burgess 2004; Burrow 2007; Fagundes 2014, 2010, 2006; Federlin 1998; Matis 1996; Neo 1996a; Neo 1996b; de Oliveira 2012; Ozgunaltay 2002; Perdigão 2012; Powell 1992, 1991; Preben 1988; Van Dijken 2000. Colour match (at 1, 2, and 3 years): Brackett 2003, 2002; Federlin 1998; Neo 1996; de Oliveira 2012; Ozgunaltay 2002; Perdigão 2012; Powell 1992, 1991; Van Dijken 2000. Marginal discolouration (at 1, 2, and 3 years): Adeleke 2012; Brackett 2003, 2002; Burgess 2004; Fagundes 2014, 2010, 2006; Federlin 1998; Neo 1996; de Oliveira 2012; Ozgunaltay 2002; Perdigão 2012; Powell 1992, 1991; Van Dijken 2000. Marginal adaptation (at 1, 2, and 3 years): Adeleke 2012; Brackett 2003, 2002; Burgess 2004; Burrow 2007; Fagundes 2014, 2010, 2006; Federlin 1998; Matis 1996; Neo 1996;; de Oliveira 2012; Ozgunaltay 2002; Perdigão 2012; Powell 1992, 1991; Preben 1988; Van Dijken 2000. Secondary caries (at 1, 2, and 3 years): Adeleke 2012; Brackett 2003, 2002; Burgess 2004; Fagundes 2014, 2010, 2006; Federlin 1998; de Oliveira 2012; Ozgunaltay 2002; Perdigão 2012; Van Dijken 2000.

Parameter	Extraction
	Surface texture (at 1 and 3 years): Brackett 2003, 2002; Burgess 2004; Federlin 1998; Perdigão 2012; Powell 1992, 1991; Van Dijken 2000.
Results/findings	Pairwise random-effects meta-analyses were completed to obtain pooled estimates of the overall risk ratio with a 95% CI for outcomes of interest. The main findings in this review suggest that there is adequate evidence that glass ionomer cement restorations showed superior retention rates compared with resin-based composite restorations in follow-ups of between 1 and 5 years (at 1, 2, 3, and 5 years; $p \leq 0.0001$). Data on loss of retention were not heterogeneous in any of the follow-ups (1 year [relative risk: 0.28; 95% CI: 0.15–0.52; I^2: 26%; 13 trials; moderate-quality evidence], 2 years [relative risk: 0.18; 95% CI: 0.07–0.43; I^2: 0%; 7 trials; moderate-quality evidence], 3 years [relative risk: 0.26; 95% CI: 0.14–0.48; I^2: 22%; 7 trials; moderate-quality evidence], and 5 years [relative risk: 0.13; 95% CI: 0.06–0.27; I^2: 0%; 2 trials; low-quality evidence]). No difference was observed for marginal adaptation for 1–3 years (1 year [relative risk: 1.18; 95% CI: 0.88–1.56; I^2: 0%; 8 trials; moderate-quality evidence], 2 years [relative risk: 0.47; 95% CI: 0.11–1.97; I^2: 1%; 2 trials; moderate-quality evidence], and 3 years [relative risk: 0.86; 95% CI: 0.73–1.01; I^2: 0%; 4 trials; moderate-quality evidence]). No difference was observed for marginal discolouration or secondary caries in all follow-ups ($p > 0.05$). Resin composite showed better colour match than glass ionomer cements only at 2 years ($p = 0.03$). Higher roughness was observed in glass ionomer cements compared with resin composite in all follow-ups (1 year: $p = 0.0003$; 3 years: $p = 0.0004$). Colour match and surface tension meta-analyses had considerable or substantial heterogeneity. The authors concluded that “the body of evidence for color match and surface texture at 1-year and 3-year recalls was judged as low or very low due to unclear risk of bias, imprecision, and inconsistency (high heterogeneity).”²⁶ (p442) Generally, the quality of evidence was graded as moderate to low. However, the authors do signal a note of caution: “this [finding in favour of resin-modified glass ionomer cement] should be interpreted with caution, because the articles included are at ‘unclear’ risk of bias. Well-designed RCTs [randomised controlled trials] with a large sample size should be conducted to confirm the findings of this review and meta-analysis.”²⁶ (p450)
Significance/direction	See results, as this varies by outcome.
Heterogeneity	Heterogeneity was generally low for three outcomes. Colour match and surface tension meta-analyses had considerable or substantial heterogeneity.
Comments	GRADE was used by the review authors. Most trials scored high or unclear for risk of bias for one or more parameters. Less than 75% of trials were judged to have adequate random sequence generation. Some analysis had high heterogeneity. The quality of the systematic review was judged as low. The HRB graded the evidence in this review as moderate to low, corresponding with the review authors’ grading.

Szesz et al. (2017)

Parameter	Extraction
First author and year of publication	Szesz et al. (2017) ³⁰³
Objectives	Compared flowable resin composite restorations with regular resin composites for improving the marginal adaptation, marginal discolouration, and retention rates of restorations placed in non-carious cervical lesions in permanent adult teeth.
Participants	Permanent dentition, non-carious cervical lesions, direct restoration material Adults with non-carious cervical lesions in permanent adult teeth The age range of 262 participants was 28–81 years, with the mean age range 40–64 years. Only one-half of the studies reported gender, and in three studies, the majority of patients were female.
Setting/context	Only one-half of the studies reported a setting, and all four of those studies reported that the trial had taken place in a university-based clinic. The study countries were Germany, Japan, Liechtenstein, and the USA.

Parameter	Extraction
Description of interventions/phenomena of interest	According to Szesz <i>et al.</i> , “flowable resin composites are low-viscosity restorative materials that differ from regular viscosity resin composites by having lower filler load and less viscous resin content. As a result, these materials are less rigid and have an elastic modulus 20% to 30% lower than that of regular viscosity composites. This reduced low elastic modulus can theoretically absorb the stresses generated during the polymerisation shrinkage of composites and during mechanical loading to which the teeth are subjected during function.” ³⁰³ (p12) Comparator: Regular resin composites
Databases and sources searched	Seven sources (MEDLINE, Scopus, Web of Science, LILACS, BBO, the Cochrane Library, and OpenSIGLE) were searched without date or language restrictions, as well as the International Association for Dental Research Abstract Archive, clinical trials registries, and dissertations and theses up to April 2017. The search strategy is presented in a table. Duplicate screening of literature was completed. Data extraction was completed by three people. It was not clear if extraction was performed in duplicate or triplicate, although it is more likely that the full texts were split into three groups. The authors prepared and registered a protocol. The authors reported that this study did not receive any funding support. Conflicts of interest were not declared.
Date range (years) of included studies	Eight randomised controlled trials published between 2003 and 2012, with 262 adult participants, were included in this review.
Number of primary studies included in the systematic review	Eight randomised controlled trials published between 2003 and 2012, with 262 adult participants, were included in this review. The funding of primary studies is not discussed.
Types of studies included	The inclusion criteria required randomised controlled trials. The reasons for exclusion and references to excluded studies were provided.
Country of origin of included studies	The study countries were Germany, Japan, Liechtenstein, and the USA.
Appraisal instruments used	The quality of the included trials was assessed using the Cochrane Collaboration’s risk of bias instrument.
Appraisal rating	Two trials were judged to be at high risk of bias, and the remaining six trials had an unclear risk of bias. Three of the eight trials were judged to have adequate random sequence generation and five were considered to have adequate blinding of outcome assessors. Publication bias was considered as part of GRADE. The authors reported that they had too few studies to complete a funnel plot. It should be noted that the authors completed a comprehensive search.
Method of analysis	All pairwise random-effects meta-analyses were performed on studies classified as having an unclear risk of bias in the key domains and from which the information about the outcome could be extracted. Three different meta-analyses for each outcome (loss of retention, marginal discolouration, and marginal adaptation) were performed based on the study follow-ups (1, 2, and 3 years).
Outcome assessed	Outcome: Marginal adaptation, marginal discolouration, and retention rates of restorations Time frame: 1–3 years (not predetermined) Outcome by primary study Retention: Baratieri 2003; Celik 2007; Karaman 2012; Kubo 2010; Li 2011; Reis 2006. Marginal discolouration: Baratieri 2003; Celik 2007; Karaman 2012; Kubo 2010; Li 2011; Reis 2006. Marginal adaptation: Baratieri 2003; Celik 2007; Karaman 2012; Kubo 2010; Li 2011; Reis 2006.
Results/findings	The main findings from the pairwise random-effects meta-analyses suggest that there is adequate evidence that resin composite viscosity does not influence retention rates at up to 3 years follow-up. The analysis showed that there was no significant difference in loss of retention between the intervention and comparator in any follow-up period (the quality of the evidence was moderate at 3-year follow-up and low at 2-year follow-up, based on GRADE) (1 year [relative

Parameter	Extraction
	risk: 0.76; 95% CI: 0.45–1.28; I²: 50%; 4 trials; undetermined evidence quality], 2 years [relative risk: 1.08; 95% CI: 0.73–1.59; I²: 40%; 4 trials; low-quality evidence], and 3 years [relative risk: 0.81; 95% CI: 0.60–1.09; I²: 0%; 3 trials; moderate-quality evidence]). According to Szesz <i>et al.</i>, “data were not heterogeneous in any of the periods, which means that all studies included in the analysis share a common effect size.”³⁰³ (p16) The evidence for marginal discolouration and marginal adaptation is low quality and therefore there is inadequate evidence upon which to judge the effectiveness of either group of resin composites on marginal discolouration (1 year [relative risk: 0.50; 95% CI: 0.06–4.02; I²: 55%; 4 trials; undetermined evidence quality], 2 years [relative risk: 0.70; 95% CI: 0.32–1.54; I²: 32%; 4 trials; low-quality evidence], and 3 years [relative risk: 0.41; 95% CI: 0.11–1.54; I²: 5%; 2 trials; low-quality evidence]) and marginal adaptation (1 year [relative risk: 0.27; 95% CI: 0.10–0.70; I²: 0%; 4 trials; undetermined evidence quality], 2 years [relative risk: 0.70; 95% CI: 0.12–3.73; I²: 71%; 3 trials; very low-quality evidence], and 3 years [relative risk: 0.34; 95% CI: 0.17–1.71; I²: 0%; 2 trials; low-quality evidence]). The analysis showed that there was no significant difference between groups for marginal discolouration in any recall period (the quality of the evidence for marginal discolouration and marginal adaptation is low for all follow-up periods based on GRADE). Flowable composites showed better results for marginal adaptation at the 1- and 3-year follow-ups (the quality of the evidence is low to very low for both follow-up periods based on GRADE). According to Szesz <i>et al.</i>, “the retention rates and marginal discolouration of resin composite restorations in non-carious cervical lesions are not affected by the resin viscosity, although flowable composites showed a better marginal adaptation. The quality of the evidence was graded as moderate for the retention rate at 3 years. All other outcomes were graded as low and very low quality.”³⁰³ (p20)
Significance/direction	Varied by outcome; see above.
Heterogeneity	Varied by outcome, combined with follow-up time point.
Comments	GRADE was used by the review authors. All trials scored high or unclear for risk of bias for one or more parameters. Less than 75% of trials were judged to have adequate random sequence generation and blinding of outcome assessment. The quality of the systematic review was judged as low. The HRB graded the evidence in this review as low which does not corresponds with all of the review authors’ ratings.

Restoration support material

De Assis *et al.* (2020)

Parameter	Extraction
First author and year of publication	De Assis <i>et al.</i> (2020) ¹²⁴
Objectives	Evaluated whether there are any differences in clinical performance (including retention) between one-step self-etching and two-step self-etching adhesive systems in non-carious cervical lesions.
Participants	Permanent dentition, non-carious cervical lesions, restoration support material Patients with restorations in which self-etching adhesive systems participated in the primary studies. In total, 822 restorations of non-carious cervical lesions were performed in 237 patients with a mean age of 45 years. Four different one-step self-etching adhesive systems and three two-step self-etching adhesive systems were used. The mean follow-up time was 18 months. The main inclusion criteria for the studies were non-carious cervical lesions with no more than three restorations per study participant. Forty-six per cent of the restorations were maxillary and 53.6% were mandibular, with a fairly homogeneous distribution of restorations. In general, restorations did not involve more than 50% of the cavosurface margin in enamel, and 75% of the restoration surface was in dentine.

Parameter	Extraction
Setting/context	The study countries or clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: Patients with restorations using one-step self-etching adhesive. Comparison: Patients with restorations using two-step self-etching adhesive. According to De Assis <i>et al.</i>, "One-step self-etching (1SSE) adhesives provide easy clinical application, reduce technical sensitivity, and are well accepted by clinicians. Although 1SSE adhesives have a simplified approach, early formulations did not promote effective dentin sealing. However, manufacturers have modified the chemical formulations of new one-step adhesives to improve their clinical performance".¹²⁴ (p599) The authors described the comparator as follows: "Two-step adhesives consist of acidic monomers dissolved in aqueous solution and a layer of hydrophobic resin as a second step. Single-step adhesives do not have this hydrophobic layer. The degree of demineralization of acidic monomers in self-etching adhesives depends on their pH, which may be mild, moderate, or strong. Self-etching adhesives are able to infiltrate the smear layer and partially dissolve the hydroxyapatite, generating a hybrid layer with incorporated minerals. The current trend is to use simplified adhesive materials, which are available from many manufacturers. Self-etching adhesive systems have become popular for clinicians because they do not require preconditioning with phosphoric acid or an overwashing step; they also provide a clinical time gain over etch-and-rinse adhesives".¹²⁴ (p599) They also stated, "Generally, non-carious cervical lesions are used as determinants of the clinical effectiveness of adhesives. This type of restoration is usually caused by stress in the cervical region of the teeth, and the cavity formed involves dentin, which makes adhesion more difficult. In addition, NCCLs [non-carious cervical lesions] present high prevalence and easy access to restoration (located in the vestibular region), do not require complicated restorative techniques, can be considered free cavities because they have a low polymerization contraction factor, and do not usually provide macromechanical retention".¹²⁴ (p599)
Databases and sources searched	The authors searched three databases: MEDLINE via PubMed, Scopus, and the Cochrane Library without limits on year of publication. The electronic search end date was July 2019 and language limitations were not mentioned. The researchers conducted a manual search for articles published in the following journals: <i>Operative Dentistry</i>, <i>Dental Materials</i>, <i>Journal of Dentistry</i>, <i>Journal of Adhesive Dentistry</i>, <i>American Journal of Dentistry</i>, <i>Brazilian Dental Journal</i>, and <i>Clinical Oral Investigations</i>. In addition, OpenGrey was used to search grey literature. This systematic review protocol was recorded in PROSPERO. Extraction and screening were completed in duplicate. The authors certified that they had no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that was presented in this article.
Date range (years) of included studies	The included studies were published in 2005, 2009, 2010, 2012, and 2016.
Number of primary studies included in the systematic review	Five randomised controlled trials, published in 2005, 2009, 2010, 2012, and 2016, were included. The sources of funding for primary studies were not reported.
Types of studies included	Randomised clinical trials were eligible for inclusion. A list of excluded studies and reason for exclusion were provided.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	The authors stated that "The findings indicated a high risk of bias for blinding of ... participants (2 studies); an unclear risk of bias to allocation (1 study), blinding of participants (2 studies), and incomplete outcome (1 study); and a low risk for other biases, where it was shown that the studies were of high quality".¹²⁴ (p601–602) All five included studies were at low risk of bias for randomisation, and all five studies were at low risk of bias for outcome assessment. De Assis <i>et al.</i> stated that "The quality of the studies was analyzed from the Cochrane scale, where the high risk of bias observed for blinding is justified by the clinical technique used in applying the adhesive, which makes it difficult to

Parameter	Extraction
	screen the examiners. The results of this review should be interpreted with caution because of the small number of clinical trials evaluated. Other randomised controlled trials with longer observation periods are still needed".¹²⁴ (p606) Publication bias is not measured or discussed.
Method of analysis	According to De Assis <i>et al.</i>, "The meta-analyses were based on the Mantel–Haenszel and inverse-variance methods. 1SSE [one-step self-etching] and 2SSE [two-step self-etching] were used in the study to assess the effects of the treatment on the body. The relative risk (RR) and 95% confidence interval (CI) were calculated for each study. The RR values were considered significant at $p=0.05$. The extracted data were analyzed using Review Manager software (RevMan) 5.3".¹²⁴ (p600)
Outcome assessed	The outcomes evaluated were retention of restoration (primary outcome), post-operative sensitivity, secondary caries, colour match, marginal discolouration, marginal adaptation, and anatomical form. In all five included studies, the researchers evaluated their outcomes through the USPHS criteria, and usually the follow-up examinations were performed every 3 months with a maximum follow-up of 24 months. All five studies evaluated retention of the restoration, along with marginal discolouration, secondary caries, and marginal adaptation. Only three studies assessed anatomical form and post-operative sensitivity. Among the included studies, four evaluated colour match. Clinical performance: Pena 2016; Tu"rku"n 2005; Perdiga"o 2012; Zhou 2009; Brackett 2010.
Results/findings	The authors reported: "Primary Outcome—Five studies were selected for quantitative analysis comparing 1SSE [one-step self-etching] adhesive systems and 2SSE [two-step self-etching] adhesive systems. The meta-analysis showed no statistically significant difference between 1SSE and 2SSE regarding retention ($p=0.23$; $RR=1.55$; $95\% CI=0.76, 3.19$)".¹²⁴ (p602) They continued, "Secondary Outcome—Regarding postoperative sensitivity, three studies were included for quantitative analysis. The data showed no statistically significant difference between 1SSE and 2SSE ($p=0.50$; $RR=3.00$; $95\% CI=0.13, 70.64$). The same was observed for secondary caries ($p=0.63$; $RR=0.68$; $95\% CI=0.14, 3.31$), color match ($p=0.41$; $RR=0.64$; $95\% CI=0.23, 1.83$),... marginal discoloration ($p=0.93$; $RR=1.02$; $95\% CI=0.65, 1.61$) and anatomical form ($p=0.56$; $RR=1.38$; $95\% CI=0.46, 4.13$). However, there was statistical difference in relation to marginal adaptation favorable to the 2SSE group ($p=0.01$; $RR=1.95$; $95\% CI=1.14, 3.34$)".¹²⁴ (p602–603) De Assis <i>et al.</i> stated that "The meta-analysis showed that there was no statistically significant difference between the results for 1SSE [one-step self-etching] and 2SSE [two-step self-etching] ($p=0.23$; $RR=1.55$; $95\% CI=0.76, 3.19$)...It is worth mentioning that the similarity between self-etching adhesive systems will allow a greater use of 1SSE systems since they will promote simplification in the technique, optimizing clinical time".¹²⁴ (p603) Additionally, they stated: "The meta-analyses showed no difference between the 1SSE [one-step self-etching] and 2SSE [two-step self-etching] adhesive systems for postoperative sensitivity, occurrence of secondary caries,... color match, marginal discoloration, and anatomical form. However, regarding marginal adaptation, there was statistical difference favorable to the 2SSE group ($p=0.01$; $RR=1.95$; $95\% CI=1.14, 3.34$)". p603–605 The authors concluded that "the results of this systematic review and meta-analysis, which only looked at self-etching adhesive systems (1SSE and 2SSE), showed minimal adjustments [changes] regarding retention, color match, marginal discoloration and anatomical form in enamel and excellent results of absence of secondary caries".¹²⁴ (p605)
Significance/direction	Both one-step self-etching and two-step self-etching adhesive systems have comparable clinical effectiveness over a follow-up period of 12–24 months, except for the outcome of marginal adaptation.
Heterogeneity	The authors did not mention measuring or discussine heterogeneity. However the Forest plots indicates that there was no statistical heterogeneity in the meta-analyses.
Comments	GRADE was not used by the review author.

Lins *et al.* (2020)

Parameter	Extraction
First author and year of publication	Lins <i>et al.</i> (2020) ¹²⁵
Objectives	Assessed whether the type of solvent (acetone-based compared with alcohol-based) in dental adhesives for composite resin restorations influences the clinical performance (including survival and 10 other parameters) of composite restorations placed in adults with non-carious cervical lesions (Class V restorations).
Participants	Permanent dentition, non-carious cervical lesions, restoration support material The included studies comprised a total of 3,959 dental restorations in 1,087 adults with non-carious cervical lesions (requiring Class V restorations), followed-up for periods ranging from 18 to 72 months. Twenty-two of the included studies used the modified USPHS criteria to evaluate dental restorations, whereas four studies used the FDI criteria, and one study used its own customised criteria.
Setting/context	The study countries were: Australia, Belgium, Brazil, Egypt, Germany, Italy, Japan, Sweden, Turkey, and the United States of America (USA). The study clinical settings were not reported. Most of the trials included in the meta-analyses reported that trained and/or experienced operators performed the composite restorations in a controlled clinical situation, which might have led to similar results for both solvents because the effects of operator mistakes were dramatically reduced due to operators strictly following the manufacturers' instructions.
Description of interventions/phenomena of interest	Intervention: Composite restorations performed with dental adhesives containing acetone-based solvents Comparison: Composite restorations performed with dental adhesives containing alcohol-based solvents The intervention under evaluation in this review was a comparison of composite restorations using either acetone- or alcohol-based solvents. The authors offer the following description of the two solvent types: "Alcohol and water are polar solvents that can create strong hydrogen bonds with collagen fibrils, maintaining the interfibrillar spaces, which improves monomer diffusion along etched dentin. Moreover, hydrogen bonds between ethanol and water increase evaporation rates, leading to more surface water removal compared with pure water. Acetone-based solvents might be a great choice for bonding agents that contain hydrophilic and hydrophobic monomers in the same bottle, as acetone can dissolve both polar and non-polar substances because of its high dipole moment and low dielectric constant." ¹²⁵ (pE238)
Databases and sources searched	Nine sources – PubMed, Scopus, Web of Science, Virtual Health Library (VHL), the Latin American and Caribbean Health Sciences Literature (LILACS) database, the Cochrane Library, OpenGrey, ClinicalTrials.gov, and ReBEC (the Brazilian Registry of Clinical Trials) – were searched, with no date or language limits or any other search filters applied. Hand-searching was also performed to find relevant articles that had not been retrieved in the electronic search of the selected databases. The protocol of this study was registered in the PROSPERO database, and its reporting followed the PRISMA guidelines. Extraction and screening were completed in duplicate. This study was financed in part by CAPES. The authors of this manuscript certified that they had no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that was presented in this article.
Date range (years) of included studies	The included studies were published from 2001 to 2019.
Number of primary studies included in the systematic review	There were 27 randomised controlled clinical trials, published from 2001 to 2019, included in the overall review; 10 of the 27 studies were included in the two meta-analyses. The sources of funding for primary studies were not reported.
Types of studies included	Randomised controlled clinical trials (the 'study design' criterion was included in the search strategy in order to avoid a high number of laboratory studies).

Parameter	Extraction
	A list of studies excluded at the full-text stage was not provided in the review. However, the reasons for exclusion were provided in the main text.
Country of origin of included studies	The studies were completed in Australia, Belgium, Brazil, Egypt, Germany, Italy, Japan, Sweden, Turkey, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	All risk of bias assessment criteria were considered to be key domains, except for the blinding of participants and personnel. According to the authors, "Four of the 27 selected studies were rated as unclear for random sequence generation. Two studies were unclear, whereas one study did not perform the allocation concealment. Twenty-two papers were rated as unclear regarding the blinding of participants and personnel. However, this third domain was not regarded as a key domain in the risk of bias assessment. One study did not blind the evaluators and eight studies were classified as unclear for this domain. Ten studies presented high risk of bias for the incomplete outcome data domain for the following reasons: the clinical criteria used to assess the results were not described; only alpha scores were reported; or only bravo scores were reported. Five studies showed high risk of bias for selective reporting, and six studies presented other biases. Overall, four papers were classified as low risk of bias. Nevertheless, six other papers were also included as low risk of bias, regardless of being checked as unclear for the blinding of participants and personnel, because this domain was not considered a key domain."¹²⁵ (E243) Twenty-two (81%) studies were at low risk of bias for randomisation. Eighteen (66%) studies were at low risk of bias for outcome assessment. The meta-analysis included only papers that the authors deemed had a low risk of bias, some of these had unclear risk of bias for the blinding of participants. Regarding publication bias, the authors stated that "Visual inspection of the funnel plot revealed a symmetric distribution, which suggests there were no publication biases for survival rates."¹²⁵ (pE245)
Method of analysis	Two meta-analyses based on 10 studies with a low risk of bias were performed; one meta-analysis examined clinical outcomes and the other examined overall survival rates. Clinical outcomes and overall survival rates were dichotomised as success or failure according to the criteria used by each of the selected studies. The prevalence of success and the total number of restorations for each group (acetone- or alcohol-based) were used to calculate the risk difference at a CI of 95%. Random-effects models were applied, and heterogeneity was tested using the I² inconsistency index.
Outcome assessed	Clinical performance parameters and overall survival rates of composite restorations placed using acetone- or alcohol-based bonding agents presented in the 10 studies that had a low risk of bias were analysed. Two separate meta-analyses were performed for: (1) clinical evaluation parameters (retention, marginal adaptation, marginal discolouration, surface texture, colour, post-operative sensitivity, secondary caries, anatomic form, and pulp vitality); and (2) survival rates (overall and at different evaluation periods: 6, 12, 18, 24, 36, 60, and 72 months). Clinical performance: Reis and Loguercio 2009; Burrow and Tyas 2012; Moretto 2013; Celik 2007; Peumans 2018; Hafer 2015; Boushell 2016; Oz 2019; Reis 2009; Scotti 2016; Abdalla and Garcia-Godoy 2006; Perdigao 2005; Ritter 2008; Ritter 2009; Ruschel 2018; Saboia 2006; Sartori 2011; Sartori 2012.
Results/findings	The overall risk difference of all clinical evaluation parameters was 0.00 (95% CI: 0.01–0.00) ($p=0.57$), whereas it was 0.01 (95% CI: 0.04–0.02; $p=0.46$) for retention; 0.00 (95% CI: 0.02–0.01; $p=0.82$) for marginal adaptation; 0.00 (95% CI: 0.01–0.01; $p=0.63$) for marginal discolouration; 0.00 (95% CI: 0.04–0.04; $p=1.00$) for surface texture, colour, and pulp vitality; 0.01 (95% CI: 0.04–0.02; $p=0.65$) for sensitivity; 0.00 (95% CI: 0.01–0.01; $p=1.00$) for secondary caries; and 0.00 (95% CI: 0.03–0.03; $p=1.00$) for anatomic form. According to the authors, "a similar clinical behavior regarding key prognostic parameters (retention, marginal adaptation, and marginal discoloration) can be expected for composite restorations placed using dental adhesives containing

Parameter	Extraction
	acetone compared with those based on alcohol, regardless of adhesive resin composition or bonding strategies (etch-and-rinse versus self-etch)."^{125 (pE248)} The overall risk difference for survival rates was 0.00 (95% CI: 0.01–0.01; p=0.91), whereas it was 0.00 (95% CI: 0.01–0.01; p=0.99) for six months, 0.00 (95% CI: 0.02–0.02; p=0.88) for 12 months, 0.14 (95% CI: 0.39–0.11; p=0.27) for 18 months, 0.01 (95% CI: 0.02–0.04; p=0.52) for 24 months, 0.00 (95% CI: 0.04–0.03; p=0.91) for 36 months, 0.01 (95% CI: 0.08–0.06; p=0.82) for 60 months, and 0.04 (95% CI: 0.20–0.12; p=0.65) for 72 months According to the authors, "A second meta-analysis was performed to compare survival rates of composite restorations placed using acetone- or alcohol-based adhesive systems over different follow-up periods. Survival rates can be described as the percentage of composite restorations that did not fail (loss or need of replacement/repair) at a certain evaluation time. There was no statistical difference between the two solvents, showing that composite restorations placed using both types of adhesives performed favourably in clinical trials with follow-ups ranging from 6 to 72 months...However, some of these results should be interpreted with caution. The follow-ups of 12 and 18 months presented high heterogeneity among studies (62% and 88%, respectively), which means the extracted data from the selected set of clinical trials varied from one to another, leading to more favourable survival rates (although not statistically significant) for restorations placed using alcohol-based bonding agents, especially at 18 months. Also, only one publication reported data for the 60-month follow-up, and the 72-month follow-up analysis also consisted of data extracted from a single study. Thus, more long-term clinical trials are necessary to allow for a reliable prediction of the performance of composite restorations placed using acetone- or alcohol-based bonding agents over time."^{125 (pE249–250)} According to the authors, "High quality of evidence by the GRADE approach was evidenced for both meta-analyses, with very strong association of at least 919 events per 1,000. Visual inspection of the funnel plot revealed a symmetric distribution, which suggests there were no publication biases for survival rates. The authors would also like to highlight that a meta-analysis including all studies, regardless of their risk of bias, was performed previously to the meta-analysis hereby presented, and the significance of their results, as well as the certainty of evidence, were similar to the statistical analysis included in the present study (that considered only studies with low risk of bias). Therefore, the authors opted to include only the last meta-analysis, without high risk of bias studies."^{125 (pE245)}
Significance/direction	The authors stated that "Based on the results of this systematic review and meta-analysis, there is no significant difference in the clinical performance of dental adhesives based on solvent type (alcohol- or acetone-based), regardless of adhesive mode of action or application."^{125 (pE252)}
Heterogeneity	Heterogeneity was assessed using the I² inconsistency index in the pooled and subgrouped meta-analyses. According to the authors, "The overall heterogeneity between studies was not significant (I²=0.00%) for both meta-analyses. The heterogeneity values for each clinical evaluation... parameter were also not significant, ranging from 0% to 38% (38% for sensitivity, 34% for retention, and 0% for the remaining criteria). The heterogeneity for survival rates at each follow-up period was not significant either, except for the 12- and 18-month follow-ups, ranging from 0% to 88% (88% for 18 months, 62% for 12 months, 46% for 24 months, and 0% for all the other follow-up periods)".^{125 (pE244–E245)}
Comments	Some limitations to the review were reported by the authors: "Methodologic variability is a limitation that must be considered in the present meta-analyses. Beveling... of the enamel margins was carried out before restorative procedures in some of the selected studies, whereas other studies did not do it. Roughening of the superficial, hypermineralized dentine surface was performed in most of the selected clinical trials, but some of them did not provide information regarding this aspect. Some papers included teeth with different levels of dentine sclerosis, and all studies had cavities of varied shapes and dimensions. All these clinical aspects can influence micro-retention, which might have affected the results of... the meta-analyses performed in this review. Furthermore, all the selected papers compared adhesives with not only different solvents, but also with distinct

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	monomer compositions. Therefore, even if some adhesive systems contained a solvent type that could have affected the clinical performance of composite restorations unfavorably, their monomer chemistry might have compensated for this disadvantage, improving their clinical results." ¹²⁵ (pE250–252)

Mara de Paula *et al.* (2019)

Parameter	Extraction
First author and year of publication	Mara de Paula <i>et al.</i> (2019)¹³⁰
Objectives	Evaluated whether the retention rates of non-carious cervical lesion restorations in adults permanent teeth that used the sandwich technique (a lining of glass ionomer cement or resin-modified glass ionomer cement) were greater than those of composite resin only restorations.
Participants	Permanent dentition, non-carious cervical lesions, restoration support material The population was adults with non-carious cervical lesion restorations. According to the authors, "All studies included the placement of multiple restorations per patient. The age of the patients selected for the clinical trials ranged from 22 to 73 years, with an average of 59.6 years. The number of participants in the studies ranged from 18 to 45, and only one study reported that the percentage of men was 72.2%. Only one study reported the use of a rubber dam for restorations. Beveling of the enamel surface was performed in all studies except one". ¹³⁰ (p500)
Setting/context	The study countries or clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: The sandwich technique (a lining of glass ionomer cement or resin-modified glass-ionomer cement) Comparator: Composite resin-only restorations. The authors mentioned, but did not adequately describe, the comparator. Mara de Paula <i>et al.</i> described the intervention as follows: "To prepare the sandwich technique, two studies used polyacrylic acid for dentin conditioning, before the GIC [glass ionomer cement] base, and one study used material primer prior to GIC application. One study did not use polyacrylic acid and did not report the use of any primer to treat the dentin surface prior to the application of the GIC base. All studies in the sandwich technique group employed conventional two-step adhesives that require phosphoric acid etching, followed by washing, subsequent application of the adhesive, and increments of CR [composite resin] over the GIC base. All studies used etch-and-rinse adhesives for CR restorations. Two studies used two-step etch-and-rinse adhesives. One study used a three-step etch-and-rinse adhesive for the control group (CR). One study had two CR groups: one that used a three-step etch-and-rinse adhesive and another that used a two-step etch-and-rinse adhesive. Regarding the materials used, two studies used RMGIC [resin-modified glass ionomer cement], while the other two used a GIC. Three studies used microfilled CRs, and one study used a flowable CR." ¹³⁰ (p500–501)
Databases and sources searched	The authors developed a search strategy for PubMed, which they then adapted for use with an additional five electronic databases: LILACS, BBO, the Cochrane Library, Scopus, and Web of Science. No restrictions were placed on the publication date or language of the search results. Grey literature was inspected using OpenSIGLE, the ProQuest Dissertations & Theses Global database, and the CAPES database. Abstracts from the annual conference of the International Association for Dental Research and its regional divisions (1990–2017) provided additional sources of investigation. Unpublished and ongoing trials were searched on the ISRCTN registry, the World Health Organization's (WHO's) International Clinical Trials Registry Platform, ClinicalTrials.gov, ReBEC (the Brazilian Registry of Clinical Trials), and the EU Clinical Trials Register. The authors prepared a study protocol and registered it with PROSPERO. Extraction and screening were completed in duplicate. Funding sources and conflict of interest were not reported.
Date range (years) of included studies	One of the included studies was published in 1991 (with follow-ups in 1992 and 1995), two studies were published in 1996, and one study was published in 2016.

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Number of primary studies included in the systematic review	Six randomised controlled trials were eligible for the qualitative analysis. Of these, three were follow-ups of the same clinical trial, so a total of four studies remained for evaluation in this review. One of the included studies was published in 1991 (with follow-ups in 1992 and 1995), two studies were published in 1996, and one study was published in 2016. The funding sources for primary studies were not reported.
Types of studies included	Randomised controlled trials only were eligible for inclusion The list of excluded studies and reason for exclusion were provided in the article text.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	The authors stated that "Sequence generation and allocation concealment were defined as key domains. In summary, all studies were classified as having unclear bias risk, as these domains were not reported in the studies".^{130 (p501)} All four trials included in the analysis were judged to have an unclear risk of bias for randomisation. Risk of bias for outcome assessment was not reported in the review. The authors reported "The primary studies included in this systematic review were classified as having unclear bias risk. Therefore, the present... meta-analysis should be interpreted with caution... Randomization and allocation concealment was not reported or insufficiently reported in 63.8% and 89.1% of RCTs [randomised controlled trials], respectively, a finding that indicates immaturity in the scientific community regarding the reporting of RCTs on this subject."^{130 (p501-2)} Publication bias was dealt with during the GRADE assessment.
Method of analysis	Mara de Paula <i>et al.</i> reported that "Dichotomized data (loss of retention, marginal adaptation, secondary caries, color match, and marginal discoloration) were collected, and a meta-analysis was performed to obtain a pooled estimate of the overall risk ratio with a 95% confidence interval. Loss of retention was the primary outcome, and all other measures were secondary outcomes."^{130 (p499)} According to the authors, "Data were analyzed for loss of retention, color match, and marginal discoloration at follow-ups of 1, 2, and 3 years. Data from secondary caries and marginal adaptation were also analyzed at the 1- and 2-year follow-ups; the 3-year follow-up was not analyzed due to lack of data".^{130 (p501)} They also stated that "Only studies classified as having low or unclear risk of bias were included in the meta-analysis. Random-effects models were employed, and heterogeneity was assessed using the Cochran's Q test and I^2 statistics. Given heterogeneity, a sensitivity analysis was conducted to identify the causes. All analyses were conducted using Review Manager 5.3 software."^{130 (p499)}
Outcome assessed	Primary outcome: Retention rates of non-carious cervical lesion restorations measured as loss of retention Secondary outcomes: Marginal adaptation, secondary caries, colour match, and marginal discoloration. At 1-, 2- and 3-year follow-up Retention rates: Neo 1996; Popescu 2016; Powell 1991; Powell 1992; Powell 1995; Teixeira 1996.
Results/findings	Loss of retention (primary outcome) According to Mara de Paula <i>et al.</i>, "No significant differences were detected between the groups at the 1- and 2-year follow-ups ($p>0.05$). However, at the 3-year follow-up, the sandwich technique presented higher retention rates (risk ratio=7.5; 95% CI: 2.1 to 27.2; $p=0.002$) than the resin-based composite restorations. Data were heterogeneous at the 2-year follow-up ($p=0.08$, $I^2=60\%$) but no heterogeneity was observed at the 1- and 3-year follow-ups ($p>0.46$, $I^2=0\%$)."^{130 (p501)} Colour match The authors reported that "No significant difference in color match was observed at any follow-up (1-year: $p=0.90$; 2-year: $p=0.73$; 3-year: $p=0.92$). The color match data were heterogeneous at the 1- and 2-year follow-ups ($p>0.06$, $I^2>57\%$), but not at the 3-year follow-up ($p=0.21$, $I^2=37\%$)."^{130 (p501)} Marginal discoloration

Parameter	Extraction
	The authors stated that “No significant differences between groups were observed at any follow-up ($p>0.22$). Data were heterogeneous at the 3-year follow-up ($p=0.15$, $I^2=52\%$) but not at the 1- and 2-year follow-ups ($p>0.32$, $I^2=0\%$)”.^{130 (p501)} Marginal adaptation According to Mara de Paula <i>et al.</i>, “No significant difference for marginal adaptation was observed between groups at any follow-up ($p>0.27$). Data were not heterogeneous at the 1-year follow-up ($p=0.72$, $I^2=0\%$), but heterogeneity could not be evaluated at the 2-year follow-up, as only one study provided information for meta-analysis”.^{130 (p501)} Secondary caries The authors reported that “No significant difference was detected at any follow-up ($p>0.25$). Heterogeneity was not applicable to any follow-up”.^{130 (p501)}
Significance/direction	The authors concluded that, “Based on the limited number of studies, outcome retention rates at the 3-year follow-up (assessed as moderate-quality evidence) were better for the sandwich technique than for CRs. Secondary outcomes, such as marginal discoloration, color match, marginal adaptation, and secondary caries, were considered low-quality evidence. Further RCTs [randomised controlled trials] with greater methodological rigor should be conducted to produce more reliable information on this subject.”^{130 (p504)}
Heterogeneity	Heterogeneity was low to high in analyses. The authors provided the following comment on heterogeneity: “heterogeneity was assessed using the Cochran Q test and I^2 statistics. Given heterogeneity, a sensitivity analysis was conducted to identify the causes.”^{130 (p499)}
Comments	GRADE was used by the review authors. According to Mara de Paula <i>et al.</i>, “Except for loss of retention, the evidence certainty was graded as low for all outcomes due to the eligible studies’ unclear bias risk and the data’s imprecision (high confidence interval). Although a high confidence interval was also observed for loss of retention, the evidence was not downgraded, as there was no change in direction in the eligible studies. The certainty of evidence for loss of retention was graded as moderate.”^{130 (p501)}

Sousa Pamplona da Silva *et al.* (2018)

Parameter	Extraction
First author and year of publication	Sousa Pamplona da Silva <i>et al.</i> (2018) ¹²⁶
Objectives	Compared HEMA-free adhesive systems with HEMA-containing systems to treat non-carious cervical lesions in permanent teeth in adults.
Participants	Permanent dentition, non-carious cervical lesions, restoration support material Population: Non-carious cervical lesions in permanent teeth in adults Twenty-two randomised controlled trials published between 1994 and 2016, involving a total of 997 adults, were included in this review. The mean ages of the participants in the 15 studies where age was known ranged from 46 to 64.7 years. The patients’ gender was not reported.
Setting/context	Seventeen studies were conducted at university centres and 3 studies did not report the setting. The review authors do not mention where the other two studies were conducted. The studies were completed in Belgium, Brazil, China, Denmark, Germany, Italy, Japan, Serbia, Sweden, Turkey, and the USA.
Description of interventions/phenomena of interest	According to da Silva <i>et al.</i>, “2-hydroxyethyl methacrylate (HEMA) seems to be the most commonly used [component in dental adhesives] and it is an important chemical component. This monomer was introduced in the adhesive composition during the 1970s with the aim of improving the wettability and diffusion into the demineralized collagen fibrils because of its high hydrophilicity. However, some long-term disadvantages have been reported, particularly with regard to its high hydrophilicity over time. The increased water uptake results in hydrolytic degradation of the adhesive interface. For this reason, manufacturers launched adhesive systems without this monomer, the so-called HEMA-free adhesives, into the market to avoid its negative effects.”^{126 (p1)} Comparator: HEMA-containing systems

Parameter	Extraction
Databases and sources searched	The authors systematically searched four databases (PubMed, the Cochrane Library, Scopus, and Web of Science) up to May 2017 with no language or date restrictions. The search strategies were provided in a table. OpenGrey and the included articles' reference lists were manually searched. A study protocol was prepared and registered with PROSPERO. The authors did not explicitly state that duplicate screening and extraction was completed. This study was financially supported by Coordenação de Aperfeiçoamento de Pessoas de Nível Superior (CAPES). Conflicts of interests were not declared.
Date range (years) of included studies	Twenty-two randomised controlled trials published between 1994 and 2016 were included.
Number of primary studies included in the systematic review	Twenty-two randomised controlled trials published between 1994 and 2016, involving a total of 997 adults, were included in this review. Funding sources of primary studies were not presented.
Types of studies included	Randomised controlled trials were specified. There reasons for excluding full-text articles were provided, but not a list of the excluded articles.
Country of origin of included studies	The studies were completed in Belgium, Brazil, China, Denmark, Germany, Italy, Japan, Serbia, Sweden, Turkey, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess the quality of primary studies.
Appraisal rating	Based on the Cochrane Collaboration's risk of bias instrument, 11 trials were judged to be at low risk of bias, and in the remaining 11 trials, the risk of bias was judged to be unclear. These 22 studies were used in the meta-analysis. Thirteen of the 22 trials were judged to have adequate random sequence generation and 19 were considered to have adequate blinding of outcome assessors. Publication bias was not discussed, although the authors had a comprehensive search strategy.
Method of analysis	The extracted data were analysed using RevMan software version 5.3. The meta-analysis was performed including studies with a low and unclear risk of bias. The meta-analysis was grouped by outcome: retention, marginal adaptation, marginal discolouration, caries, and post-operative sensitivity. Each single outcome and the overall effect (clinical performance by combined outcomes) was analysed. The data were dichotomised as either acceptable or unacceptable according to the classification criteria used by each study. The prevalence of unacceptable restorations (failures/events) and the total number of restorations for each group were used to calculate the risk difference with a 95% CI. Random-effects models were employed, and heterogeneity was tested using the I^2 Inconsistency Index. If some of the information needed for the meta-analysis was absent from any of the selected studies, the authors were contacted to provide the missing data. Five attempts of contacts with authors were made for each study. If after the contact attempts there was no response from the authors, or the authors did not provide the data, the study was not included in the meta-analysis.
Outcome assessed	Outcome: Clinical performance or restoration effectiveness The main outcomes were retention, marginal adaptation, marginal discolouration, secondary caries, and post-operative sensitivity. Time frame: The study recall time frames ranged from 1 to 13 years for the 22 studies. Two studies have very long follow-up time frames, at 8 and 13 years. The remaining 20 studies' follow-up time frames were 1–4 years. Outcome by primary studies: Retention: Brackett 2005; Dutra-Correa 2013; Horsted-Bindslev 1996; Kurokawa 2007; McCoy 1998; Perdigão 2005; Reis 2009; Ritter 2008; Ritter 2009; Scotti 2016; Saboia 2006; Soderholm 2013; Stojanac 2013; Swift 2001; Turkun 2003; Van Dijken 1994; Van Dijken 2007; Van Dijken 2008; Van Dijken 2013; Van Landuyt 2014; Zhou 2009. Marginal discolouration: Brackett 2005; Dutra-Correa 2013; Horsted-Bindslev 1996; Kurokawa 2007; McCoy 1998; Perdigão 2005; Reis 2009; Ritter 2008; Ritter 2009; Scotti 2016; Saboia 2006; Soderholm 2013; Stojanac 2013; Swift 2001; Turkun 2003; Van Dijken 2013; Van Landuyt 2014; Zhou 2009. Marginal adaptation: Brackett 2005; Dutra-Correa 2013; Horsted-Bindslev 1996; Kurokawa 2007; Perdigão 2005; Reis 2009; Ritter 2008; Ritter 2009; Scotti 2016; Saboia 2006; Soderholm 2013; Stojanac 2013; Swift 2001; Turkun 2003; Van Dijken 2013; Van Landuyt 2014; Zhou 2009.

Parameter	Extraction
	Secondary caries: Brackett 2005; Dutra-Correa 2013; Kurokawa 2007; Perdigão 2005; Reis 2009; Ritter 2008; Ritter 2009; Scotti 2016; Saboia 2006; Soderholm 2013; Stojanac 2013; Swift 2001; Turkun 2003; Van Dijken 2013; Van Landuyt 2014; Zhou 2009. Post-operative sensitivity: Brackett 2005; Dutra-Correa 2013; Kurokawa 2007; Perdigão 2005; Reis 2009; Ritter 2008; Ritter 2009; Scotti 2016; Saboia 2006; Soderholm 2013; Stojanac 2013; Swift 2001; Turkun 2003; Van Dijken 2013; Van Landuyt 2014; Zhou 2009. Clinical performance by combined outcomes: Brackett 2005; Dutra-Correa 2013; Häfer 2015; Horsted-Bindslev 1996; Kurokawa 2007; McCoy 1998; Perdigão 2005; Reis 2009; Ritter 2008; Ritter 2009; Scotti 2016; Saboia 2006; Soderholm 2013; Stojanac 2013; Swift 2001; Turkun 2003; Van Dijken 1994; Van Dijken 2007; Van Dijken 2008; Van Dijken 2013; Van Landuyt 2014; Zhou 2009.
Results/findings	The main finding from the pairwise random-effects meta-analysis is that when HEMA-free adhesive systems were compared with HEMA-containing adhesive systems, the evidence is inconclusive regarding which system is better, as performance is similar for both. There was no overall risk difference (standardised mean difference: 0.00; 95% CI: -0.01 to 0.01; I²: 10%) and no difference for restoration effectiveness (standardised mean difference: 0.03; 95% CI: -0.01 to 0.07; I²: 50%; 21 trials; 1,704 restorations), marginal discolouration (standardised mean difference: 0.02; 95% CI: -0.01 to 0.04; I²: 43%; 17 trials; 1,210 restorations), marginal adaptation (standardised mean difference: -0.01; 95% CI: -0.04 to 0.01; I²: 35%; 16 trials; 1,198 restorations), secondary caries (standardised mean difference: 0.00; 95% CI: -0.01 to 0.01; I²: 0%; 16 trials; 1,148 restorations), or post-operative sensitivity (standardised mean difference: -0.00; 95% CI: -0.02 to 0.01; I²: 0%; 16 trials; 1,141 restorations). None of the comparisons between HEMA-free adhesive systems and HEMA-containing adhesive systems were significantly different. According to da Silva <i>et al.</i>, "the results of the meta-analysis for RE [restoration effectiveness] showed no significant difference between the two groups compared (HEMA-free compared with HEMA-containing systems). Therefore, both HEMA-free and HEMA-containing adhesive systems had a good behaviour for RE in NCCL [non-carious cervical lesion] restorations within the reviewed studies. Thus, it can be stated that even monomers, or a blend of monomers, without HEMA, may interpenetrate, cure, and play their main initial role in the RE of the composite resin."¹²⁶ (p12)
Significance/direction	No difference for any outcome
Heterogeneity	Low to moderate; varied by outcome
Comments	GRADE was not used by the review authors. One-half of the trials scored unclear for risk of bias for one or more parameters. Less than 75% of trials were judged to have adequate random sequence generation. The quality of the systematic review was judged as critically low using AMSTAR 2 as the authors did not control for unclear risk of bias and did not discuss the effects of bias or heterogeneity on their analysis. The HRB graded the evidence in this review as low.

Schroeder *et al.* (2017)

Parameter	Extraction
First author and year of publication	Schroeder <i>et al.</i> (2017) ¹²⁷
Objectives	Compared composite restorations in non-carious cervical lesions in adults' permanent teeth bonded using self-etch adhesives with composite restorations bonded using etch-and-rinse adhesives for post-operative sensitivity, retention rates, and marginal discolouration.
Participants	Permanent dentition, non-carious cervical lesions, support materials Adult permanent teeth with non-carious cervical lesions requiring composite restorations (1,486 participants) More than one-half (23/42) of the primary studies did not report mean age. For the 19 studies that reported mean age, the authors reported great variation in the

Parameter	Extraction
	mean age range (35–61 years) of adult participants involved. Only one-half of the primary studies reported a gender breakdown, and the proportions of male participants ranged between 33% and 75%.
Setting/context	The study settings were not reported. The studies were completed in Germany, Japan, Korea, Liechtenstein, Switzerland, and the USA.
Description of interventions/phenomena of interest	Self-etch adhesives for bonding composite restorations of non-carious cervical lesions Schroeder <i>et al.</i> (2017) described the intervention as “placement of composite restorations with self-etch adhesives” ^{127 (p37)} and the comparator as “composite restorations placed with an etch-and-rinse adhesive.” ^{127 (p37)}
Databases and sources searched	A comprehensive search of seven databases (MEDLINE, Scopus, Web of Science, LILACS database, BBO, the Cochrane Library, and OpenSIGLE) was performed in May 2016 without date or language restrictions. The authors provide their search strategy in a table. In addition, the authors searched International Association for Dental Research Abstract database and grey literature via trial registries. Dissertations and theses were searched using the ProQuest Dissertations & Theses Global and CAPES databases. A protocol was completed and registered. It is unclear who screened abstracts, but full-text articles were screened by two reviewers. Two reviewers extracted relevant information. This study was partially supported by the Brazilian Council for Scientific and Technological Development.
Date range (years) of included studies	Fifty articles based on 42 randomised controlled trials, published between 2003 and 2015, were included in this review.
Number of primary studies included in the systematic review	Fifty articles based on 42 randomised controlled trials were included in this review, and follow-ups of the same studies were merged for analysis. The studies were published between 2003 and 2015. Forty of the 42 studies reported their sample size; the total sample size of these studies was 1,486 participants, the average sample size per primary study was 37, and the sample size range was 8–90. The sources of funding for primary studies were not reported.
Types of studies included	Randomised clinical trials were specified. The excluded trials are referenced and their reasons for exclusion are provided in the text.
Country of origin of included studies	The studies were completed in Germany, Japan, Korea, Liechtenstein, Switzerland, and the USA.
Appraisal instruments used	The Cochrane Collaboration’s risk of bias instrument was used to assess the risk of bias.
Appraisal rating	Based on the Cochrane Collaboration’s risk of bias instrument, 3 of the 42 trials were judged to be at high risk of bias and 11 were judged to be at unclear risk of bias. The remaining 28 trials were judged to be at low risk of bias, and only these were included in the meta-analysis. Thirty (71%) of the 42 trials were judged to have adequate random sequence generation and 32 (76%) were considered to have adequate blinding of outcome assessors. Publication bias was not discussed.
Method of analysis	The extracted data were analysed using RevMan 5.3. Data from all outcomes of the eligible studies were dichotomous. To summarise the risk of post-operative sensitivity after restoration, loss of retention, and marginal discolouration for each study, the authors calculated the relative risk with a 95% CI. Pairwise random-effects meta-analyses were completed. Heterogeneity was assessed using the Cochran Q test and the I ² Inconsistency Index. No subgroup analysis was performed. Additionally, whenever heterogeneity was detected, the authors performed sensitivity analysis to identify whether the heterogeneity was caused by any of the included studies.
Outcome assessed	Outcome: Post-operative sensitivity, retention rates, and marginal discolouration Time frame: No minimum follow-up period was established since one of the outcomes of interest was post-operative sensitivity after restoration placement. One study had baseline data only. For the remaining 41 studies, the last follow-up time point ranged from one year to eight years after the intervention. Eleven studies had follow-up periods of three years or longer.

Parameter	Extraction
	Outcome by primary studies: Post-operative sensitivity: Armstrong 2012; Bittencourt 2005; Blunck 2013; Daudt 2013; Dutra Correa 2013; Ermis 2013; Fron 2011; Kim 2009; Loguercio 2008; Loguercio 2015; Moosavi 2013; Olivera 2013; Paula 2015; Perdigao 2012; Ritter 2008; Sartori 2011; Turkun 2003; Van Dijken 2013; Van Landuyt 2014. Retention rates (at 1, 2, 3, and 5 years): Araujo 2013; Armstrong 2012; Bittencourt 2005; Blunck 2013; Burgess 2013; Burrrow 2017; Daudt 2013; Dutra Correa 2013; Ermis 2013; Fron 2011; Hafer 2015; Kim 2009; Lawson 2015; Loguercio 2008; Loguercio 2015; Moosavi 2013; Olivera 2013; Paula 2015; Perdigao 2012; Ritter 2008; Sartori 2011; Tuncer 2013; Turkun 2003; Van Dijken 2004; Van Dijken 2010; Van Dijken 2013; Van Landuyt 2014. Marginal discolouration (at 1, 2, 3, and 5 years): Araujo 2013; Armstrong 2012; Bittencourt 2005; Blunck 2013; Burgess 2013; Burrrow 2017; Daudt 2013; Dutra Correa 2013; Ermis 2013; Fron 2011; Hafer 2015; Kim 2009; Lawson 2015; Loguercio 2008; Loguercio 2015; Moosavi 2013; Olivera 2013; Paula 2015; Perdigao 2012; Ritter 2008; Sartori 2011; Tuncer 2013; Turkun 2003; Van Dijken 2004; Van Dijken 2010; Van Dijken 2013; Van Landuyt 2014.
Results/findings	The results of this pairwise random-effects meta-analysis suggest that there is evidence that using either self-etch adhesives or etch-and-rinse bonding strategy composite restorations in non-carious cervical lesions in adults' permanent teeth does not influence the risk of post-operative sensitivity (relative risk: 1.04; 95% CI: 0.81–1.34; I²: 0%; 10 trials; 169 participants; low-quality evidence), which, according to Schroeder <i>et al.</i>, “reinforces the fact that the adhesive strategy is not responsible for post-operative sensitivity”.^{127 (p49)} However, there is evidence that using etch-and-rinse adhesives to bond composite restorations in non-carious cervical lesions in adults' permanent teeth can result in a better reduction of marginal discolouration when compared with using self-etch adhesives at 18 months to two years (relative risk: 1.51; 95% CI: 1.21–1.90; I²: 12%; 22 trials; 169 participants; low-quality evidence) and at 4–5 years (relative risk: 1.81; 95% CI: 1.28–2.55; I²: 0%; 2 trials; 101 participants; low-quality evidence); of note, the findings at 1 and 3 years were not significant. In addition, when considering the loss of restoration, the moderate-quality evidence is inconclusive, as no significant differences between etch-and-rinse compared with self-etch adhesives were observed in any of the 1- to 5-year follow-up periods. However, the number of participants dwindled and the percentage heterogeneity increased from low to high. For example, at one year: relative risk: 1.07; 95% CI: 0.72–1.58; I²: 3%; 20 trials; 2,781 participants; and at 4–5 years: relative risk: 0.60; 95% CI: 0.27–1.32; I²: 55%; three trials; 518 participants. In conclusion, Schroeder <i>et al.</i> pointed out that “composite resin restorations placed with self-etch and etch-and-rinse adhesives produce restorations with a similar retention rate and post-operative sensitivity; however using etch-and-rinse adhesives can reduce marginal discolouration.”^{127 (p51)}
Significance/direction	Varied by outcome and follow-up time points.
Heterogeneity	Heterogeneity was generally low except for the meta-analysis of retention at the 4–5-year follow-up time point, and the meta-analysis of marginal discolouration at the 3-year follow-up time point, where heterogeneity was high in both cases.
Comments	GRADE was not used by the review authors. The numbers of participants was below 200 for some outcomes. Two-thirds of the trials scored high or unclear for risk of bias for one or more parameters. Just under 75% of the trials were judged to have adequate random sequence generation. The quality of the systematic review was judged as moderate. The HRB graded the evidence in this review as moderate.

Moraes Coelho Santos *et al.* (2014)

Parameter	Extraction
First author and year of publication	Moraes Coelho Santos <i>et al.</i> (2014) ¹²⁸

Parameter	Extraction
Objectives	Assessed the effect of different adhesive systems, surface treatments, and tooth preparation techniques on the retention of tooth-coloured restorative materials placed in non-carious cervical lesions.
Participants	Permanent dentition, non-carious cervical lesions, restoration support material Non-carious cervical lesions in permanent teeth in adults The authors included 27 randomised clinical studies published between 1991 and 2013. The studies included 1,249 adults (1,674 restorations of permanent teeth) aged 18–88 years with a mean age of 53 years. Gender was not reported. The follow-up periods ranged from 3 to 13 years.
Setting/context	The study countries or settings were not reported.
Description of interventions/phenomena of interest	Intervention: Different adhesive systems, surface treatments, and tooth preparation techniques A non-carious cervical lesion is characterised by a slow and gradual loss of mineralised dental tissue in the absence of dental caries. The result is a saucer- or wedge-shaped defect that appears along the cementum–enamel junction. Non-carious cervical lesions may require the placement of a restoration due to hypersensitivity, aesthetic concerns, prevention of food entrapment, the need for denture retention, or for halting the progression of the defect. The most common materials used to restore non-carious cervical lesions are resin composites, glass ionomer cements, resin-modified glass ionomers, and polyacid-modified resin composites. The presence of mineral casts in tubular dentine and the presence of a hypermineralised layer are considered to be potential barriers to primer diffusion and resin infiltration. In order to increase the bond strength of composite materials and overcome the obstacles that jeopardise effective resin infiltration on non-carious cervical lesions, some studies have suggested roughening the surface of the non-carious cervical lesion using a carbide or diamond bur and/or placing retentive grooves. Many studies have reported a high failure rate for the simplified adhesives (two-step etch-and-rinse or one-step self-etch adhesive system), and this has been attributed to the lack of a separated hydrophobic layer on the simplified versions. More recent studies, however, have observed good retention rates for one-step self-etch adhesives. A high retention rate has been reported for resin-modified glass ionomer restorative materials in non-carious cervical lesions. Comparator: Each other
Databases and sources searched	The Cochrane Central Register of Controlled Trials (CENTRAL), Embase via Ovid, LILACS, and MEDLINE (via Ovid) electronic databases were searched, with no language restrictions, from 1990 to 2013. The search strategy is presented in an appendix. The International Association for Dental Research Abstract database and grey literature databases were also searched. The reference lists of the included articles were screened for additional studies. The authors did not report preparing a protocol. Duplicate screening and extraction were completed. The authors reported no conflicts of interest. The source of funding for the review was not reported.
Date range (years) of included studies	The authors included 27 randomised clinical studies published between 1991 and 2013.
Number of primary studies included in the systematic review	The authors included 27 randomised clinical studies published between 1991 and 2013. The sources of funding for primary studies were not reported.
Types of studies included	Randomised clinical trials were specified in the eligibility criteria. The full-text studies and their associated reasons for exclusion were presented in a table.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess bias in the included trials.
Appraisal rating	Nine of the 27 trials were judged to be at high risk of bias and 18 had an unclear risk of bias based on the Cochrane Collaboration's risk of bias instrument. Seventeen out of 27 studies were judged to have adequate randomisation and 9 had adequate blinding of the outcome assessor. The authors' only mention of the risk of bias or quality assessment was that they completed one. Publication bias was not measured.

Parameter	Extraction
Method of analysis	First, adhesive systems were classified into five categories, as follows: three-step etch-and-rinse, two-step etch-and-rinse, two-step self-etch, one-step self-etch, and glass ionomer materials (including glass ionomer cement and resin-modified glass ionomer). All of the studies that compared similar adhesive systems (for example, a three-step etch-and-rinse compared with a two-step etch-and-rinse) were included in a meta-analysis. If a study had multiple study groups that all used the same category of adhesive system, the results of those study groups were combined into a single comparison group. Interventions were grouped by adhesive type and restoration type. The primary outcome (event) under consideration was the risk of loss of a non-carious cervical lesion restoration during the observation period of the clinical study using the restoration as the unit of observation. Meta-analysis was performed using Review Manager 5.1.5. The authors used fixed-effects pairwise meta-analysis, as per Cochrane guidance. The I^2 Inconsistency Index was used to determine heterogeneity across studies. The Mantel-Haenszel statistic was used to test the null hypothesis at the 0.05 level of significance. The risk ratio and the absolute risk difference were used to compare adhesive system performance.
Outcome assessed	Assessed effectiveness of tooth-coloured materials, adhesive systems, surface treatments, and preparation techniques for the restoration of non-carious cervical lesions at 3 years follow-up or longer. Outcome: Retention, which was measured as loss of tooth-coloured restorative materials. There was inadequate data to measure the effects of other outcomes on retention. Time frame: three years or longer follow-up period Outcome by primary studies: Two-step etch-and-rinse compared with three-step etch-and-rinse for retention of restoration: Aw 2005; van Dijken 2000; van Dijken 2013. Two-step self-etch compared with three-step etch-and-rinse for retention of restoration: Matis 2004; McCoy 1998; van Dijken 2007. One-step self-etch compared with three-step etch-and-rinse for retention of restoration: Ritter 2008; van Dijken and Pallesen 2008; van Dijken 2013; van Landuyt 2011. Three-step etch-and-rinse compared with glass ionomer for retention of restoration: Ozgunaltay and Onen 2002; van Dijken and Pallesen 2008; van Dijken 2000. Two-step etch-and-rinse compared with two-step self-etch for retention of restoration: Burrow and Tyas 2007; Kubo 2006; van Dijken 2010; van Dijken 2007. Two-step etch-and-rinse compared with glass ionomer for retention of restoration: Burrow and Tyas 2007; Matis 1996; van Dijken 2000.
Results/findings	Twelve of the 27 studies analysed the influence of co-variables on the success of the non-carious cervical lesion restorations. The most common co-variables reported in the studies included identification of wear facets, the degree of dentine sclerosis, and the size, shape, and location of the lesion. Eleven of the 27 studies reported that they used enamel bevelling when placing resin composites, but just one evaluated the influence of bevelling on retention. Ten studies reported dentine preparation by bur roughening, and three studies performed it only when sclerotic dentine was present. Ten studies mentioned dentine sclerosis, but just one study found a significantly lower retention rate for wide and sclerotic lesions. None of the selected studies evaluated the influence of additional retentive features on the success of the non-carious cervical lesion restorations. Meta-analysis was used to determine the relative risk of loss of tooth-coloured non-carious cervical lesion restorations between different categories of adhesive systems. The effect of tooth preparation could not be similarly analysed. The current best evidence indicates that glass ionomer cement has a significantly lower risk of loss of a non-carious cervical lesion restoration compared with either a three-step etch-and-rinse (risk ratio: 1.63; 95% CIs: 1.10–2.43; I^2: 0%; 369 participants; three trials) or a two-step etch-and-rinse adhesive system (risk ratio: 6.46; 95% CIs: 3.50–11.89; I^2: 0%; 206 participants; three trials).

Parameter	Extraction
	A three-step etch-and-rinse adhesive system has a significantly lower risk of loss of a non-carious cervical lesion restoration compared with a two-step etch-and-rinse adhesive system (risk ratio: 2.80; 95% CIs: 1.67–4.69; I²: 59%; 338 participants; three trials), although the meta-analysis had significant heterogeneity. No significant difference could be observed in the risk of loss of a tooth-coloured non-carious cervical lesion restoration between a three-step etch-and-rinse adhesive system and either a two-step self-etch (risk ratio: 1.02; 95% CIs: 0.82–1.28; I²: 0%; 550 participants; 3 trials) or a one-step self-etch adhesive system (risk ratio: 1.06; 95% CIs: 0.76–1.49; I²: 0%; 631 participants; four trials), indicating equal effect. A two-step self-etch adhesive system has a significantly lower risk of loss of a non-carious cervical lesion restoration compared with a two-step etch-and-rinse adhesive system (risk ratio: 1.52; 95% CIs: 1.20–1.92; I²: 0%; 383 participants; four trials). The authors' conclusions repeat the results above.
Significance/direction	Results listed by outcome
Heterogeneity	The authors reported that "In the meta-analysis comparing a three-step etch-and-rinse adhesive system to a two-step etch-and-rinse adhesive system, the three studies demonstrated some heterogeneity. The observation period for two of the studies was 3 years, and 5 years for the third study. The major difference between the studies, however, was that the study of Aw <i>et al.</i> beveled the enamel of the NCCL restoration before application of the adhesive system and insertion of the restorative material whereas the study of van Dijken did not." ^{128 (p1377)}
Comments	GRADE was not used by the review authors. All trials scored high or unclear for risk of bias for one or more parameters. Less than 75% of trials were judged to have adequate random sequence generation and blinding of outcome assessment. The quality of the systematic review was judged as critically low as they did not control for the high or unclear risk of bias in their analyses or discuss its implications. The HRB graded the evidence in this review as low.

Chee *et al.* (2012)

Parameter	Extraction
First author and year of publication	Chee <i>et al.</i> (2012) ¹²⁹
Objectives	Compared simplified adhesives (two-step self-etch and one-step self-etch) with conventional adhesives (three-step etch-and-rinse and two-step etch-and-rinse) for treatment of non-carious cervical lesions in the permanent teeth of adults.
Participants	Permanent dentition, non-carious cervical lesions, restoration support material Population: Adults (n= 1,032) with non-carious cervical lesions in their permanent teeth The mean age of participants across studies was 52.9 years (SD: 6.0), although this did not take into account four studies where median age or age ranges were not reported, and three studies where age was not reported. The mean age range, where reported, was 45–61.8 years. Gender was not reported.
Setting/context	Most included studies reported university dental hospitals as the research setting. The study countries of origin were not reported.
Description of interventions/phenomena of interest	According to Chee <i>et al.</i>, "the 3-step etch-and-rinse approach conventionally involves etching the tooth with 30–40% phosphoric acid, followed by the application of a primer and subsequently an adhesive resin...Two-step etch-and-rinse systems combine the primer and adhesive into one bottle but maintain a separate etching step to remove the smear layer and demineralise the surface layer of enamel and dentine. Self-etch systems penetrate through the smear layer and incorporate it into the hybrid layer to varying degrees dependent upon their acidity. They consist of either a self-etching primer accompanied by an adhesive resin applied as a subsequent step, or a self-etch adhesive which does not require a separate primer."^{129 (p444)} Comparator: Three-step etch-and-rinse and two-step etch-and-rinse

Parameter	Extraction
Databases and sources searched	Four electronic databases were searched up to August 2011: the Cochrane Oral Health Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and Embase. No language restrictions were applied. A search strategy was provided. In addition, studies were identified by hand-searching nine selected journals. Manufacturers were asked for unpublished trials. It is not clear whether a protocol was prepared before completing the review. It is not clear how many people screened the literature or extracted the data. The source of funding for the review was not reported and conflicts of interest were not declared.
Date range (years) of included studies	Twenty-six randomised controlled trials published between 1996 and 2011, involving 1,032 adults, were included.
Number of primary studies included in the systematic review	Twenty-six randomised controlled trials published between 1996 and 2011, involving 1,032 adults and comparing at least two adhesives in non-carious cervical lesions in permanent teeth, and with at least 18 months of follow-up, were included in this review. The funding sources of primary studies were not provided.
Types of studies included	The inclusion criteria required randomised controlled trials only. Reasons for exclusion during full-text screening were provided, but the list of excluded studies was not.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess the risk of bias in the primary trials.
Appraisal rating	Based on the Cochrane Collaboration's risk of bias instrument, 10 trials were judged to be at high risk of bias, and the risk of bias was unclear in the remaining 16 trials. Six of the 26 trials were judged to have adequate random sequence generation and 15 were considered to have adequate blinding of outcome assessors. Publication bias was not discussed.
Method of analysis	Following the data extraction and quality assessment process, trial authors were contacted in order to obtain further information on any unclear or missing data. Included studies for which the necessary data could not be extracted from the report or retrieved by the review authors were not included in the data synthesis. Trials were assessed for clinical heterogeneity. If they were similar (in terms of participants, interventions, and outcomes measured), formal assessment of heterogeneity was planned using the chi-square test and the I^2 Inconsistency Index. Subgroup analysis was to be carried out to examine the effect of follow-up period and risk of bias on the results. The planned meta-analysis was not possible due to clinical heterogeneity, high or unclear risk of bias, and missing data. A narrative analysis was reported.
Outcome assessed	Outcome: Restoration retention or loss, marginal adaptation, and marginal discolouration Time frame: At least 18 months follow-up Actual: Varied from 18 months to 8 years Outcome by primary studies: Restoration retention or loss: No studies found. Marginal discolouration of clinically acceptable restoration: Aw 2005; Brackett 2003; Brackett 2005; Kim 2009; Kubo 2006; Kubo 2009; Loguercio 2007; Loguercio 2010; Matis 2004; Merte 1998; Neo 1996; Onal and Pamir 2005; Ozgunaltay and Onen 2002; Peumans 2007; Reis and Loguercio 2009; Reis 2010; Ritter 2008; Ritter 2009; Santiago 2010; Turkun 2003; Van Dijken 2000; Van Dijken 2004; Van Dijken 2010; Van Landuyt 2011. Marginal integrity of clinically acceptable restoration: Aw 2005; Brackett 2003; Brackett 2005; Brackett 2010; Kim 2009; Kubo 2006; Kubo 2009; Loguercio 2007; Loguercio 2010; Matis 2004; Merte 1998; Neo 1996; Onal and Pamir 2005; Ozgunaltay and Onen 2002; Peumans 2007; Reis and Loguercio 2009; Reis 2010; Ritter 2008; Ritter 2009; Santiago 2010; Turkun 2003; Van Dijken 2000; Van Dijken 2004; Van Dijken 2010; Van Landuyt 2011.
Results/findings	The planned meta-analysis was not possible due to clinical heterogeneity, high or unclear risk of bias, and missing data. A narrative analysis was reported. Trials

Parameter	Extraction
	were assessed for clinical heterogeneity. Narrative comparisons were made between adhesive systems and between the four types of bonding strategy. The included studies demonstrated wide variation between adhesives of the same category, and the follow-up time points varied between 18 months and 8 years. The findings for marginal integrity were as follows: three-step etch-and-rinse ranged between 90% and 100% clinically acceptable; two-step etch-and-rinse ranged between 51% and 100%; two-step self-etch ranged between 76% and 100%; and one-step self-etch ranged between 67% and 100%. The findings for marginal discolouration were as follows: three-step etch-and-rinse ranged between 87% and 100% clinically acceptable; two-step etch-and-rinse ranged between 83% and 100%; two-step self-etch all scored 100%; and one-step self-etch ranged between 35% and 100%. The worst clinical performance reported in terms of marginal integrity was found for one-step etch-and-rinse with 51% of restorations considered clinically acceptable at 36 months. However, two other studies found 100% clinical acceptability for this adhesive at 18 and 36 months, respectively. One-step self-etch (iBond) had the poorest reported clinical performance in terms of marginal discolouration, with 35% of restorations clinically acceptable at an unidentified follow-up time point. Frequently, data from studies were either reported inadequately or were inappropriate for use in meta-analyses. Hence, this review was limited to the qualitative or narrative description of studies. According to Chee <i>et al.</i>, "there was insufficient evidence to make firm recommendations for the use of one adhesive system or bonding strategy over another. The proportion of information obtained from studies with an unclear or high risk of bias was high. The null hypothesis of no difference could not be supported or rejected with the data currently available...There is not enough evidence to support one adhesive or bonding strategy over another for treatment of non-carious cervical lesions."¹²⁹ (p450)
Significance/direction	The planned meta-analysis was not possible due to clinical heterogeneity, high or unclear risk of bias, and missing data. A narrative analysis was reported.
Heterogeneity	The planned meta-analysis was not possible due to clinical heterogeneity, high or unclear risk of bias, and missing data. A narrative analysis was reported.
Comments	GRADE was not used by the review authors. All trials scored high or unclear for risk of bias for one or more parameters. Less than 75% of trials were judged to have adequate random sequence generation and blinding of outcome assessment. Meta-analysis was not completed due to clinical heterogeneity. The quality of the systematic review was judged as moderate using AMSTAR 2. The HRB graded the evidence in this review as low.

Restoration processes or techniques

Rocha *et al.* (2018)

Parameter	Extraction
First author and year of publication	Rocha <i>et al.</i> (2018) ¹³¹
Objectives	Evaluated the influence of different dentine surface treatments on the retention rate of resin composite restorations in non-carious cervical lesions.
Participants	Permanent dentition, non-carious cervical lesions, restoration technique Resin composite restorations in non-carious cervical lesions in adults Seven randomised clinical trials published between 2010 and 2015, with 299 participants (and 947 restorations), were included in this review. More than one-half of the participants (n=176, 59%) were male, and the ages of the participants ranged from 20 to 80 years. The longest follow-ups were 18–96 months.
Setting/context	The study settings were not reported. The study countries were Brazil, Chile, Turkey, and the USA.

Parameter	Extraction
Description of interventions/phenomena of interest	Intervention: Tooth surface treatment may include surface irrigation with ethylenediaminetetraacetic acid (EDTA), adhesive application with a friction technique, or drying the dentine before applying the adhesive. Comparator: No surface treatment The included studies evaluated different surface treatments, such as using an adhesive system with a frictional technique, drying the dentine, and removing sclerotic dentine by using a bur and applying EDTA before primer use.
Databases and sources searched	Eight databases were searched up to December 2016: PubMed via MEDLINE LILACS, IBECs, Web of Science, BBO, Scopus, Scielo, and the Cochrane Library. The search strategy is presented in the paper. The authors prepared a protocol and published it on PROSPERO. There were language restrictions (English, Portuguese, and Spanish). The references cited in included papers were searched for additional studies. Duplicate screening was completed. It was not clear whether duplicate extraction was completed. The authors reported that they had no conflicts of interest. The source of funding for the review was not reported.
Date range (years) of included studies	Seven randomised clinical trials published between 2010 and 2015 were included in this review.
Number of primary studies included in the systematic review	Seven randomised clinical trials published between 2010 and 2015, with 299 participants (and 947 restorations), were included in this review. Data regarding retention rate, type of surface treatment, and the main characteristics of studies were analysed. The funding sources of primary studies were not provided.
Types of studies included	Only clinical trials evaluating dentine surface treatments in resin composite restorations in non-carious cervical lesions were included. The references excluded at full-text screening and their reasons for exclusion were presented. The sources of funding for primary studies were not presented.
Country of origin of included studies	The study countries were Brazil, Chile, Turkey, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	Two of the seven studies were judged to be at high risk of bias and five had a low risk of bias. All seven studies had adequate randomisation and five had adequate blinding for outcome assessment.
Method of analysis	Pairwise random-effects meta-analyses were completed for three outcomes following Cochrane Collaboration guidance. Subgroup analysis was completed by intervention. Outcome by primary studies: Retention following removal of sclerotic dentine by using a bur: Dalkilic 2012; vanDijken 2010. Retention following application of an adhesive system with a frictional technique: Loguercio 2011; Zander Grande 2014. Retention following application of an adhesive system to dried dentine: Perdigao 2014; Zander Grande 2011.
Outcome assessed	Retention of resin composite restoration (measured by partial or complete loss) The longest follow-ups were 18–96 months (not predetermined). Retention of resin composite restoration (measured by partial or complete loss): van Dijken 2010; Loguercio 2011; Dalkilic 2012; Luque-Martinez 2015; Zander-Grande2014; Zander-Grande 2011; Perdigao 2014.
Results/findings	The subgroup analyses were presented, as the single analysis had considerable statistical heterogeneity whereas the subgroup analyses by intervention had no statistical heterogeneity. Retention following removal of sclerotic dentine by using a bur: risk ratio: –0.15; 95% CI: –0.24 to –0.05; I²: 0%; 246 restorations; 2 studies; low-quality evidence of reduced risk of restoration loss following removing sclerotic dentine by using a bur Retention following application of an adhesive system with a frictional technique: relative risk: –0.11; 95% CI: –0.19 to –0.02; I²: 0%; 227 restorations; 3 studies; low-quality evidence of reduced risk of restoration loss following application of an adhesive system with a frictional technique Retention following application of an adhesive system to dried dentine: risk ratio: –0.01; 95% CI: –0.06 to 0.03; I²: 0%; 258 restorations; 3 studies; low-quality evidence of similar risk of restoration loss following application of an adhesive system to dried dentine

Parameter	Extraction
	The analysis considering the mechanical removal of dentine surface with a bur and the application of an adhesive system in a frictional mode showed that these treatments improved retention rates of the resin composite restorations in non-carious cervical lesions ($p < 0.05$). The authors concluded that "There is evidence in the literature suggesting that the mechanical removal of dentine surface with a bur and the application of an adhesive system in a frictional mode could improve the retention rates of resin composite restorations in non-carious cervical lesions."^{131 (p9)}
Significance/direction	Results listed by outcome
Heterogeneity	No statistical heterogeneity was detected in subgroup analyses.
Comments	GRADE was not used by the review authors. Only 20% of trials scored high for risk of bias for one or more parameters. Less than 75% of trials were judged to have adequate blinding of outcome assessment. The quality of the systematic review was judged as critically low using AMSTAR 2 as they did not control for the high or unclear risk of bias in their analyses or discuss its implications. The HRB graded the evidence in this review as low.

Szesz *et al.* (2016)

Parameter	Extraction
First author and year of publication	Szesz <i>et al.</i> (2016) ¹³²
Objectives	Compared selective etching of enamel margins with no etching to improve the retention rates and marginal discolouration of cervical composite restorations in non-carious cervical lesions in permanent teeth of adults.
Participants	Permanent dentition, non-carious cervical lesions, restoration technique Population: Adults (n= 242) with non-carious cervical lesions in their permanent teeth The number of patients included in these trials ranged from 8 to 39. The mean age of all participants included in the clinical trials was 48.8 years, ranging from 18 to 78 years. The proportion of males ranged from 27% to 61%. Gender was not reported in four studies.
Setting/context	Only 2 of the 10 included trials reported their setting, and both were based in a university setting. The study countries were Germany, Japan, Liechtenstein, and the USA.
Description of interventions/phenomena of interest	The authors do not provide a detailed description of the intervention aside from pointing out that "selective etching of enamel margins with phosphoric acid has been recommended prior to the application of self-etch adhesives."^{132 (p2)} Comparator: No etching of enamel margins
Databases and sources searched	The authors searched seven sources (MEDLINE via PubMed, Scopus, Web of Science, LILACS, BBO, the Cochrane Library, and OpenSIGLE) up to 15 April 2016 without restrictions. The PubMed and Cochrane Library search strategies are provided in a table. In addition, the authors searched International Association for Dental Research Abstract database and grey literature via trial registries. Dissertations and theses were searched using the ProQuest Dissertations & Theses Global and CAPES databases. A protocol was completed and registered. Two reviewers screened the literature and three extracted the data. It is not clear whether at least two authors screened the literature and extracted the data in duplicate or if they divided the work between them. This study was partially funded by the Brazilian Council for Scientific and Technological Development. Conflicts of interest were not declared.
Date range (years) of included studies	Ten randomised controlled trials published between 2005 and 2014, with 242 adult participants, were included in this review.
Number of primary studies included in the systematic review	Ten randomised controlled trials published between 2005 and 2014, with 242 adult participants, were included in this review. The sources of funding for primary studies were not presented.
Types of studies included	The authors specified randomised controlled trials in their inclusion criteria.

Parameter	Extraction
	Studies excluded at full-text screening were referenced and reasons for exclusion reported.
Country of origin of included studies	The study countries were Germany, Japan, Liechtenstein, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess the risk of bias in the primary studies.
Appraisal rating	Based on the Cochrane Collaboration's risk of bias instrument, three trials were judged to be at high (unclear) risk of bias and seven trials were judged to be at low risk of bias. Seven of the 10 trials were judged to have adequate random sequence generation and nine were considered to have adequate blinding of outcome assessors. Only studies with low risk of bias are included in the meta-analysis. The authors reported that publication bias was addressed through a comprehensive search.
Method of analysis	Dichotomised data were collected and meta-analyses for paired data were performed to obtain a pooled estimate of the overall odds ratios with a 95% CI. Due to the matched nature of the data (split-mouth design), the authors imputed an external correlation of 0.5 for groups from the same study (as this information was not available in any of the studies). Only studies classified as having a low risk of bias in the key domains were used in the meta-analysis. The random-effects pairwise models were employed. Heterogeneity was assessed using the Cochran Q test and the I² Inconsistency Index. In the presence of substantial heterogeneity ($p < 0.1$; I²: >75%), sensitivity analysis was conducted to determine whether excluding one or more studies would reduce the heterogeneity or not. Sensitivity analyses using lower (0.1) and higher (0.9) external correlations were performed to check the impact of such imputation in all meta-analyses. The impact of excluding studies at high risk of bias was also assessed through a sensitivity analysis. All analyses were conducted using the software Comprehensive Meta-Analysis. No subgroup analyses were performed.
Outcome assessed	Outcome: Marginal adaptation, discolouration, and retention of composite restorations in non-carious cervical lesions in the adult population Time frame: 1–5 years (not predetermined) Outcome by primary studies: Loss of retention: Fron 2011; Oliveira 2013; Ozel 2010; Pena 2014; Perdigao 2014; Van Meerbeek 2015. Marginal discolouration: Fron 2011; Oliveira 2013; Ozel 2010; Pena 2014; Perdigao 2005; Perdigao 2014; Van Meerbeek 2015. Marginal adaptation: Fron 2011; Oliveira 2013; Ozel 2010; Pena 2014; Perdigao 2005; Perdigao 2014; Van Meerbeek 2015.
Results/findings	The random-effects pairwise meta-analysis was robust and based on trials with a low risk of bias. Four different meta-analyses for each outcome (loss of retention, marginal discolouration, and marginal adaptation) were performed based on the study follow-ups (1 year; 18 months to 2 years; 3 years; and 4–5 years). At the 4–5 years follow-up, only studies conducted over the course of 5 years were included in the meta-analysis because the studies with follow-ups at 4 years were classified as being at high risk of bias. Loss of retention (not significant) 1 year (odds ratio: 3.09; 95% CI: 0.55–17.27; I²: 0%; 2 trials) 18 months to 2 years (odds ratio: 0.57; 95% CI: 0.22–1.50; I²: 0%; 4 trials) 3 years (odds ratio: 0.23; 95% CI: 0.08–0.67; I²: 0%; 3 trials) 5 years (odds ratio: 1.03; 95% CI: 0.38–2.76; I²: 0.22%; 2 trials) Marginal discolouration (not significant at 1 year, but significant thereafter) 1 year (odds ratio: 0.83; 95% CI: 0.14–4.89; I²: 66.78%; 4 trials) 18 months to 2 years (odds ratio: 0.50; 95% CI: 0.26–0.95; I²: 45.71%; 7 trials) 3 years (odds ratio: 0.21; 95% CI: 0.09–0.51; I²: 57.25%; 3 trials) 5 years (odds ratio: 0.25; 95% CI: 0.09–0.71; I²: 75.36%; 2 trials) Marginal adaptation (not significant at 1 year, but significant thereafter) 1 year (odds ratio: 0.94; 95% CI: 0.56–1.58; I²: 0%; 4 trials) 18 months to 2 years (odds ratio: 0.49; 95% CI: 0.30–0.80; I²: 15.19%; 6 trials) 3 years (odds ratio: 0.41; 95% CI: 0.20–0.83; I²: 65.11%; 3 trials) 5 years (odds ratio: 0.19; 95% CI: 0.09–0.35; I²: 40.69%; 2 trials)

Parameter	Extraction
	The meta-analyses undertaken in this review revealed that, except for at 1-year follow-up, there was a significantly lower marginal discolouration and better marginal adaptation during all follow-up periods when selective enamel etching was performed. Significantly reduced loss of restorations at the three-year follow-up was also observed when the selective enamel etching technique was used. Szesz <i>et al.</i> conclude that “the selective enamel etching prior to application of self-etch adhesive systems in non-carious cervical lesions can produce composite restorations with better esthetics (lower marginal discolouration rates and better marginal integrity) and higher longevity (higher retention rates).” ^{132 (p10)} The authors also reported that “high heterogeneity was detected in some meta-analyses (three in the marginal discolouration and one for the marginal adaptation), however, the authors could not identify the source of such heterogeneity, which may be related to the subjectivity of the outcomes evaluated.” ^{132 (p8)}
Significance/direction	Varied by outcome and follow-up time point; see above
Heterogeneity	Heterogeneity was low for the retention outcome. Heterogeneity was moderate to high for the marginal discolouration outcome. Heterogeneity was low for the marginal adaptation outcome up to and including the two-year follow-up time point, but increased thereafter.
Comments	GRADE was not used by the review authors. Only trials with a low risk of bias were included in meta-analyses. The sample size for each outcome were not provided but were less than 200. There was high statistical heterogeneity for marginal discolouration at three years. The quality of the systematic review was judged as moderate using AMSTAR 2. The HRB graded the evidence in this review as moderate.

Schroeder *et al.* (2015)

Parameter	Extraction
First author and year of publication	Schroeder <i>et al.</i> (2015) ¹³³
Objectives	Compared enamel bevelling with no enamel bevelling to improve the retention of composite restorations in non-carious cervical lesions lesions in the permanent teeth of adult patients.
Participants	Permanent dentition, non-carious cervical lesions, restoration technique Population: Adults with non-carious cervical lesions requiring composite restorations The age range of the 164 participants included in the clinical trials was similar in the three trials that reported age (22–59 years). Only one of the four trials reported gender; 55% of participants were male.
Setting/context	All trials took place in a university setting. The study countries were Germany, Liechtenstein, and the USA.
Description of interventions/phenomena of interest	According to Schroeder <i>et al.</i> , “considering the enamel substrate, the placement of an enamel bevel may be a good option, taking into consideration that laboratory studies have shown that this procedure can reduce marginal microleakage, reduce the risk of fracture in the marginal enamel, result in better adhesion and yield to improved aesthetics.” ^{133 (p778)} Comparator: No enamel bevelling
Databases and sources searched	Seven data sources (MEDLINE, Scopus, Web of Science, LILACS, BBO, the Cochrane Library, and OpenSIGLE) were searched up to June 2014 without restrictions. A search strategy for PubMed and the Cochrane Library is provided in a table. In addition, the authors searched and grey literature via trial registries. Dissertations and theses were searched using the ProQuest Dissertations & Theses Global and CAPES databases. A protocol was completed and registered. Two researchers screened the full-text articles. It is not clear who screened the abstracts or if they were screened in duplicate. It is not clear if data extraction was done in duplicate. This study was partially funded by the Brazilian Council for Scientific and Technological Development.

Parameter	Extraction
	Conflicts of interests were not declared.
Date range (years) of included studies	Four randomised controlled trials published between 2003 and 2013, with 164 adult participants, were included in this review.
Number of primary studies included in the systematic review	Four randomised controlled trials published between 2003 and 2013, with 164 adult participants, were included in this review. There is no statement on the funding of primary studies.
Types of studies included	Randomised clinical trials were specified in the inclusion criteria. The excluded full-text studies were referenced and reasons for exclusion were provided.
Country of origin of included studies	The study countries were Germany, Liechtenstein, and the USA.
Appraisal instruments used	The Cochrane Collaboration's risk of bias instrument was used to assess the quality of the primary trials.
Appraisal rating	Based on the Cochrane Collaboration's risk of bias instrument, two trials were judged to have a high risk of bias, one had an unclear risk of bias, and one trial had a low risk of bias. Two of the four trials were judged to have adequate random sequence generation and three were considered to have adequate blinding of outcome assessors. Publication bias was not discussed.
Method of analysis	The extracted data were analysed using RevMan 5. Data from eligible studies were either dichotomous (retention rates) or ordinal (marginal discolouration). Marginal discolouration (mostly modified United States Public Health Service (USPHS) criteria [Alpha, Bravo, Charlie, and Delta]) was dichotomised into "no", corresponding to Alpha scores, and "yes", corresponding to Bravo, Charlie, and Delta scores. To summarise the retention rate and marginal discolouration for each study, the authors calculated the risk difference with a 95% CI. Random-effects pairwise models were employed. Heterogeneity was assessed using Cochran's Q test and the I ² Inconsistency Index. No subgroup analysis was performed.
Outcome assessed	Outcome: Retention of composite restorations and marginal discolouration in non-carious cervical lesions in the permanent teeth of adults Time frame: At least 1-year follow-up(predetermined). The two studies included in the meta-analysis had a short-term follow-up of 12 months and 18 months. Outcome by primary studies: Retention rates: Costa 2013; Perdigao 2005. Marginal discolouration: Costa 2013; Perdigao 2005.
Results/findings	The pairwise random-effects meta-analyses in this review suggest that the evidence for enamel bevelling prior to restoration of non-carious cervical lesions requiring resin composite is inconclusive, as there was no difference between bevelled and non-bevelled restorations at the short-term follow-up of 12–18 months. The overall risk difference was 0.0 (95% CI: –0.04 to 0.04; I ² : 0%; 148 restorations; two trials) for the retention rate ($p=0.91$), and 0.05 (95% CI: –0.02 to 0.13; I ² : 0%; 144 restorations; two trials) for marginal discolouration ($p=0.17$). However, this finding is based on only two trials with noted limitations. According to Schroeder <i>et al.</i> , "the present study did not indicate any superiority of the restorations where enamel bevelling was performed, and the extrapolation of these conclusions to the overall practice should be done with caution." ¹³³ (p786) This conclusion was based on one randomised controlled trial with a low risk of bias and one trial with a high risk of bias, both with small sample sizes.
Significance/direction	No difference
Heterogeneity	Heterogeneity was not an issue.
Comments	GRADE was not used by the review authors. The numbers of participants were less than 200 for each outcome. Most trials scored high or unclear for risk of bias for one or more parameters. Less than 75% of trials were judged to have adequate random sequence generation. The quality of the systematic review was judged as moderate using AMSTAR 2. The HRB graded the evidence in this review as moderate.

Qin *et al.* (2014)

Parameter	Extraction
First author and year of publication	Qin <i>et al.</i> (2014)¹³⁴
Objectives	Compared the clinical effectiveness (retention, marginal defects and marginal discolouration) of self-etching adhesives, with or without previous enamel bevelling and selective phosphoric acid etching, in restorations of non-carious cervical lesions in adults permanent teeth.
Participants	Permanent dentition, non-carious cervical lesions, restoration technique There was no explicit reporting on participant data. However, the authors highlighted the following points when outlining their inclusion criteria: 1. Patients were at least 18 years of age, with an acceptable oral hygiene level. 2. Participants presented with non-carious cervical lesions, to be restored on vital teeth without mobility. 3. All non-carious cervical lesions had cervical margins on the dentine and incisal margins on the enamel of their permanent teeth.
Setting/context	The study countries or clinical settings were not reported.
Description of interventions/phenomena of interest	Intervention: Self-etching adhesives with selective enamel etching Comparator: Self-etching adhesives without selective enamel etching Commenting on the interventions, the authors stated that “self-etching [SE] adhesives present various advantages over total-adhesive procedures: they are less technique sensitive and less time-consuming, and they are expected to induce less post-operative sensitivity. However, unlike bonding to dentin, the strength and longevity of adhesion to enamel using SE [self-etching] adhesives have been controversial issues. The etching pattern of enamel using SE adhesives appears to be less retentive than that produced by phosphoric acid. As a result, selective etching of enamel with phosphoric acid prior to the application of dentin adhesives has been proposed to improve the durability of the enamel bond.” ¹³⁴ (p30)
Databases and sources searched	Four databases were searched (MEDLINE via the PubMed database, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, and the Wiley Online Library) for articles published up to 20 August 2013. Searches were limited to articles written in the English language. The authors did not report conducting any additional searches. The authors did not report preparing a protocol. Extraction and screening were completed in duplicate. No funding sources were reported. The authors declared that there were no conflicts of interest that could influence their work.
Date range (years) of included studies	The included trials were published in 1993, 2005 (two studies), 2006, 2007 (two studies), 2010, and 2011.
Number of primary studies included in the systematic review	Eight randomised controlled trials, published in 1993, 2005 (two studies), 2006, 2007 (two studies), 2010, and 2011, were included. The sources of funding of primary studies were not reported.
Types of studies included	Randomised controlled clinical trials only were eligible for inclusion. A list of excluded studies was not reported. However, the reasons for exclusion were provided.
Country of origin of included studies	The study countries were not reported.
Appraisal instruments used	The Cochrane Collaboration’s risk of bias tool was employed to assess the risk of bias in the included studies.
Appraisal rating	Seven of the eight included studies had an unclear risk of bias and one had a high risk of bias. All eight studies had an unclear risk of bias for randomisation. Seven of the eight included studies had a low risk of bias for outcome assessment, and one study had an unclear risk of bias for outcome assessment. Commenting on the risk of bias and how it affected analysis and quality of evidence, the authors stated that “Regarding clinical investigations, in accordance with the Cochrane Collaboration’s tool for assessing the risk of bias, all eight studies were described as randomized, but none of them were double-blinded. However, blinding the operator to the intervention used was not possible. Furthermore, the outcome evaluators were double-blinded to the adhesive

Parameter	Extraction
	protocol used in any given restorative treatment. Two articles were judged to have a high risk of attrition bias because their follow-up loss rates were greater than 20%.”¹³⁴ (p306) Publication bias was not discussed.
Method of analysis	Commenting on the method of analysis used, the authors stated that “Dichotomized data were collected, and a meta-analysis was performed using the Mantel–Haenszel method to obtain a pooled estimate of the overall risk ratios with 95% confidence intervals. Between-study heterogeneity was assessed by processing the Q statistic. In the presence of substantial heterogeneity ($p < 0.1$, $I^2 > 50\%$), a random-effects model was applied to evaluate the data, and a sensitivity analysis was conducted to determine whether excluding one or more studies would reduce the heterogeneity or not. To explore for statistical heterogeneity, the sources of any possible variables, in terms of differences in clinical conditions or in methodological or assessment methods, were considered.”¹³⁴ (p306)
Outcome assessed	Restoration retention, prevalence of marginal defects, and marginal discolouration were evaluated. Clinical effectiveness: Kubo 2006; Peumans 2005; Peumans 2007; Fron 2011; Abdalla and Garcia-Godoy 2007; Van Meerbeek 2005; Peumans 2010; Van Meerbeek 1993.
Results/findings	Commenting on the findings, the authors stated that “The outcomes of the identified studies were divided into three analysis units based on the types of clinical outcome parameters, in terms of restoration retention, the prevalence of marginal defects, and marginal discoloration. Further subgroup analysis for 2- and 5-year follow-up was performed within each group. For restoration retention, the included studies were heterogeneous (chi-squared test =262.70, degrees of freedom =3, $p < 0.00001$, $I^2 = 99\%$) at two-year follow-up. Thus, a random-effects model was created for data estimation. In the forest plots, the black diamonds overlapped with the equivalence lines, and the overall RR value showed that $p = 0.21$, indicating that the differences between the selective etching and non-selective etching groups were not statistically significant. In addition, when each study was deleted in turn from the meta-analysis, we identified one article with contrasting results. This study was excluded, and the remaining articles were found to be homogeneous (chi-squared test =0.75, df [degrees of freedom] =2, $p = 0.60$, $I^2 = 0\%$). Then, a fixed-effects model was used, and a similar conclusion was obtained for the overall effect, with $p = 0.44$. Although one heterogeneous study was excluded, it did not unduly influence the overall estimate. For the estimation of marginal defects and marginal discoloration, homogeneity existed among the included studies. Thus, a fixed-effects model was applied to evaluate the overall RR value. When the available data from two articles at 5-year follow-up were also summarized, the prevalence of marginal defects in the non-selective etching group was significantly greater than that in the selective etching group ($p = 0.0001$). The measurement selections for clinical outcomes and the analysis procedures were consistent with previous descriptions. Finally, the prevalence of marginal discoloration in the non-selective etching group was significantly greater than that in the selective etching group ($p = 0.008$).”¹³⁴ (p306)
Significance/direction	Commenting on the significance/direction of the results, the authors stated “In conclusion, based on the results of this analysis, fewer defects at the restoration margins were recorded following the selective enamel etching approach. The restoration retention and marginal discoloration outcomes based on previous etching of the enamel had no significant differences compared with the non-selective etching group. These conclusions were based on data from observation durations of up to 5 years.”¹³⁴ (p311)
Heterogeneity	Commenting on heterogeneity, the authors stated that: “Between-study heterogeneity was assessed by processing the Q statistic. In the presence of substantial heterogeneity ($p < 0.1$, $I^2 > 50\%$), a random-effects model was applied to evaluate the data, and a sensitivity analysis was conducted to determine whether excluding one or more studies would reduce the heterogeneity or not. To explore for statistical heterogeneity, the sources of any possible variables, in terms of differences in clinical conditions or in methodological or assessment methods, were considered.”¹³⁴ (p306).

Parameter	Extraction
Comments	GRADE was not used by the review authors.

Appendix K: High-level summaries of included systematic reviews

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Primary dentition			
Non-cavitated caries			
Non-invasive treatment			
Ancira-González <i>et al.</i> (2018)	Compared the effectiveness of fluoride varnishes, gels, casein phosphopeptide-amorphous calcium phosphate, and other remineralisation agents with each other in the management of white spot lesions in children's primary teeth.	There was low-quality evidence that fluoride varnishes were superior to placebo or no intervention as a remineralisation agent. In addition, there was low-quality evidence that casein phosphopeptide-amorphous calcium phosphate combined with fluoride toothpaste had the same remineralising effect as fluoride toothpaste alone. Furthermore, there was low-quality evidence that fluoride varnish had the same effect as pit-and-fissure resin sealants, Nd:YAG laser, and chlorhexidine. Finally, there was low-quality evidence that fluoride varnish alone was inferior to fluoride varnish plus chlorhexidine or Nd:YAG laser.	Low
Microinvasive treatment			
Lam <i>et al.</i> (2020)	Evaluated the effectiveness of different types of pit-and-fissure sealants, as compared with no treatment measures among children and adolescents, to arrest of pit-and-fissure occlusal caries.	There was low-quality evidence that resin-based sealants plus application of 5% sodium fluoride varnish had the same arresting effect as fluoride varnish alone.	Low
Cavitated caries			
Non-invasive treatment			
Tolba <i>et al.</i> (2019)	Evaluated the effectiveness (in arresting caries) of the application of 12% silver diamine fluoride compared with 38% silver diamine fluoride in cavitated dentine caries in children's primary teeth.	The findings indicated moderate-quality evidence from two trials that the number or proportion of caries arrested was lower in the 12% silver diamine fluoride group compared with the 38% silver diamine fluoride group at 24 and 30 months follow-up periods, and these differences were statistically significant. The black discolouration of the carious dentine after silver diamine fluoride treatment was the most notable side effect.	Moderate

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Trieu <i>et al.</i> (2019)	Evaluated dentine caries arrest capabilities of silver diamine fluoride compared with those of sodium fluoride in the carious teeth of children aged 12 years and under.	The findings indicated moderate-quality evidence from five trials that silver diamine fluoride, when compared to sodium fluoride, was a more effective fluoride containing reagent for dentine caries arrest in children at 18 months and at 30 months follow-up periods.	Moderate
Direct restoration material			
Dias <i>et al.</i> (2018)	Compared failure and clinical performance of glass ionomer cement with composite resin in Class II restorations in primary teeth.	The findings indicated moderate-quality evidence that glass ionomer cement and composite resin were similar on failure and three aspects of clinical performance (marginal discolouration, marginal adaptation, and anatomical form) in Class II restorations in primary teeth. In addition, there was moderate-quality evidence that glass ionomer cements were significantly better than composite resins at preventing the occurrence of secondary carious lesions in primary teeth.	Moderate
Weber Pires <i>et al.</i> (2018)	Evaluated the clinical performance of different conventional restorative materials placed in posterior primary teeth.	The authors found low-quality evidence that the relative risk of failure was significantly higher for glass ionomer cement when compared with compomer, resin-modified glass ionomer cement, amalgam, and composite resin. The materials with the highest probability of failure were glass ionomer cement (0.99), followed by amalgam, with a much lower probability (0.008); compomer (0.004); resin-modified glass ionomer cement (0.0009); and composite resin (0.0008).	Low
Raggio <i>et al.</i> (2016)	Compared glass ionomer cements with other restorative materials (amalgam, resin composite, or polyacid-modified resin composite) to prevent adjacent (secondary) carious lesions in the margins of occlusal and occlusoproximal restorations in primary teeth.	There was moderate-quality evidence that secondary caries prevention in the margins of occlusal restorations was equal in both groups. In addition, there was moderate-quality evidence that caries prevention in the margins of occlusoproximal restorations, when examined on their own, was better in the glass ionomer cements group.	Moderate

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Santos <i>et al.</i> (2016)	Compared glass ionomer cements, composite resins, and compomers, known as adhesive restorations, in order to determine which is superior in terms of restoration survival in the primary (molar) teeth of children.	The review authors identified low-quality evidence that the median survival time of silver-reinforced glass ionomer cement was less than that of glass ionomer cement and resin-modified glass ionomer cement, and two studies found that glass ionomer cement had a lower median survival time than both resin-modified glass ionomer cement and compomer. There was low-quality evidence that composite resin, compomer, and resin-modified glass ionomer cement did not differ significantly regarding the number of restorations that survived up to 24 months. The authors overall conclusion was that low-quality evidence that the adhesive-based materials were equal in performance to each other for restoring primary teeth in children, excluding silver-reinforced glass ionomer cement, which was inferior and not recommended for use in primary teeth.	Low
Indirect restoration material			
Badar <i>et al.</i> (2019)	Assessed the outcomes (retention and absence of pulpal symptoms) of placement of a crown using the Hall technique on primary carious molars in children and compared it with conventional dental restorations or stainless steel crowns.	The meta-analysis using three trials comparing the Hall technique to restore primary carious molars with conventional methods found that the Hall technique was more successful than the comparative treatment modalities, but this evidence was very low quality.	Very low
Innes <i>et al.</i> (2015)	Compared the effectiveness and safety of all types of preformed crowns (using the Hall technique) with conventional filling materials for restoring primary molar teeth in children.	The main findings suggested low-quality evidence that crowns were more likely to reduce the risk of major failure, pain, and infection in the long term compared with using fillings. In addition, there was low-quality evidence that crowns fitted using the Hall technique were more likely to reduce discomfort at the time of treatment compared with using other restorations. Finally, there was low-quality evidence that the incidence of gingival bleeding was not different across interventions.	Low
Comparison direct and indirect restoration material			

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Chisini <i>et al.</i> (2018)	Investigated the longevity of posterior restorations in primary teeth and the reasons for failure.	The restoration success rates for each type of material, based on low-quality evidence, were: amalgam: 82% at 3 years; composite resin: 79% at 4 years; glass ionomer cement: 89% at 4 years; compomers: 91% at 3 years; resin-modified glass ionomer cement: 94% at 4 years; modified resin glass ionomer cement: 57% at 3 years; and steel crowns: 96% at 3 years. Based on low-quality evidence, the overall annual failure rate ranges were as follows: composite resin: 2–13% over 4 years; amalgam: 1–28% over 3 years; glass ionomer cement: 0.8–17% over 4 years; compomers: 2–15% over 3 years; resin-modified glass ionomer cement: 1–17% over 4 years; steel crowns: 1–19% over 3 years; and modified resin glass ionomer cement: 10–29% over 3 years. The main finding in this review suggested that there was little consensus regarding the best material for posterior restorations in primary teeth, due to a wide range of time points for data collection and different year end points for individual studies.	Low
Aiem <i>et al.</i> (2017)	Evaluated the clinical effectiveness (success or failure of restorations based on five criteria) of all types of aesthetic preformed crowns for restoring primary teeth, compared with conventional filling materials or other types of crowns.	The authors could not conclude on the direction of the findings on the clinical effectiveness of interventions (aesthetic preformed crowns) and comparators (conventional filling materials or other types of crowns) for restoring primary teeth due to clinical and methodological heterogeneity between the primary studies. The authors reported that due to the risk of bias, changing the recommendations for posterior teeth is not advised. Regarding restoration failures of the commercialised preformed paediatric crowns, zircon crowns appeared to be the best choice to restore incisors for a follow-up of only 6 months. Zircon crowns should be evaluated over periods of at least 1 year in primary anterior and posterior teeth. Overall the evidence was low quality.	Low
Restoration support material			

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Schwendicke <i>et al.</i> (2015)	Evaluated the risk of restoration failure (proportion of teeth requiring retreatment) following restoration due to dentine caries in primary molar teeth, comparing restorations with cavity lining to restorations without cavity lining. The follow-up was 1 or more years	There was low-quality evidence that there was no difference in failure of adhesive restorations with and without the placement of a liner in primary teeth.	Low
Restoration technique			
Aïem <i>et al.</i> (2020)	Compared the efficacy (measured by pulp exposure and absence of pulpal or periodontal complications or restorative failures) of three caries removal techniques – complete caries removal, selective caries removal, and stepwise caries removal – for deep carious lesions in vital (absence of irreversible pulpitis or pulpal necrosis) primary teeth.	During clinical protocol, the pulp exposure risk was lower for selective caries removal compared with complete caries removal based on moderate-quality evidence. At the end of the treatment follow-up, pulpo-periodontal complications (clinical and/or radiographic failures) were similar in the selective caries removal and complete caries removal groups based on moderate-quality evidence. The intention-to-treat meta-analysis based on United States Public Health Service (USPHS) criteria for testing composite restorations demonstrated significantly higher restorative success for complete caries removal when compared with selective caries removal (low-quality evidence). The intention-to-treat meta-analysis based on the Frencken criteria found no difference between selective caries removal compared with complete caries removal (low-quality evidence). Two trials compared pulp exposure at the time of intervention in stepwise caries removal with complete caries removal. The odds of pulp exposure in the stepwise caries removal group were significantly lower compared with the complete caries removal group (low-quality evidence). The pulpo-periodontal complications at follow-up (clinical and/or radiographic failures) did not differ significantly between the stepwise caries removal and complete caries removal groups (low-quality evidence). Two trials compared pulp exposure in selective caries removal with stepwise caries removal. There was no difference in the risk of pulp exposure in the selective caries removal and stepwise caries removal groups (low-quality evidence). In addition, the risk of pulpal or periodontal complications (clinical and radiographic failures) in the selective caries removal and stepwise caries removal groups were not different.	Moderate or low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Pedrotti <i>et al.</i> (2019)	Evaluated whether selective carious tissue removal of soft dentine from deep cavitated lesions in primary teeth increases the risk of experiencing restoration failure compared with complete carious tissue removal.	There was moderate-quality evidence that restorations placed following selective carious tissue removal of soft dentine from deep cavitated lesions in primary teeth increased the risk of experiencing restoration failure compared with complete carious tissue removal.	Moderate
Aparecida Silva Martins <i>et al.</i> (2018)	Evaluated the clinical evidence of partial caries removal in the primary dentition, regardless of liner and restorer materials, measuring the longevity of the restorative treatment and clinical and radiographic success.	There was low-quality evidence that partial caries removal had high clinical and radiographic success rates and the longevity of the associated restorations was satisfactory. The longevity of restorations in primary molars preceded by partial caries removal compared with restorations preceded by total caries removal was not statistically significantly different.	Low
Deng <i>et al.</i> (2018)	Compared the efficiency (operation time, bacterial count, and restoration survival) and efficacy (acceptability and preference) of chemomechanical caries removal (Papacarie) in primary molar caries in children and adolescents with the conventional drilling method (controls).	There was low-quality evidence that microbiota in caries dentine was significantly reduced using the Papacarie treatment compared with the conventional drilling method. There was very low-quality evidence that pain scores evaluated before and after caries removal were reduced in both the Papacarie and conventional drilling method. There was low-quality evidence of longer time required for the Papacarie treatment compared with conventional drilling method. The children reported less pain and anxiety were experienced with the Papacarie method compared with the conventional drilling method and this was graded as very low-quality evidence. There were no significant differences in retention of restoration and incidence of secondary caries at follow-up with the Papacarie method compared with the conventional drilling method based on very low-quality evidence.	Low or very low
Restoration material and technique			

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Tedesco <i>et al.</i> (2018)	Determined the best treatment for dentine carious lesion arrestment and the success rate of different treatments of the dentine carious lesions of primary teeth. The purpose of the review was to bridge a gap in the evidence by considering whether lesions of different depths and the number of surfaces involved affect treatment outcomes.	There was very low-quality evidence that resin composite restoration had a higher success rate than resin sealant. However, when caries arrest was considered as the primary outcome, no difference was observed between the restorative treatments. For the studies that considered only the occlusal surface without information about the depth of progression, the success rates were similar in all mixed-treatment comparisons based on very low-quality evidence. The treatment with the highest probability of success was using conventional restorative treatment with composite resin or conventional restorative treatment with compomer. After that, the ranking was: (2) atraumatic restorative treatment, (3) conventional restorative treatment with high-viscous glass ionomer cement, (4) conventional restorative treatment with amalgam, and (5) conventional restorative treatment with resin composite. The primary outcome of the comparison dentine carious lesions on occlusoproximal surfaces, without information about the depth of progression, was a comparison of success rates. The Hall technique, compared with non-restorative caries treatment, had a statistically significantly higher success rate based on very low-quality evidence. No other mixed-treatment comparisons were statistically significantly better than their comparators in this analysis. The rank probability showed that the best result for occlusoproximal cavities was the Hall technique for applying a stainless-steel crown based on very low-quality evidence. After that, the final ranking was: (2) non-restorative caries treatment, (3) conventional restorative treatment using compomer, (4) conventional restorative treatment using high-viscosity glass ionomer cement, (5) conventional restorative treatment using resin composite, (6) atraumatic restorative treatment, (7) conventional restorative treatment using amalgam, and (8) ultraconservative treatment. Three studies evaluated caries arrest on occlusal and smooth surfaces of primary teeth, and three treatment comparisons were statistically significantly better than their comparators based on very low-quality evidence: 38% silver diamine fluoride (two applications per year) compared with silver diamine fluoride (one application per year), low-viscosity glass ionomer cement compared with silver diamine fluoride (two applications per year), and interim restorative treatment compared with silver diamine fluoride (one application of either 30% or 38%). The rank probability showed that the best performance for this type of dentine carious lesion was two	Very low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
		annual applications of 38% silver diamine fluoride per year, and this was significantly better than other silver diamine fluoride treatment doses and frequencies (1). After that, the final ranking was low-viscosity glass ionomer cement (2), one annual application of silver diamine fluoride (3), three applications per year of silver diamine fluoride (4), three applications per year of sodium fluoride (5), and interim restorative treatment (6).	

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Permanent dentition			
Non-cavitated caries			
Non-invasive treatment			
Oliveira <i>et al.</i> (2018)	Assessed the effect of professionally applied silver diamine fluoride compared with no, placebo, or other active intervention in preventing and arresting caries in exposed root surfaces of adults.	There was moderate-quality evidence that silver diamine fluoride applications had a better preventive effect in comparison with placebo and were as effective as either chlorhexidine or sodium fluoride varnish in preventing new root carious lesions in adults' permanent teeth. There was low-quality evidence that silver diamine fluoride applications provided a higher caries arrest effect than placebo treatments in root carious lesions in adults permanent teeth.	Moderate or low
Tao <i>et al.</i> (2018)	Evaluated the efficacy of combining casein phosphopeptide-amorphous calcium phosphate and fluorides compared to fluorides monotherapy on patients with early carious lesions in permanent teeth.	Based on low-quality evidence and analysis of laser fluorescence results, the random-effects pairwise meta-analysis showed that the combination of casein phosphopeptide-amorphous calcium phosphate and fluoride treatment was better at decreasing the size of early occlusal carious lesions than fluoride monotherapy. However, there was low-quality evidence that fluoride combined with casein phosphopeptide-amorphous calcium phosphate achieved the same results as fluoride monotherapy for early carious lesions on smooth surfaces.	Low
Hendre <i>et al.</i> (2017)	Evaluated the effectiveness (preventing, arresting, or remineralising) of silver diamine fluoride in the management of root caries in older adults.	There was moderate-quality evidence that silver diamine fluoride effectively arrested root caries in older adults.	Moderate
Wierichs and Meyer-Lueckel (2015)	Evaluated results of clinical studies investigating chemical agents to reduce initiation of root carious lesions or inactivate existing ones (arrest root carious lesions).	There was low-quality evidence that dentifrice containing 5,000 ppm fluoride and professionally applied chlorhexidine or silver diamine fluoride varnish inactivated existing and/or reduced the initiation of root carious lesions.	Low
Non-cavitated caries and cavitated			
Comparison of non-invasive, minimally invasive, and minimally invasive treatment			

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Schwendicke <i>et al.</i> (2015a)	Compared non-invasive, microinvasive, and minimally invasive treatments with each other, with no active treatment or a placebo treatment, or with standard oral home care for treating pit-and-fissure lesions in permanent posterior teeth in adults.	The analysis based on very-low-quality evidence showed that microinvasive and minimally invasive treatments were potentially effective in avoiding invasive retreatments following earlier treatment of pit-and-fissure lesions in permanent posterior teeth. In addition, there was some very low-quality evidence that non-invasive treatments might also be effective in avoiding invasive retreatments following earlier treatment of pit-and-fissure lesions in permanent posterior teeth. Based on very low-quality evidence, the need for any retreatment was significantly higher in microinvasively sealed lesions than in those that received non-invasive or minimally invasive treatments.	Very low
Cavitated caries			
Direct restoration material			
Medeiros Maran <i>et al.</i> (2020)	Evaluated survival or clinical performance (two primary outcomes: colour match and surface texture and 6 secondary outcomes) of nanofilled/nanohybrid restorations compared with hybrid composite restorations in patients with direct posterior restorations.	The meta-analyses revealed no significant differences between nanofilled and hybrid composite for colour match (moderate evidence) or surface texture (moderate evidence). The meta-analyses revealed no significant differences between nanohybrid and hybrid for colour match (moderate or low evidence), surface texture (moderate evidence or low) The low-quality evidence was at the 72-month follow-up period and the moderate-quality evidence was at earlier follow-ups.	Moderate or low
Raiane Mamede Veloso <i>et al.</i> (2019)	Evaluated whether the clinical performance (failure measured by eight criteria) of bulk-fill resin composites is comparable to that of conventional composites in restored permanent posterior (molars and premolars) teeth.	There was moderate-quality evidence that the clinical performance of bulk-fill and conventional resin composites in direct restorations of posterior teeth was similar, within a follow-up period of 12 to 72 months.	Moderate

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
CADTH (2018)	Evaluated the comparative efficacy of direct dental restorations made of composite resin compared with amalgam for the treatment of dental caries in posterior permanent teeth Evaluated the comparative safety of dental restorations made of composite resin compared with amalgam in children and adults.	CADTH reported that it found one additional study, and this study (Kemaloglu <i>et al.</i>, 2016) reported zero events of restoration failure and secondary caries in either treatment arm at 3 years, or 100% survival in both arms. CADTH reported that due to methodological and clinical heterogeneity, incorporation of the data from this 2016 split-mouth randomised controlled trial with the 2014 Cochrane systematic review data ¹¹ was not possible. Therefore, there is no additional evidence for findings on efficacy and the Rasines Alcaraz <i>et al.</i> review remain valid. (Rasines Alcaraz 2014) With respect to safety, there was low -quality evidence that statistically significant differences in urinary mercury excretion between patients receiving amalgam and those receiving composite resin at follow-up time points of up to 5–6 years were reported in two large trials. One of two large trials reported that the prevalence of micoralbuminuria was found to be statistically significantly higher in the amalgam-treated group at 3- and 5-year follow-ups bit this finding was based on low-quality evidence. There were some statistically significant findings on physical development, neuropsychological function, and psychosocial outcomes in one of the two large trials, but not consistently across both, and these findings were based on low-quality evidence. There was low-quality evidence that there were no observed statistically significant differences between treatment groups in evaluations of neurological symptoms, immune function, and urinary porphyrin excretion. There was low -quality evidence that post-operative sensitivity did not differ between amalgam and composite resin restorations at follow-ups between 2 and 52 weeks, although a statistically significant difference was reported at 36 months follow-up in two studies, favouring the composite resin group.	No additional evidence for efficacy and low-quality evidence for safety See Rasines Alcaraz <i>et al.</i> (2014)

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
de Castro Kruly <i>et al.</i> 2018	Compared the clinical behaviour (marginal integrity/adaptation, marginal discolouration, recurrent caries, retention of composite restorations, and post-operative sensitivity) of restorations performed with low polymerisation shrinkage resin composite (bulk fill) resins in comparison with methacrylates-based (conventional) resin composite (in humans with Class I or II restorations in the permanent dentition).	There was low-quality evidence that restorations conducted with low polymerisation shrinkage composites, such as silorane, ormocer, and bulk-fill type, demonstrated a clinical performance similar to direct conventional resin composites restorations.	Low
Monsarrat <i>et al.</i> (2017)	Evaluated the clinical performance (such as survival rates or quality of restorations) of the first generation of ormocer-based fillings against those of conventional composite resin restorations and glass ionomer restorations; and explored the influence of different clinical factors and the impact of the quality of studies on published results.	There was low-quality evidence that the clinical performance of the first generation of ormocer-based fillings was similar to conventional composite restorations. No factor emerged to explain global failures although an increase of age, an increase of the proportion of females, and a decrease of the number of restorations per patient were associated with fewer marginal adaptation failures for ormocers in Class I/II cavities.	Low
Hayes <i>et al.</i> (2016)	Compared the clinical performance of restorative materials for the treatment of root caries in the permanent teeth of adult patients.	There was insufficient and low-quality evidence to recommend any specific material for routine use in the restoration of root carious lesions; all had high failure rates. There is a need to evaluate restorative materials in a more generalised population, as many of the studies, included in Hayes <i>et al.</i> 's systematic review, were confined to post-radiation, xerostomic patients.	Low
Moraschini <i>et al.</i> (2015)	Compared the failure rates of amalgam and composite resin in occlusal and occlusoproximal restorations in posterior permanent teeth.	There was very low-quality evidence that resin composite had higher failure rates and higher secondary caries rates than amalgam. In addition, there was very low-quality evidence that restoration fracture was the same for both amalgam and resin composite.	Very low
Rasines Alcaraz <i>et al.</i> (2014)	Compared the restoration failure of direct composite resin fillings with amalgam fillings for permanent posterior teeth.	There was low-quality evidence that resin composite had higher failure rates and higher secondary caries rates than amalgam. In addition, there was low-quality evidence that restoration fracture was the same for both amalgam and resin composite.	Low
Sharif <i>et al.</i> (2014a)	Compared the effects of replacing resin composite with repairing it (with resin composite) in the management of defective resin composite dental restorations in permanent molar and premolar teeth.	No trials met the inclusion criteria.	No evidence

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Sharif <i>et al.</i> (2014b)	Compared the effects (retention, survival) of replacing (with amalgam) compared with repair (with amalgam) in the management of defective amalgam dental restorations in permanent molar and premolar teeth.	No trials met the inclusion criteria.	No evidence
Indirect restoration material			
Bustamante-Hernández <i>et al.</i> (2020)	Evaluated the clinical behaviour (survival) and the possible complications of posterior region onlays in adults' permanent posterior teeth by the type of material used for the onlay restoration 1 year or more after restoration intervention.	Based on very low-quality evidence, the estimated percentage survival for onlays was 94.2% (95% CI: 92.3–96.1). The survival, based on very low-quality evidence, varied by type of onlay material: hybrids (99%), feldspathic ceramic reinforced with lithium disilicate (98%); conventional feldspathic ceramic reinforced with leucite (93%), and resin composites (90%).	Very low
Becker Rodrigues <i>et al.</i> (2019)	Evaluated the difference in longevity of tooth-supported ceramic prostheses designed by a computer-aided design/computer-aided manufacturing system compared with a conventional manufacturing (milling) system.	The meta-analysis results suggested that the longevity of tooth-supported ceramic prostheses made by the computer-aided design/computer-aided manufacturing system was lower than that of crowns made by the conventional milling technique, but the findings were based on low-quality evidence.	Low
Sampaio <i>et al.</i> (2019)	Evaluated the survival rate of indirect composite and ceramic inlays, onlays, and overlays following different manufacturing methods in children and adults teeth.	There was low-quality evidence that the pooled estimated survival rates at the follow-up times of 5 and 10 years were 97% and 89%, respectively. After 5 years, survival rate for pressable glass ceramics was 95% (low-quality evidence). For the stratified group, survival rates at the follow-up times of 5 and 10 years were 88% and 93%, respectively (low-quality evidence).	Low
Vagropoulou <i>et al.</i> (2018)	Investigated whether different types of indirect restorations (inlay, onlay, both inlay and onlay, and crown) used for single permanent anterior, premolar, or molar teeth had different biological or technical complications, or different survival rates.	Based on the narrative and descriptive analysis of the included studies, there was low-quality evidence that the mean survival rate of inlays was 90.9% at 5 years, while for onlays and crowns it was 93.5% and 95.4%, respectively. For the fourth study group, consisting of both inlays and onlays, the survival rate was found to be 99.4%. This means that there was low-quality evidence that indirect restorations demonstrated survival rates over 90%, which was judged to be very high by the review authors. There was no evidence for comparisons between direct and indirect restoration materials.	Low or no evidence

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Morimoto <i>et al.</i> (2016)	Evaluated the survival rate of resin and ceramic inlays, onlays, and overlays at 5 years and 10 years in permanent teeth (deduced from reported age range and intervention), and identified the types of complications associated with the main negative clinical outcomes.	The main findings from this review suggested that there was very low-quality evidence that ceramic inlays, onlays, and overlays produced acceptable high restoration survival rates of over 90% regardless of the ceramic material, study design, or study setting. The pooled estimated survival rate was 95% at 5 years follow-up (95% for glass ceramic and 92% for feldspathic porcelain) and the survival rate decreased to 91% after 10 years follow-up (93% for glass ceramic and 91% for feldspathic porcelain). According to 13 included studies reporting 106 failures out of 4,800 restorations, the fracture/chipping rate of teeth and/or inlay, onlay, and overlay restorations was 4%. The incidence of endodontic problems was reported as 3%.	Very low
Grivas <i>et al.</i> (2014)	Evaluated clinical performance (longevity, colour match, and post-operative sensitivity) at 12 months or longer of indirect composite inlays compared with direct composite restorations as well as with ceramic and gold inlays in adults with permanent vital teeth restorations.	There was low-quality evidence that the survival rate of composite inlays ranged from 100% after 3 years to 51% after 10 years and was not significantly different to ceramic or gold materials. There was conflicting evidence on colour match over time and there was no difference for post-operative sensitivity at 1-month follow-up. Five studies that compared indirect composite inlays with direct composite fillings had follow-up periods ranging from 3.5 to 11 years, and the survival rates for indirect composite inlays varied from 100% after 3.5 years to 87.3% after 11 years based on low-quality evidence. The authors report that the studies provide insufficient evidence to identify whether there is a difference in longevity between indirect composite inlays and direct composite fillings. Most of the studies concurred that differences between composite inlays and direct composite fillings with respect to aesthetic quality (colour match and marginal discolouration) and post-operative sensitivity were insignificant. Based on low-quality evidence, composite inlays had similar longevity, colour match, and post-operative sensitivity as ceramic inlays, gold inlays, and direct composite fillings.	Low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Fron Chabouis <i>et al.</i> (2013)	Compared performance of composite inlays and onlays with ceramic inlays or onlays for restoring posterior permanent teeth in adults.	There was low-quality evidence that the overall 3-year success rate was 94.2% for composite inlays and 97.1% for ceramic inlays. The reported clinical acceptable scores showed considerable heterogeneity between trials and could not be combined. Visual examination of results of the two trials for each measure indicated no difference in outcome.	Low
Comparison direct and indirect restoration material			
Vetromilla <i>et al.</i> (2020)	Evaluated restorative treatment types and materials for large tooth cavity restorations in permanent posterior teeth in adults with respect to tooth or restoration longevity, and ranked them from best to worst.	Based on the results of randomised controlled trials (highest source of primary evidence), the best annual failure rate for direct restorations was for amalgam (at 1.9%), and for indirect restorations it was metal ceramic (at 0.3%); however, these findings were based on very low-quality evidence. Based on very low-quality evidence, the highest annual failure rate for any method was for zirconia-based ceramic (at 5.1%). Indirect composite resin (3.5%) had a marginally higher failure rate than direct composite resin (2.7%). The failure rate for gold was 0.75%. For randomised controlled trials, direct methods appear to perform better than indirect methods, but this comparison was based on very low-quality evidence.	Very low
Angeletaki <i>et al.</i> (2016)	Evaluated the clinical parameters of longevity (secondary caries, post-operative sensitivity, marginal discolouration, and colour match) for direct and indirect composite restorations in posterior (molar or premolar) teeth at follow-ups of 3 years or over.	. There was low-quality evidence that there were similar survival rates, failure rates, post-operative sensitivity, and colour match of composite restorations in premolars for direct and indirect techniques based on low-quality evidence. In addition, there was low-quality evidence that direct restorations were statistically significantly less likely to experience marginal discolouration.	Low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Antonelli da Veiga <i>et al.</i> (2016)	Compared the differences in clinical performance and longevity of direct and indirect resin composite restorations in Class I and Class II cavities in permanent molar and premolar teeth, with at least 2 years of follow-up.	There was moderate-quality evidence of no difference in terms of clinical longevity between direct and indirect resin composite restorations. This conclusion remains valid even when the type of restored tooth was considered. The most common general failures reported were fracture of restoration, anatomical form, tooth fracture, and marginal adaptation for direct resin composite; marginal discolouration, marginal adaptation, fractures, and debonding of restoration for indirect resin composite; and secondary caries for direct inlay/onlay.	Moderate
Grivas <i>et al.</i> (2014)	Evaluated clinical performance (longevity, colour match, and post-operative sensitivity) at 12 months or longer of indirect composite inlays compared with direct composite restorations as well as with ceramic and gold inlays in adults with permanent vital teeth	Grivas <i>et al.</i> ¹¹⁰ , mentioned above, evaluated clinical performance (longevity, colour match, and post-operative sensitivity) at 12 months or longer of indirect composite inlays compared with direct composite restorations as well as with ceramic and gold inlays in adults with permanent vital teeth restorations. Five studies that compared indirect composite inlays with direct composite fillings had follow-up periods ranging from 3.5 to 11 years, and the survival rates for indirect composite inlays varied from 100% after 3.5 years to 87.3% after 11 years based on low-quality evidence. The authors report that the studies provide insufficient evidence to identify whether there is a difference in longevity between indirect composite inlays and direct composite fillings. Most of the studies concurred that differences between composite inlays and direct composite fillings with respect to aesthetic quality (colour match and marginal discolouration) and post-operative sensitivity were insignificant.	Low
Restoration support material			
Schenkel <i>et al.</i> (2019)	Compared the effects of using dental cavity liners with those of not using liners in the placement of Class I and Class II resin-based composite posterior restorations in permanent teeth in children and adults.	There was low-quality evidence that the use of liners did not add any benefit to the routine resin-based restorations in permanent posterior teeth in adults in the studies examined. There was no evidence for children aged under 15 years by 2019.	Low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Reis <i>et al.</i> (2015)	Compared the effects of posterior resin composite restorations that were bonded using self-etching with posterior resin composite restorations that were bonded using etch-and-rinse adhesives on the risk and intensity of post-operative sensitivity in permanent dentition (posterior restorations) of adult patients.	There was high-quality evidence that the type of adhesive strategy (etch-and-rinse or self-etch) for posterior resin composite restoration did not seem to influence the risk and intensity of post-operative sensitivity in posterior resin composite restorations.	High
Restoration technique			
Arcanjo Frota Barros <i>et al.</i> (2020)	Evaluated the risk or benefit (pulp exposure, dentine deposition, microbiological examination, quality of the restoration, and success of maintaining pulpal health) of selective caries removal for the treatment of dentinal caries in permanent teeth compared with non-selective (complete) or stepwise caries removal.	There was very low-quality evidence that selective removal resulted in greater success of maintaining pulp vitality compared with both non-selective (complete) and stepwise excavation.	Very low
Göstemeyer <i>et al.</i> (2019)	Evaluated the efficacy of atraumatic restorative treatment compared with conventional restorative treatment for restoring root carious lesions in older adults.	There was moderate-quality evidence that that there was no significant difference in the failure rates of atraumatic restorative technique compared with conventional restorative treatment.	Moderate
Solon de Mello <i>et al.</i> (2019)	Evaluated whether the survival rates of indirect restorations cemented with self-adhesive resin cement in permanent teeth are influenced by the presence or absence of selective enamel etching.	There was moderate-quality evidence of no statistically significant difference in clinical longevity of indirect restorations cemented with self-adhesive resin cement in permanent teeth, with or without selective enamel etching, for the time periods 36 months, 48 months, and 78 months.	Moderate
Deng <i>et al.</i> (2016)	Evaluated the effects of laser treatment of direct pulp capping in patients who required this treatment for their deep carious lesions on the success of restorations.	There was low-quality evidence that the success rate of the laser treatment (89.9%) during pulp capping was statistically significantly higher than that of control groups (67.2%) who had pulpectomy or pulpotomy.	Low
Mixed dentition			
Non-cavitated caries			
Non-invasive treatment			
Khijmatgar <i>et al.</i> (2020)	Evaluated the remineralisation potential of NovaMin compared with placebo or no intervention in humans with evidence of demineralisation (white spot lesions and/or cavitation) on teeth.	There was low-quality evidence based on one trial that there was no statistically significant difference between the NovaMin and the control group (Crest toothpaste) in remineralising capacity.	Low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Ma <i>et al.</i> (2019)	Evaluated the efficacy of casein phosphopeptide-amorphous calcium phosphate compared with no intervention or placebo for the remineralisation of white spot lesions.	There was moderate-quality evidence that there was no significant difference between using tooth mousse with casein phosphopeptide-amorphous calcium phosphate or fluoride toothpaste with active tooth mousse and the comparators (standard fluoride toothpaste or standard fluoride toothpaste with placebo tooth mousse).	Moderate
Chong <i>et al.</i> (2018)	Compared the retention, effectiveness, and safety of different types of slow-release fluoride devices on preventing, arresting, or reversing the progression of carious lesions on all surface types of primary (deciduous) and permanent teeth at 12 months following treatment.	There was low-quality evidence based on one trial to determine whether slow-release fluoride devices (glass beads) help reduce dental decay. The incidence of decayed, missing, and filled permanent teeth or primary teeth or their surfaces at 2 years was statistically significantly better in treated than in non-treated populations at 2 years. Caries increment was significantly lower at 24 months in the intervention group. The primary study authors stated that no irritations or other harms were reported.	Low
Paula <i>et al.</i> (2017)	Compared different remineralisation agents (fluoride products, casein phosphopeptide-amorphous calcium phosphate, and ICON plc. resin) and techniques with each other for the treatment of white spot lesions in both permanent and primary teeth. There was no age cut-off, and both permanent and primary teeth were included.	Most of the 13 studies included in this narrative analysis reported that therapy with remineralising agents reduces white spot lesions (in terms of their size or visual appearance) and this finding is based on moderate-quality evidence. Most of the six studies evaluating remineralising agents reported that such agents reduced white spot lesions (in terms of their size or visual appearance), although only two demonstrated a statistically significant improvement, and this finding was based on moderate-quality evidence. Three studies of the effects of casein phosphopeptide-amorphous calcium phosphate on remineralising white spot lesions demonstrated improvements, and the improvements were significant in two of these studies, and this finding is based on moderate-quality evidence. One study on ICON resin, based on low-quality evidence, indicated significant regression of white spot lesions, either in size or in their clinical visual appearance. There was moderate-quality evidence that when fluoride was compared with casein phosphopeptide-amorphous calcium phosphate, both products demonstrated improvements but neither product was significantly better than the other.	Moderate or low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Gao <i>et al.</i> (2016)	Compared professionally applied fluoride therapy with other active treatments, with placebo, or with no intervention in remineralising and arresting dental caries in primary and permanent teeth in children.	There was low-quality evidence to suggest that fluoride varnish was an effective remineralising agent for targeting early caries in primary teeth and very low-quality evidence that silver diamine fluoride was more effective than controls for remineralising and arresting the progression of active caries in both primary and permanent teeth in children and adolescents.	Low or very low
Lenzi <i>et al.</i> (2016)	Evaluated the effectiveness of professional topical fluoride application (gels or varnishes) on the reversal of incipient enamel carious lesions in primary or permanent dentition in children.	There was very low-quality evidence that fluoride varnish was an effective treatment for the reversal of incipient carious lesions in primary and permanent dentition. Additionally, there was very low-quality or no evidence as to the effectiveness of fluoride gel as a treatment for the reversal of incipient carious lesions in primary and permanent dentition.	Very low
Li <i>et al.</i> (2014)	Compared the use of casein phosphopeptide-amorphous calcium phosphate in any modality with the use of fluoride toothpastes or mouthwashes, placebos, topical creams, and chewing gum in order to assess their long-term (>3 months) remineralising effect on early carious lesions.	There was low-quality evidence that casein phosphopeptide-amorphous calcium phosphate was better than no intervention; however, it offered no advantage as a supplement to fluoride.	Low
Microinvasive treatment			
Chen <i>et al.</i> (2021)	Evaluated the caries-arresting effectiveness of infiltration and sealing for proximal non-cavitated carious lesions and beyond, including different dentition types and caries risk levels in humans.	For both primary and permanent dentition, there was moderate-quality evidence that both infiltration and sealing were more effective at reducing lesion progression than both placebo and non-invasive treatments. There was low-quality evidence that the overall positive effects of infiltration and sealing were significantly better in those classified as having high or low caries risk compared with the effects of control interventions.	Moderate or low
Elrashid <i>et al.</i> (2019)	Evaluated the efficacy (clinical performance) of resin infiltration (compared with placebo or control material) on non-cavitated proximal carious lesions in primary and permanent teeth in humans.	The risk of carious lesion progression with resin infiltration was significantly lower in primary teeth and in permanent teeth compared with that of control or placebo based on moderate-quality evidence.	Moderate
Faghihian <i>et al.</i> (2019)	Evaluated the efficacy (clinical performance) of the resin infiltration technique in arresting initial caries progression in both primary and permanent teeth compared with control groups such as placebo, fluoride therapy, and oral health instruction.	There was moderate-quality evidence that resin infiltration significantly reduced the risk of caries progression in primary and permanent teeth compared with the control groups.	Moderate

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Chatzimarkou <i>et al.</i> (2018)	The objective of this review was to provide a comprehensive synthesis of resin infiltration effects, in vivo, on early proximal carious lesions in primary and permanent teeth.	There was moderate-quality evidence that resin infiltration combined with non-invasive oral hygiene measures resulted in significantly (86%) lower odds for early proximal carious lesion progression when compared with non-invasive methods (control) at 18–24-month follow-up period, and there were similar findings with respect to resin infiltration for 36-month follow-up.	Moderate
Krois <i>et al.</i> (2018)	Evaluated microinvasive treatments compared with each other, non-invasive treatments, placebo or no treatment to arrest early non-cavitated proximal carious lesions in primary and permanent teeth of children, adolescents, and young adults.	There was moderate-quality evidence that sealing and/or infiltration was effective for arresting early (non-cavitated) proximal lesions compared with non-invasive treatment and no intervention. However, there was moderate-quality evidence that sealing was not superior or inferior to infiltration for arresting proximal caries.	Moderate
Liang <i>et al.</i> (2018)	Compared the effectiveness of microinvasive interventions with non-invasive measures (e.g. fluoride), a placebo, or no treatment in arresting non-cavitated proximal carious lesions and analysed their effectiveness in acting on carious lesions of different depths.	There was moderate-quality evidence in favour of resin infiltration and sealant for arresting the progression of non-cavitated proximal caries. However, there is insufficient and low-quality evidence to judge the effectiveness of glass ionomer cements or resin sealant at different caries depths.	Moderate or low
Dorri <i>et al.</i> (2015)	Compared microinvasive treatments with non-invasive measures, invasive measures, no intervention, or a placebo for managing proximal carious lesions in primary and permanent dentition in children and adults.	There was moderate-quality evidence for microinvasive treatment (resin infiltration or sealing) for managing proximal carious lesions in primary and permanent dentition over non-invasive professional treatment (e.g. fluoride varnish) or advice (e.g. to floss).	Moderate
Ammari <i>et al.</i> (2014)	Evaluated effectiveness (caries arrest and control) of sealing and/or infiltration compared with placebo or other materials or techniques to treat non-cavitated proximal lesions in primary and permanent teeth.	There was moderate evidence favouring infiltration over placebo to arrest caries in non-cavitated proximal lesions in primary and permanent teeth.	Moderate
Non-cavitated caries and cavitated			
Non-invasive treatment			

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Marcilio Santos <i>et al.</i> (2020)	Evaluated the effectiveness (antimicrobial effect and lesion progression or regression) and safety (adverse events) of ozone therapy compared with no treatment, sham, or any other antibacterial intervention (including pharmacological and non-pharmacological treatments) for treating cavitated and non-cavitated dental caries in participants of any age.	There was low-quality evidence that ozone therapy was more effective for reducing lesion progression and severity compared with no ozone (compressed air) or no treatment. Additionally, there was low-quality evidence that ozone therapy was less effective than chlorhexidine digluconate in the short and medium term, but not in the long term, for reducing the total bacterial count. Analysis of this outcome based on bacteria species indicates that chlorhexidine was effective in reducing both <i>Streptococcus mutans</i> and <i>Lactobacillus</i>, but the effect was stronger for <i>Lactobacillus</i> based on low-quality evidence. At the time of temporary restoration removal, based on low-quality evidence, ozone therapy demonstrated a significantly higher reduction in total bacterial counts compared with sealant, and no difference after final excavation and permanent restoration. There was a significant decrease in lesion progression favouring the sealant group over the ozone group at long-term follow-up; however, there was no difference at short- and medium-term follow-ups. The results showed no significant difference in lesion progression between ozone added to sealant and sealant alone in the short- and long term based on low-quality evidence. One included study compared lesion progression following ozone therapy with fluoride varnish and showed no significant reduction in lesion progression between groups at long-term follow-up. Another study assessed the effects of ozone therapy compared with fluoride gel and presented improvement in favour of ozone therapy for lesion progression at long-term follow-up. The meta-analysis of two trials found no statistically significant difference between ozone and fluoride with respect to the severity of carious lesions following treatment. All these findings are based on very low-quality evidence. No adverse events were reported for any of the five comparisons	Low or very low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Chibinski <i>et al.</i> (2017)	Evaluated the efficacy of silver diamine fluoride in controlling (arresting) caries progression in children's primary or permanent teeth when compared with active treatments (different doses of silver diamine fluoride, fluoride varnish, sealant, atraumatic restorative technique) or placebos (water or saline).	There was moderate-quality evidence that the arrestment of caries in primary teeth at 12 months promoted by silver diamine fluoride (at both 38% and 30% concentrations, and nanosilver fluoride) was significantly higher than that by other active material or placebo. There was not enough evidence to assess the effectiveness in permanent molars.	Moderate or no evidence
Gao <i>et al.</i> (2016b)	Evaluated the effectiveness of silver diamine fluoride in arresting dental caries in primary or permanent teeth in children, using prospective clinical studies.	Two studies investigating the caries-arresting effect of 38% silver diamine fluoride in permanent teeth did not find that it was better than its comparators based on very low-quality evidence. The pooled analysis of eight studies found that the caries-arresting rate of 38% silver diamine fluoride treatment in children's primary teeth was 81%. Apart from staining the arrested carious lesions black, the 19 clinical trials did not report any significant complication arising from silver diamine fluoride use among children based on very low-quality evidence.	Very low
Microinvasive and invasive treatment			
de Amorim <i>et al.</i> (2018)	The authors evaluated the survival rate of atraumatic restorative treatment glass ionomer restorations and atraumatic restorative treatment sealants in primary and permanent posterior teeth.	There was very low-quality evidence that the survival rates of single-surface and multiple-surface atraumatic restorative treatment restorations in primary posterior teeth over the first 2 years were 94.3% and 65.4%, respectively. Additionally there was very low-quality evidence that single-surface atraumatic restorative treatment restorations in permanent posterior teeth over the first 3 years had a survival rate of 87.1%, and multiple-surface atraumatic restorative treatment restorations in permanent posterior teeth over the first 5 years had a survival rate of 77%. Based on very low-quality evidence, the weighted mean annual failure rates of completely lost atraumatic restorative treatment sealants in permanent posterior teeth over the first 3 and 4 years were 10.7% and 9.6%, respectively. The mean annual dentine-cariou-lesion failure percentages in previously sealed pits and fissures using atraumatic restorative treatment sealants in permanent posterior teeth were 0.9% at 3 years and 1.9% at 5 years, again based on very low-quality evidence.	Very low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Non-invasive and microinvasive treatment			

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Urquhart <i>et al.</i> (2019)	Compared non-restorative treatments with other active intervention(s), or with no treatment or a placebo, for the arrest or reversal of non-cavitated and cavitated carious lesions in primary and permanent teeth in children and adults.	There was a series of findings from this large-scale systematic review: • There was low-quality evidence that the combination of either infiltrates or sealants with 5% sodium fluoride varnish for arrest or reversal of non-cavitated carious lesions on occlusal surfaces in primary and permanent teeth is superior to most other treatments. • There was very low-quality evidence that the combination of resin infiltration and 5% sodium fluoride varnish may not be the most effective intervention for non-cavitated carious lesions on approximal surfaces in primary and permanent teeth, but it was better than no treatment. • There was very low-quality evidence that sealants or resin infiltration were more effective than no treatment intervention for arrest or reversal of non-cavitated carious lesions on approximal surfaces in primary and permanent teeth. • There was low-quality evidence that 30% silver diamine fluoride solution, applied annually, is better than 30% silver diamine fluoride solution applied once a week for 3 weeks or 5% sodium fluoride varnish applied once a week for 3 weeks on any coronal surface for arrest or reversal of carious lesions. • There was low-quality evidence that 38% silver diamine fluoride solution, applied biannually, was better than 38% silver diamine fluoride solution applied annually, or 12% silver diamine fluoride solution applied annually on any coronal surface for arrest or reversal of carious lesions. • There was low-quality evidence that 5% sodium fluoride varnish was more effective than some other non-invasive treatments or no treatment for arresting or reversing carious lesions on any coronal surface of primary and permanent teeth. • There was low-quality evidence that the use of 1.23% acidulated phosphate fluoride gel on facial/lingual lesions for arresting or reversing such lesions was more effective than oral health education, although only at longer follow-up times. • There was low-quality evidence to suggest that 5000 ppm fluoride (1.1% sodium fluoride) toothpaste or gel was more effective than no intervention for arresting or reversing non-cavitated and cavitated carious lesions on root surfaces in permanent teeth.	Low or very low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Microinvasive and restorative treatment			
Marzouk <i>et al.</i> (2019)	Evaluated bisphenol A exposure in humans from resin-based dental sealants and restorations which contain bisphenol A glycidyl methacrylate by retrieving all clinical studies that measured urinary BPA (uBPA) concentrations in patients before and after resin-based dental treatments. In addition, the authors explored the degree to which baseline bisphenol A concentrations were associated with prior resin-based dental treatments.	There was low-quality evidence that urinary bisphenol A concentrations increased 24 hours after treatment. There was also some suggestion of an increase at 7 days post-treatment. Beyond 1 week of treatment, the evidence was uncertain.	Low
Paula <i>et al.</i> (2019)	Estimated the release of bisphenol A, after the use of composite resins and/or dental sealants, to determine if the increase is higher than the acceptable daily exposure and may cause harmful effects to the health of children, adolescents, and pregnant adults. However, harmful effects were not examined.	All 15 studies of salivary content showed an increase in the levels of bisphenol A within 1 hour of the treatments, either with composite resins or with sealants and these findings were based on low-quality evidence. This increase in bisphenol A in most studies ranges from 2 to 42 ng/mL (nanograms per millilitre), although there are some reports of extreme values ranging from 120 to 931 ng/mL. In follow-ups, the levels decrease over time, for example from treatment to after 1 week. Some studies have evaluated the levels of bisphenol A by the number of surfaces restored or sealed, with an exponential increase in levels from six surfaces upwards. On the other hand, one study performed the evaluation after the treatment followed by mouthwash, demonstrating an abrupt decrease in levels. Two of the four studies that evaluated levels of bisphenol A in the blood reported that it was not detected in serum at any of the follow-up time points, however, these findings were based on low-quality evidence. Five studies evaluating urinary levels of bisphenol A immediately after treatment reported that levels increase slightly after resin-based treatments, but not as markedly as levels detected in saliva. One study measured the estrogenic assay, and an increase immediately after treatment from 0.1 to 1.43 parts per million (ppm) was observed, with only one type of fissure sealant (Delton®); however, levels decreased to below 0.1 ppm after 24 hours. This finding was based on low-quality evidence.	Low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Treatment technique			
Wang <i>et al.</i> (2016)	Compared the effects (survival and failure) of rubber dam isolation compared with other types of isolation (cotton roll) used for direct and indirect restorative treatments in children's molars.	Low-quality evidence that dental restorations had a significantly higher survival rate in the rubber dam isolation group compared with the cotton roll isolation group at 6 months in participants receiving composite restorative treatment of non-carious cervical lesions. Low-quality evidence that the rubber dam group had a lower risk of failure at 2 years in children undergoing proximal atraumatic restorative treatment in primary molars. Low-quality evidence from one trial that reported limited data showing that rubber dam usage during fissure sealing might shorten the treatment time.	Low
Cavitated caries			
Direct restoration material			
Arbildo-Vega <i>et al.</i> (2020)	Evaluated the clinical performance (based on 11 parameters) of bulk-fill direct resin composites used in direct restorations in human teeth and compared them with conventional direct resin composites.	There was low-quality evidence that there were no significant differences in clinical performance of bulk-fill resin composites compared with conventional resin composites, regardless of the type of restoration, type of tooth restored, or technique used. Additionally, there was low-quality evidence that there were no significant differences between bulk-fill resin composites and conventional resin composites on the absence of fractures, absence of discolouration or marginal staining, adequate marginal adaptation, absence of secondary caries, adequate colour stability and translucency, proper surface texture, proper anatomical form of the restoration, adequate integrity of the tooth without the presence of wear, adequate restoration integrity, and proper occlusion.	Low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Kielbassa <i>et al.</i> (2016 and 2017)	Compared the clinical performance of high-viscosity glass ionomer cement covered with a resinous coating with the use of amalgam (no studies), resin composite, or other glass ionomer cements in Class I and Class II restorations of posterior primary or permanent teeth.	In a narrative analysis based on low-quality evidence, the authors reported that two of the three included studies reported high survival of Class I restorations and good colour matching using either glass ionomer cement or resin-modified glass ionomer cement. On the other hand, the third study reported a high proportion of unsatisfactory multi-surface Class II restorations. The three trials reported no differences in survival between high-viscosity glass ionomer cement and resin composite or other glass ionomer cements.	Low
Restoration support material			
Elkady <i>et al.</i> 2020	Evaluated the effect of chlorhexidine as a cavity pretreatment or mix-in on the survival of atraumatic restorative treatment restorations in primary or permanent teeth with occlusal or occlusoproximal cavities.	There was moderate-quality evidence that there were no significant differences in the survival of atraumatic restorative treatment restorations between chlorhexidine as a cavity pretreatment or mix-in compared with no treatment.	Moderate
Da Rosa <i>et al.</i> (2019)	Evaluated the role of calcium hydroxide liner in the treatment of deep carious lesions in primary or permanent teeth with respect to restoration failure.	There was low-quality evidence that calcium hydroxide liner did not reduce restoration failure or increase clinical success of selective or stepwise removal of carious tissue. For primary teeth, the quality of evidence was very low that calcium hydroxide liner had better clinical success for deep carious lesion treatments than glass ionomer cement, and low-quality evidence of no difference in success was compared with inert materials or adhesive systems. For permanent teeth, there was very low-quality evidence that calcium hydroxide liner did not increase the clinical success of deep carious lesion treatments.	Low or very low
Göstemeyer and Schwendicke (2016)	Evaluated the risk of retention loss and failure of adhesively placed resin-based restorations after degradation inhibitory cavity pretreatment with chlorhexidine, ethanol wet-bonding, or quaternary ammonium compounds compared with no treatment, placebo, or alternative pretreatments.	There was low -quality evidence that risk of retention loss or failure was not significantly decreased after pretreatment with chlorhexidine, ethanol wet-bonding, or quaternary ammonium compounds compared with no treatment, placebo, or alternative pretreatments using intention-to-treat analysis. Scenario analyses found that great uncertainty was introduced by participant attrition at follow-up. According to trial sequential analysis, no firm evidence was reached.	Low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Schwendicke <i>et al.</i> (2015b)	Compared the antibacterial effects of different cavity liners with each other, a placebo, or no liner.	There was low-quality evidence and conflicting evidence upon which to judge the performance of different liners for their antibacterial effects.	Low
Pereira-Cenci <i>et al.</i> (2013)	Compared antibacterial agents incorporated into composite restorations with composite restorations containing no antibacterial agents for the prevention of negative clinical outcomes.	No trials met the inclusion criteria.	No evidence
Restoration material and support material			
Schwendicke <i>et al.</i> (2016)	Compared the survival of combinations of adhesive and restorative materials placed in one of two types of cavitated lesions (cervical cavitated lesions or load-bearing posterior cavitated lesions) with each other in permanent and primary teeth. The lesions may or may not be due to caries.	There was low-quality evidence that conventional or bulk-fill resin composites seem suitable for load-bearing lesions. Of note, bulk fills had not all been placed in bulk but in increments in included studies, which possibly artificially improved this material class' performance. There was low-quality evidence that etch-and-rinse adhesives might be preferable in permanent teeth while self-etch systems might be suitable for primary teeth.	Low
Restoration technique			

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Cardoso <i>et al.</i> (2020)	Evaluated the efficiency (time for treatment, caries removal, anaesthesia, and colony-forming units count) of alternative methods (chemomechanical methods, laser, and air- and/or sono-abrasion) for caries removal, compared with the conventional mechanical method (rotary or hand instruments), for removing dental caries from primary and permanent decayed teeth.	The alternative methods had longer treatment times compared with the conventional methods based on very low-quality evidence. Both conventional and alternative approaches reduced cariogenic flora within the cavities based on very low-quality evidence. Alternative methods for caries removal showed a tendency to produce more comfortable treatment experiences and had reduced requests for anaesthesia based on very low-quality evidence. Although every method decreased self-reported pain in patients when compared with conventional mechanical treatment, the chemomechanical treatments were statistically significantly better than the other alternative methods (Er:YAG, and Er,Cr:YSGG laser systems) based on very low-quality evidence. The vector system also resulted in significantly less induced pain based on very low-quality evidence. However, smell and taste were found to be factors for increased anxiety. The longevity and survival of restorations performed by each method did not significantly differ from each other based on very low-quality evidence. Papacarie was the most studied chemomechanical treatment and presented efficiency for caries removal and high acceptance by patients based on very low-quality evidence.	Very low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Zhang <i>et al.</i> (2020)	Evaluated the extent of microleakage from tooth cavities in humans prepared by Er,Cr:YSGG lasers compared with microleakage from cavities prepared by traditional burs, and the effectiveness of acid etching on the adhesive potential of self-etch and etch-and-rinse adhesives after laser preparation compared with no etching.	The incidence of microleakage was not statistically significantly higher after employing a traditional bur compared with the Er,Cr:YSGG laser both on the dentine and the whole marginal line based on very low-quality evidence. In addition, the results of the enamel margin subgroup revealed a non-significant increase in microleakage in the Er,Cr:YSGG laser group. It was reported that prior acid etching improved the adhesive potential of self-etching adhesives and significantly decreased microleakage after laser preparations based on very low-quality evidence. The significant difference was detected both in the enamel and dentine margin subgroups. Prior acid etching did not improve the adhesive potential of the etch-and-rinse adhesives and incidence of microleakage when compared with no etching was not different based on very low-quality evidence. The result revealed substantial statistical heterogeneity among the studies. Prior acid etching did not improve the adhesive potential of the etch-and-rinse adhesives and incidence of microleakage when compared with no etching based on very low-quality evidence. The result revealed substantial statistical heterogeneity among the studies.	Very low
Li <i>et al.</i> (2019)	Evaluated the clinical efficacy (operation time, pain, and long-term outcomes) of the Er:YAG laser for caries removal and cavity preparation in children compared with that of the conventional mechanical method.	There was low-quality evidence that the operation time required for the Er:YAG laser treatment was longer than the conventional mechanical method. However, there was low-quality evidence that the pain caused by the Er:YAG laser was reduced compared to the conventional mechanical method. Additionally, there was low-quality evidence that there were no statistical differences for retention rates, complete restoration, marginal discolouration, and marginal adaption between the Er:YAG laser and conventional mechanical method.	Low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Cianetti <i>et al.</i> (2017)	Evaluated the effectiveness (treatment time, need for anaesthesia, clinical performance, and pulpal complications) and degree of acceptance (pain, discomfort, and fear) by children and adolescents of the use of Sonic and ultrasonic devices with oscillating tips compared with conventional rotating drills to remove carious tissue from primary or permanent teeth.	The effectiveness of sonic and ultrasonic tips for managing pain and dental fear in children and adolescents who required caries removal remains unproven due to the very low-quality evidence available, although there were signals that time required for treatment was longer for the sonic and ultrasonic tips than for the mechanical drill, and the other measures (need for anaesthesia, clinical performance, pulpal complications, pain, discomfort, and fear) favoured the sonic and ultrasonic tips over the mechanical drill.	Very low
Dorri <i>et al.</i> (2017)	Compared atraumatic restorative treatment with conventional treatment (the drill and fill approach) for managing dental carious lesions in the primary and permanent teeth of children and adults.	Compared with conventional treatment using high-viscosity glass ionomer cement, atraumatic restorative treatment may increase the risk of restoration failure in the primary dentition over a follow-up period ranging from 12 to 24 months based on low-quality evidence. Pain experienced by children during the procedure using atraumatic restorative treatment was similar to conventional treatment based on low-quality evidence. Comparisons of atraumatic restorative treatment with conventional treatment using composite or resin-modified glass ionomer cement for restoration failure over a 24-month follow-up period were not different based on low-quality evidence. Comparison of atraumatic restorative treatment with conventional treatment placing resin-modified glass ionomer cement restorations in the permanent teeth of older adults with root carious lesions over a 6-month follow-up period was not different based on low-quality evidence. Comparison of atraumatic restorative treatment with conventional treatment placing resin-modified glass ionomer cement restorations in the permanent teeth of older adults with root carious lesions over a 6-month follow-up period was not different based on low-quality evidence.	Low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Tao <i>et al.</i> (2017)	Evaluated the comparative clinical success (restoration loss, pulpal vitality, and post-operative sensitivity) and efficacy (procedure time, requirement for anaesthesia and acceptability) of erbium laser, compared with traditional drilling, in individuals with carious lesions.	Compared with conventional treatment using high-viscosity glass ionomer cement, atraumatic restorative treatment may increase the risk of restoration failure in the primary dentition over a follow-up period ranging from 12 to 24 months based on low-quality evidence. Pain experienced by children during the procedure using atraumatic restorative treatment was similar to conventional treatment based on low-quality evidence. Comparisons of atraumatic restorative treatment with conventional treatment using composite or resin-modified glass ionomer cement for restoration failure over a 24-month follow-up period were not different based on low-quality evidence. Comparison of atraumatic restorative treatment with conventional treatment placing resin-modified glass ionomer cement restorations in the permanent teeth of older adults with root carious lesions over a 6-month follow-up period was not different based on low-quality evidence.	Moderate or low
Montedori <i>et al.</i> (2016)	Compared laser-based methods with conventional mechanical methods for removing dental caries in deciduous and permanent teeth measuring the outcomes pain, anaesthesia, durability of restoration, pulp damage.	There was insufficient evidence to suggest that either lasers or drills were better at caries removal based on low-quality evidence. The incidence of moderate or high pain, based on low-quality evidence, was greater in the drill group compared with the laser group using the 6-face rating scale. The need for anaesthesia, based on low-quality evidence, was significantly higher in the drill group than in the laser group in children and adults. There was very low-quality evidence that there was no difference in marginal integrity and durability of restoration between the laser and drill comparisons evaluated. Only two trials investigated the recurrence of caries, but no events occurred during the 6-month follow-up period (very low-quality evidence). There was very low-quality evidence and insufficient evidence of a difference between laser or drill in terms of pulpal inflammation or necrosis.	Low or very low
Hamama <i>et al.</i> (2015)	Compared the time required for chemomechanical (sodium hypochlorite-based agent, known as Carisolv, and enzyme-based agent, known as Papacarie) caries removal with the other conventional caries removal methods in primary and permanent teeth.	There was very low-quality evidence that the shortest estimated mean excavation time was recorded during rotary caries excavation (2.99 minutes), followed by the enzyme-based (Papacarie) chemomechanical caries removal method (6.36 minutes) and the hand excavation method (6.98 minutes).	Very low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Schwendicke <i>et al.</i> (2015)	Evaluated and compared the effects (with respect to risk of complications, pain, time required for excavation, and/or number of bacteria remaining) of using different criteria for caries removal in primary and permanent teeth.	There was low-quality evidence that the risk of complications was highest when excavating until only non-stainable dentine remained, and lowest when not attempting to remove all softened dentine. There was low-quality evidence that the risk of pain significantly decreased if self-limiting chemomechanical excavation or fluorescence-assisted lasers were used instead of excavating until all dentine was hard. There was low-quality evidence that, when not attempting to remove all softened dentine, the time required for excavation was shortest, while the greatest number of bacteria remained. There was low-quality evidence that not attempting to remove all softened dentine resulted in the highest number of bacteria remaining and the highest chance of leaving any cultivable bacteria. However, none of these detected differences were statistically significant.	Low
Li <i>et al.</i> (2014)	Evaluated CariSolv for chemomechanical caries removal from primary or permanent teeth, compared with the conventional rotary instrument, for the outcomes complete caries removal rate, the treatment time (in minutes), and the use of local anaesthesia.	There was moderate-quality evidence that there was not a statistically significant difference in complete caries removal between CariSolv group and rotary instruments group in teeth with caries. Additionally, there was moderate-quality evidence that the treatment time required for caries removal using CariSolv was significantly longer than the time required for the rotary instrument group. Finally, there was moderate-quality evidence that fewer patients in the CariSolv group experienced discomfort and used local anaesthesia than in the rotary instrument group.	Moderate
Schwendicke <i>et al.</i> (2013)	Compared one- or two-step incomplete removal with complete caries removal of primary or permanent teeth with primary carious lesions requiring a restoration with respect to risk of pulpal exposure, post-operative pulpal symptoms, overall failure, and caries progression.	Pairwise random-effects meta-analysis, based on low-quality evidence, showed significant risk reduction for pulpal exposure and a non-significant reduction for pulpal symptoms for teeth treated with one- or two-step incomplete excavation. There was low-quality evidence based on inconclusive limited data that risk of failure seemed to be similar for both complete and incomplete excavation.	Low
Permanent dentition			
Non-cariou cervical lesions			
Factors influencing direct restoration material			

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
de Oliveira Correia <i>et al.</i> (2020)	Evaluated how tooth- and cavity-related properties of non-carious cervical lesions in humans' permanent teeth that already had resin composite restorations affect the retention of such restorations.	There was low-quality evidence that the location of the tooth in the dental arch and the presence of wear facets interfere with the retention rate of resin restorations in non-carious cervical lesions. In contrast, there was low-quality evidence that other aspects – such as dentine sclerosis, shape, size, depth, occlusogingival distance, and margin location of the cavity – demonstrated no influence on the retention rate.	Low
Direct restoration material			
Bezerra <i>et al.</i> (2020)	The study evaluated, through a systematic review and meta-analysis, the clinical performance/longevity of composite resin restorations and glass ionomer cements restorations used in adults with non-carious cervical lesions.	The authors found low-quality evidence that there was no difference in the colour, surface texture, and incidence of secondary caries for composite resin restorations and glass ionomer cements restorations used in adults with non-carious cervical lesions at follow-up. In addition, there was low-quality evidence that there was a difference in marginal discolouration, and marginal adaptation at 36 months follow-up only, with better results obtained from restorations with glass ionomer cements over composite resin. Finally, there was low-quality evidence that there was a difference in retention at 36 months, with better results obtained from restorations with glass ionomer cements over composite resin.	Low
Boing <i>et al.</i> (2018)	Compared retention and colour match of glass ionomer cement restorations with resin-based composite restorations in non-carious cervical lesions in the permanent teeth of adults.	The authors found low to moderate-quality evidence in favour of glass ionomer cement, when compared with resin-based composites, for retention up to 3 years (moderate-quality evidence) and for 5 years (low-quality evidence).	Moderate or low
Szesz <i>et al.</i> (2017)	Compared flowable resin composite restorations with regular (or conventional) resin composites for improving the marginal adaptation, marginal discolouration, and retention rates of restorations placed in non-carious cervical lesions in permanent adult teeth.	There was low-quality evidence that resin composite viscosity does not influence retention rates at 3 years follow-up. There was low-quality evidence that resin composite viscosity does not influence marginal discolouration and marginal adaptation at 2- and 3-years follow-up but does influence marginal adaption at 1-year follow-up.	Low
Restoration support material			

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
De Assis <i>et al.</i> (2020)	Evaluated whether there are any differences in clinical performance (including retention) between one-step self-etching and two-step self-etching adhesive systems in non-carious cervical lesions.	There was moderate-quality evidence that there was no statistically significant difference in retention of restoration between the use of one-step self-etching compared with two-step self-etching adhesive systems in non-carious cervical lesions. In addition, there was moderate-quality evidence that there was no statistically significant difference in post-operative sensitivity, incidence of secondary caries, colour match, marginal discolouration, and anatomical form between the use of one-step self-etching compared with two-step self-etching adhesive systems for restoration of non-carious cervical lesions. Finally, there was moderate-quality evidence that there was a statistically significant difference in marginal adaption with two-step self-etching adhesive systems performing better than one-step self-etching for restoration of non-carious cervical lesions.	Moderate
Lins <i>et al.</i> (2020)	Assessed whether the type of solvent (acetone-based compared with alcohol-based) in dental adhesives for composite resin restorations influences the clinical performance (including survival and 10 other parameters) of composite restorations placed in adults with non-carious cervical lesions (Class V restorations).	There was moderate-quality evidence that there is no significant difference in the clinical performance of composite restorations in follow-ups of 6–72 months using adhesives based on solvent type (alcohol-based compared with acetone-based), on retention, marginal adaptation, and marginal discolouration. In addition, there was moderate-quality evidence that there was no statistical difference in survival between the two solvents, indicating that composite restorations placed using either type of adhesive had equal survival rates up to 72 months.	Moderate
Mara de Paula <i>et al.</i> (2019)	Evaluated whether the retention rates of non-carious cervical lesion restorations in adults permanent teeth that used the sandwich technique (a lining of glass ionomer cement or resin-modified glass ionomer cement) were greater than those of composite resin only restorations.	There was low-quality evidence that there was no significant difference in restoration retention between the sandwich technique and composite resin on its own at the 1- and 2-year follow-ups. In addition, there was low-quality evidence that the sandwich restoration technique had higher retention rates than resin composite on its own at the 3-year follow-up. Finally, there was low-quality evidence that there was no significant difference in restoration colour match, marginal discolouration, marginal adaption, or incidence of secondary caries between the sandwich technique and composite resin on its own at the 1- 2- and 3-year follow-ups.	Low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Sousa Pamplona da Silva <i>et al.</i> (2018)	Compared 2-hydroxyethyl methacrylate (HEMA)-free adhesive systems with HEMA-containing systems to treat non-carious cervical lesions in permanent teeth in adults.	There was low-quality evidence that there was no difference in restoration effectiveness between HEMA-free adhesive systems and HEMA-containing adhesive systems.	Low
Schroeder <i>et al.</i> (2017)	Compared composite restorations in non-carious cervical lesions in adults' permanent teeth bonded using self-etch adhesives with composite restorations bonded using etch-and-rinse adhesives for post-operative sensitivity, retention rates, and marginal discolouration.	There was moderate-quality evidence that using either self-etch adhesives or etch-and-rinse bonding strategy composite restorations in non-carious cervical lesions in adults' permanent teeth did not influence the risk of post-operative sensitivity. In addition, there was moderate-quality evidence that using etch-and-rinse adhesives to bond composite restorations in non-carious cervical lesions in adults' permanent teeth can result in a better reduction of marginal discolouration when compared with using self-etch adhesives at 18 months to 2 years and at 4–5 years follow-up. Finally, there was moderate-quality evidence that there was no difference in retention between etch-and-rinse compared with self-etch adhesives.	Moderate
Moraes Coelho Santos <i>et al.</i> (2014)	Assessed the effect of different adhesive systems, surface treatments, and tooth preparation techniques on the retention of tooth-coloured restorative materials placed in non-carious cervical lesions.	There was low-quality evidence that glass ionomer cement has a significantly lower risk of loss of a non-carious cervical lesion restoration compared with either a three-step etch-and-rinse or a two-step etch-and-rinse adhesive system. Also, a three-step etch-and-rinse adhesive system had a significantly lower risk of loss of a non-carious cervical lesion restoration compared with a two-step etch-and-rinse adhesive system. In addition, there was low-quality evidence that there was no significant difference in the risk of loss of a tooth-coloured non-carious cervical lesion restoration between a three-step etch-and-rinse adhesive system and either a two-step self-etch or a one-step self-etch adhesive system, indicating equal effect. Finally, a two-step self-etch adhesive system had a significantly lower risk of loss of a non-carious cervical lesion restoration compared with a two-step etch-and-rinse adhesive system based on low-quality evidence.	Low
Chee <i>et al.</i> (2012)	Compared simplified adhesives (two-step self-etch and one-step self-etch) with conventional adhesives (three-step etch-and-rinse and two-step etch-and-rinse) for treatment of non-carious cervical lesions in the permanent teeth of adults.	There was low-quality evidence that one- or two-step adhesives had similar clinical performance for treating non-carious cervical lesions as other adhesive systems.	Low

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Schwendicke <i>et al.</i> (Schwendicke 2016)	Compared the survival of combinations of adhesive and restorative materials placed in one of two types of cavitated lesions (cervical cavitated lesions or load-bearing posterior cavitated lesions) with each other in permanent and primary teeth. The lesions may or may not be due to caries.	This review is classified as a mixed dentition review however we have moved some of its findings to this section of the review as they pertain to non-carious cervical lesions. There was low-quality evidence that resin-modified glass ionomer cements or, if aesthetics is an issue, conventional resin composites or compomers placed via two-step self-etch adhesives or three-step etch-and-rinse adhesives might be preferred to restore cervical lesions. Additionally, there was low-quality evidence that adhesives combining primer and bonding (two-step etch-and-rinse or one-step self-etch adhesives) were inferior to support restoration of cervical lesions with conventional resin composites or compomers.	Low
Restoration technique			
Rocha <i>et al.</i> 2018 ¹³¹	Evaluated the influence of different dentine surface treatments on the retention rate of resin composite restorations in non-carious cervical lesions.	There was low-quality evidence of reduced risk of restoration loss following removing sclerotic dentine by using a bur. In addition, there was low-quality evidence of reduced risk of restoration loss following application of an adhesive system with a frictional technique. Moreover, there was low-quality evidence of similar risk of restoration loss following application of an adhesive system to dried dentine.	Low
Szesz <i>et al.</i> (2016)	Compared selective etching of enamel margins with no etching to improve the retention rates and marginal discolouration of cervical composite restorations in non-carious cervical lesions in permanent teeth of adults.	There was moderate-quality evidence that the selective enamel etching technique was better than controls for improving the marginal adaptation, discolouration (low at 3 years only), and retention of composite restorations in non-carious cervical lesions in the adult population.	Moderate or low
Schroeder <i>et al.</i> (2015)	Compared enamel bevelling with no enamel bevelling to improve the retention of composite restorations in non-carious cervical lesions in the permanent teeth of adult patients.	There was moderate-quality evidence that outcomes for bevelling prior to restoration were similar to no bevelling.	Moderate

Author (year)	Research question	Evidence summary	Overall GRADE or quality of evidence
Qin <i>et al.</i> (2014)	Compared the clinical effectiveness (retention, marginal defects and marginal discolouration) of self-etching adhesives, with or without previous enamel bevelling and selective phosphoric acid etching, in restorations of non-carious cervical lesions in adults' permanent teeth.	There was low-quality evidence that the differences in restoration retention between self-etching adhesives, with or without previous enamel bevelling were not statistically significant. In addition, there was low-quality evidence that the prevalence of marginal defects and marginal discolouration in the self-etching adhesives without previous enamel bevelling group was significantly higher than that in the self-etching adhesives with enamel bevelling group.	Low

Appendix L: Results of quality assessment of each review

Author (year)	*PIC O	Protocol prior to review and report deviations	Justify primary study design for inclusion	Comprehensive literature search	Duplicate screening	Duplicate data extraction	List of excluded studies	Detailed characteristics of primary studies	Method for assessment of bias	Source of funding for primary studies	*Methods for meta-analyses	*Discussed heterogeneity	*Meta-analysis and risk of bias in analyses	*Risk of bias in discussion of results	Publication bias (search, measure [10 sources], and GRADE)	Conflicts of interest and funding	Overall quality rating of review
Primary dentition																	
Non-cavitated caries																	
Non-invasive treatment																	
Ancira-González et al. (2018)	Yes	No	Yes	Yes	Yes	No	No	Partial yes	Yes	No	No meta-analyses	Yes	No meta-analyses	No	No meta-analyses	No	Low
Microinvasive treatment																	
Lam et al. (2020)	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Low
Cavitated caries																	
Non-invasive treatment																	
Tolba et al. (2019)	Yes	No	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	No meta-analyses	Yes	No meta-analyses	No	No meta-analysis	Yes	Low
Trieu et al. (2019)	Yes	No	No	Yes	Yes	Yes	No	Yes	Partial yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate

Author (year)	*PIC O	Protoc ol prior to review and report deviati ons	Justify prima ry study design for inclusi on	Comprehe nsive literature search	Duplic ate screen ing	Duplica te data extract ion	List of exclud ed studie s	Detailed characteri stics of primary studies	Method for assessm ent of bias	Source of fundin g for primar y studies	*Meth ods for meta-analysi s	*Discusse d heterogen eity	*Meta-analysi s and risk of bias in analysi s	*Risk of bias in discuss ion of results	Publicat ion bias (search, measur e [10 sources] , and GRADE)	Confli cts of intere st and fundi ng	Overall quality rating of review
Direct restoratio n material																	
Dias <i>et al.</i> (2018)	Yes	Yes	Yes	Yes	Yes	No	No	Partial yes	Yes	No	Yes	Yes	Yes	Yes	No	No	Moder ate
Weber Pires <i>et al.</i> (2018)	Yes	Yes	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	No	No	No	Yes	Critical ly low
Raggio <i>et al.</i> (2016)	Yes	Yes	Yes	Partial yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Low
Santos <i>et al.</i> (2016)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	No	No	Low
Indirect restoratio n material																	
Badar <i>et al.</i> (2019)	Yes	Yes	No	Yes	Yes	Yes	Yes	Partial yes	Partial Yes	No	Yes	No	No	No	No	Yes	Critical ly low
Innes <i>et al.</i> (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Low
Compariso n direct and indirect restoratio n material																	
Chisini <i>et al.</i> (2018)	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No meta-analysi s	Yes	No meta-analysi s	Yes	No meta-analysi s	No	Moder ate
Aiem <i>et al.</i> (2017)	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No meta-analysi s	Yes	No meta-analysi s	Yes	No meta-analysis	Yes	Moder ate

Author (year)	*PIC O	Protocol prior to review and report deviations	Justify primary study design for inclusion	Comprehensive literature search	Duplicate screening	Duplicate data extraction	List of excluded studies	Detailed characteristics of primary studies	Method for assessment of bias	Source of funding for primary studies	*Methods for meta-analyses	*Discussed heterogeneity	*Meta-analysis and risk of bias in analyses	*Risk of bias in discussion of results	Publication bias (search, measure [10 sources], and GRADE)	Conflicts of interest and funding	Overall quality rating of review
Restoration support material																	
Schwendicke <i>et al.</i> (2015)	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Low
Restoration technique																	
Aïem <i>et al.</i> (2020)	Yes	No	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate
Pedrotti <i>et al.</i> (2019)	Yes	No	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate
Aparecida Silva Martins <i>et al.</i> (2018)	No	No	No	Partial yes	Yes	Yes	No	No	Yes	No	No meta-analyses	No	No meta-analyses	Yes	No meta-analyses	Yes	Low
Deng <i>et al.</i> (2018)	Yes	No	No	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	No	No	No	Yes	Critically low
Restoration material and technique																	
Tedesco <i>et al.</i> (2018)	Yes	Yes	No	Yes	Yes	Yes	Yes	Partial yes	Yes	No	No	Yes	No	Yes	No	Yes	Critically low
Premanent dentition																	
Non-cavitated caries																	

Author (year)	*PIC O	Protocol prior to review and report deviations	Justify primary study design for inclusion	Comprehensive literature search	Duplicate screening	Duplicate data extraction	List of excluded studies	Detailed characteristics of primary studies	Method for assessment of bias	Source of funding for primary studies	*Methods for meta-analysis	*Discussed heterogeneity	*Meta-analysis and risk of bias in analysis	*Risk of bias in discussion of results	Publication bias (search, measure [10 sources], and GRADE)	Conflicts of interest and funding	Overall quality rating of review
Non-invasive treatment																	
Oliveira <i>et al.</i> (2018)	Yes	Yes	No	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	No	No	No	Yes	Critical ly low
Tao <i>et al.</i> (2018)	Yes	Partial yes	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	No	Yes	No	Yes	Low
Hendre <i>et al.</i> (2017)	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	No	No meta-analysis	No	No meta-analysis	Yes	Yes	No	Low
Wierichs and Meyer-Lueckel (2015)	Yes	No	No	Yes	Yes	No	Yes	Partial yes	Yes	Yes	No	No	No	Yes	No	Yes	Critical ly low
Non-cavitated caries and cavitated																	
Comparison of non-invasive, microinvasive, and minimally invasive treatment																	
Schwendicke <i>et al.</i> (2015a)	Yes	No	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Low
Cavitated caries																	

Author (year)	*PICO	Protocol prior to review and report deviations	Justify primary study design for inclusion	Comprehensive literature search	Duplicate screening	Duplicate data extraction	List of excluded studies	Detailed characteristics of primary studies	Method for assessment of bias	Source of funding for primary studies	*Methods for meta-analyses	*Discussed heterogeneity	*Meta-analysis and risk of bias in analyses	*Risk of bias in discussion of results	Publication bias (search, measure [10 sources], and GRADE)	Conflicts of interest and funding	Overall quality rating of review
Direct restoration material																	
Medeiros Maran <i>et al.</i> (2020)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate
Raiane Mamede Veloso <i>et al.</i> (2019)	Yes	No	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
CADTH (2018)	Yes	Yes	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	No meta-analyses	Yes	No meta-analyses	Yes	No meta-analyses	Yes	Moderate
de Castro Kruly <i>et al.</i> 2018	Yes	Yes	Yes	Partial yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	No	Yes	No	Yes	Low
Monsarrat <i>et al.</i> (2017)	Yes	No	Yes	Yes	No	No	No	Partial yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Low
Hayes <i>et al.</i> (2016)	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	No	No meta-analyses	Yes	No meta-analyses	Yes	No meta-analyses	No	Moderate
Moraschini <i>et al.</i> (2015)	Yes	No	Yes	Yes	Yes	No	Partial yes	Partial yes	Yes	No	No	No	No	No	Yes	No	Critically low
Rasines Alcaraz <i>et al.</i> (2014)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Low

Author (year)	*PIC O	Protocol prior to review and report deviations	Justify primary study design for inclusion	Comprehensive literature search	Duplicate screening	Duplicate data extraction	List of excluded studies	Detailed characteristics of primary studies	Method for assessment of bias	Source of funding for primary studies	*Methods for meta-analyses	*Discussed heterogeneity	*Meta-analysis and risk of bias in analyses	*Risk of bias in discussion of results	Publication bias (search, measure [10 sources], and GRADE)	Conflicts of interest and funding	Overall quality rating of review
Sharif <i>et al.</i> (2014a)	Yes	Yes	Yes	Yes	Yes	Not applicable	Yes	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Yes	Empty review
Sharif <i>et al.</i> (2014b)	Yes	Yes	Yes	Yes	Yes	Not applicable	Yes	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Yes	Empty review
Indirect restoration material																	
Bustamante-Hernández <i>et al.</i> (2020)	Yes	Yes	No	No	Yes	Yes	No	Partial yes	Yes	No	No	Yes	No	No	Yes	Yes	Critically low
Becker Rodrigues <i>et al.</i> (2019)	Yes	No	No	Yes	Yes	Yes	No	Partial yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Critically low
Sampaio <i>et al.</i> (2019)	Yes	No	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate
Vagropoulou <i>et al.</i> (2018)	Yes	Partial yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No meta-analyses	Yes	No meta-analyses	Yes	No meta-analyses	Yes	Moderate
Morimoto <i>et al.</i> (2016)	Yes	No	Yes	Yes	No	Yes	No	Partial yes	Partial yes	No	No	Yes	No	No	No	Yes	Critically low
Grivas <i>et al.</i> (2014)	Yes	No	No	Partial yes	No	Yes	No	Partial yes	Yes	No	No meta-analyses	Yes	No meta-analyses	Yes	No meta-analyses	No	Moderate

Author (year)	*PICO	Protocol prior to review and report deviations	Justify primary study design for inclusion	Comprehensive literature search	Duplicate screening	Duplicate data extraction	List of excluded studies	Detailed characteristics of primary studies	Method for assessment of bias	Source of funding for primary studies	*Methods for meta-analyses	*Discussed heterogeneity	*Meta-analysis and risk of bias in analyses	*Risk of bias in discussion of results	Publication bias (search, measure [10 sources], and GRADE)	Conflicts of interest and funding	Overall quality rating of review
Fron Chabouis <i>et al.</i> (2013)	Yes	Partial yes	Yes	Yes	Yes	No	Yes	Partial yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Critically low
Comparison direct and indirect restoration material																	
Vetromilla <i>et al.</i> (2020)	Yes	Yes	No	Partial yes	Yes	Yes	No	Partial yes	Yes	No	No	Yes	No	No	No	Yes	Critically low
Angeletaki <i>et al.</i> (2016)	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes	Low
Antonelli da Veiga <i>et al.</i> (2016)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate
Restoration support material																	
Schenkel <i>et al.</i> (2019)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Low
Reis <i>et al.</i> (2015)	Yes	Partial yes	Yes	Yes	Yes	No	Partial yes	Partial yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate
Restoration technique																	
Arcanjo Frota Barros <i>et al.</i> (2020)	Yes	No	No	Partial yes	Yes	Yes	No	Partial yes	Yes	No	No	No	No	Yes	No	Yes	Critically low

Author (year)	*PIC O	Protocol prior to review and report deviations	Justify primary study design for inclusion	Comprehensive literature search	Duplicate screening	Duplicate data extraction	List of excluded studies	Detailed characteristics of primary studies	Method for assessment of bias	Source of funding for primary studies	*Methods for meta-analyses	*Discussed heterogeneity	*Meta-analysis and risk of bias in analyses	*Risk of bias in discussion of results	Publication bias (search, measure [10 sources], and GRADE)	Conflicts of interest and funding	Overall quality rating of review
Göstemeyer <i>et al.</i> (2019)	Yes	No	Yes	Partial yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes	No	Critically low
Solon de Mello <i>et al.</i> (2019)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Deng <i>et al.</i> (2016)	Yes	No	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Critically low
Mixed dentition																	
Non-cavitated caries																	
Non-invasive treatment																	
Khijmatgar <i>et al.</i> (2020)	Yes	No	No	Yes	Yes	Yes	No	Partial yes	Yes	No	No meta-analysis	Yes	No meta-analysis	Yes	No meta-analysis	Yes	Moderate
Ma <i>et al.</i> (2019)	Yes	Yes	No	Partial yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate
Chong <i>et al.</i> (2018)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No meta-analysis	Yes	No meta-analysis	Yes	No meta-analysis	Yes	High
Paula <i>et al.</i> (2017)	Yes	No	Yes	Yes	No	No	Yes	Partial yes	Yes	Yes	No meta-analysis	Yes	No meta-analysis	Yes	No meta-analysis	Yes	Moderate

Author (year)	*PIC O	Protoc ol prior to review and report deviati ons	Justify prima ry study design for inclusi on	Compre hensive literature search	Duplic ate screen ing	Duplica te data extract ion	List of exclud ed studie s	Detailed characteri stics of primary studies	Method for assessm ent of bias	Source of fundin g for primar y studies	*Meth ods for meta-analysi s	*Discusse d heterogen eity	*Meta-analysi s and risk of bias in analysi s	*Risk of bias in discuss ion of results	Publicat ion bias (search, measur e [10 sources] , and GRADE)	Confli cts of intere st and fundi ng	Overall quality rating of review
Gao <i>et al.</i> (2016)	Yes	No	No	Partial yes	Yes	No	No	No	Yes	No	No	No	No	No	Yes	Yes	Critical ly low
Lenzi <i>et al.</i> (2016)	No	Partial yes	Yes	Yes	Yes	Yes	No	Partial yes	Partial yes	No	Yes	Yes	No	Yes	No	No	Low
Li <i>et al.</i> (2014)	Yes	No	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	No	No meta-analysi s	Yes	No meta-analysi s	Yes	No meta-analysi s	Yes	Moder ate
Microinva sive treatment																	
Chen <i>et al.</i> (2021)	Yes	No	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	No	Yes	No	Yes	Low
Elrashid <i>et al.</i> (2019)	Yes	Partial yes	Yes	Yes	No	No	No	Partial yes	Yes	No	Yes	Yes	Yes	No	No	Yes	Low
Faghihian <i>et al.</i> (2019)	Yes	Yes	Yes	Yes	Yes	No	Yes	Partial yes	Yes	No	Yes	Yes	No	No	Yes	No	Critical ly low
Chatzimar kou <i>et al.</i> (2018)	Yes	No	No	Yes	Yes	Yes	No	Partial yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Low
Krois <i>et al.</i> (2018)	Yes	Partial yes	Yes	Yes	No	Yes	Yes	Partial yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Low
Liang <i>et al.</i> (2018)	Yes	No	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moder ate
Dorri <i>et al.</i> (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Low
Ammari <i>et al.</i> (2014)	Yes	No	No	Yes	Yes	No	Yes	Partial yes	Yes	No	Yes	Yes	Yes	Yes	No	No	Moder ate
Non-cavitated																	

Author (year)	*PIC O	Protoc ol prior to review and report deviati ons	Justify prima ry study design for inclusi on	Comprehe nsive literature search	Duplic ate screen ing	Duplica te data extract ion	List of exclud ed studie s	Detailed characteri stics of primary studies	Method for assessm ent of bias	Source of fundin g for primar y studies	*Meth ods for meta-analysi s	*Discusse d heterogen eity	*Meta- analysi s and risk of bias in analysi s	*Risk of bias in discuss ion of results	Publicat ion bias (search, measur e [10 sources] , and GRADE)	Confli cts of intere st and fundi ng	Overall quality rating of review
caries and cavitated																	
Non-invasive treatment																	
Marclio Santos <i>et al.</i> (2020)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Low
Chibinski <i>et al.</i> (2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	No	Yes	Yes	No	Yes	No	Yes	Low
Gao <i>et al.</i> (2016b)	Yes	No	No	Partial yes	Yes	Yes	No	Partial yes	Yes	No	No	Yes	Yes	No	No	Yes	Critical ly low
Microinva sive and invasive treatment																	
de Amorim <i>et al.</i> (2018)	Yes	Partial yes	No	Partial yes	No	Yes	Yes	No	Yes	No	No	No	No	Yes	No	Yes	Critical ly low
Non-invasive and microinva sive treatment																	
Urquhart <i>et al.</i> (2019)	Yes	No	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Low
Microinva sive and restorativ e treatment																	

Author (year)	*PIC O	Protocol prior to review and report deviations	Justify primary study design for inclusion	Comprehensive literature search	Duplicate screening	Duplicate data extraction	List of excluded studies	Detailed characteristics of primary studies	Method for assessment of bias	Source of funding for primary studies	*Methods for meta-analyses	*Discussed heterogeneity	*Meta-analysis and risk of bias in analyses	*Risk of bias in discussion of results	Publication bias (search, measure [10 sources], and GRADE)	Conflicts of interest and funding	Overall quality rating of review
Marzouk <i>et al.</i> (2019)	Yes	No	No	Yes	Yes	Yes	Yes	Partial yes	Partial yes	No	No meta-analyses	Yes	No meta-analyses	Yes	No meta-analysis	Yes	Moderate
Paula <i>et al.</i> (2019)	Yes	Partial yes	No	Partial yes	Yes	Yes	No	Partial yes	Yes	No	No meta-analyses	No	No meta-analyses	No	No	Yes	Critically low
Treatment technique																	
Wang <i>et al.</i> (2016)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No meta-analyses	Yes	No meta-analyses	Yes	No meta-analyses	Yes	High
Cavitated caries																	
Direct restoration material																	
Arbildo-Vega <i>et al.</i> (2020)	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	No	No	Yes	No	Yes	Critically low
Kielbassa <i>et al.</i> (2016 and 2017)	Yes	No	Yes	Partial yes	Yes	No	No	Partial yes	Yes	Yes	No meta-analyses	No	No meta-analyses	No	No meta-analyses	No	Critically low
Restoration support material																	
Elkady <i>et al.</i> 2020	Yes	Partial yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate

Author (year)	*PICO	Protocol prior to review and report deviations	Justify primary study design for inclusion	Comprehensive literature search	Duplicate screening	Duplicate data extraction	List of excluded studies	Detailed characteristics of primary studies	Method for assessment of bias	Source of funding for primary studies	*Methods for meta-analyses	*Discussed heterogeneity	*Meta-analysis and risk of bias in analyses	*Risk of bias in discussion of results	Publication bias (search, measure [10 sources], and GRADE)	Conflicts of interest and funding	Overall quality rating of review
Da Rosa <i>et al.</i> (2019)	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	No	No	No	Yes	Critically low
Göstemeyer and Schwendicke (2016)	Yes	No	Yes	Partial yes	Yes	Yes	Yes	Partial yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Low
Schwendicke <i>et al.</i> (2015b)	Yes	No	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	No	No	No	No	No	Yes	Yes	Critically low
Pereira-Cenci <i>et al.</i> (2013)	Yes	Yes	Yes	Yes	Yes	Not applicable	Yes	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Yes	Empty review
Restoration material and support material																	
Schwendicke <i>et al.</i> (2016)	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Low
Restoration technique																	
Cardoso <i>et al.</i> (2020)	Yes	Partial yes	No	Yes	Yes	Yes	No	Partial yes	Partial yes	No	No meta-analyses	Yes	No	Yes	No meta-analyses	Yes	Low
Zhang <i>et al.</i> (2020)	Yes	No	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	No	Yes	No	Yes	No	Yes	Critically low
Li <i>et al.</i> (2019)	Yes	No	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate

Author (year)	*PIC O	Protocol prior to review and report deviations	Justify primary study design for inclusion	Comprehensive literature search	Duplicate screening	Duplicate data extraction	List of excluded studies	Detailed characteristics of primary studies	Method for assessment of bias	Source of funding for primary studies	*Methods for meta-analyses	*Discussed heterogeneity	*Meta-analysis and risk of bias in analyses	*Risk of bias in discussion of results	Publication bias (search, measure [10 sources], and GRADE)	Conflicts of interest and funding	Overall quality rating of review
Cianetti <i>et al.</i> (2017)	Yes	No	No	Yes	Yes	Yes	Yes	Partial yes	Yes	No	No meta-analyses	Yes	No meta-analyses	Yes	No meta-analysis	Yes	Moderate
Dorri <i>et al.</i> (2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Low
Tao <i>et al.</i> (2017)	Yes	No	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate
Montedor <i>i et al.</i> (2016)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Low
Hamama <i>et al.</i> (2015)	Yes	No	Yes	Partial yes	Yes	No	Yes	Yes	Yes	No	No	No	Yes	No	No	Yes	Critically low
Schwendicke <i>et al.</i> (2015)	Yes	No	No	Yes	Yes	No	Yes	Partial yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Low
Li <i>et al.</i> (2014)	Yes	No	Yes	Yes	Yes	Yes	No	Partial yes	Partial yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate
Schwendicke <i>et al.</i> (2013)	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Low
Permanent dentition																	
Non-carious cervical lesions																	
Factors influencing direct restoration material																	

Author (year)	*PICO	Protocol prior to review and report deviations	Justify primary study design for inclusion	Comprehensive literature search	Duplicate screening	Duplicate data extraction	List of excluded studies	Detailed characteristics of primary studies	Method for assessment of bias	Source of funding for primary studies	*Methods for meta-analyses	*Discussed heterogeneity	*Meta-analysis and risk of bias in analyses	*Risk of bias in discussion of results	Publication bias (search, measure [10 sources], and GRADE)	Conflicts of interest and funding	Overall quality rating of review
de Oliveira Correia <i>et al.</i> (2020)	Yes	Yes	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Direct restoration material																	
Bezerra <i>et al.</i> (2020)	Yes	Yes	No	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	No	Yes	No	Yes	Low
Boing <i>et al.</i> (2018)	Yes	No	Yes	Yes	Yes	No	Yes	Partial yes	Yes	No	Yes	Yes	No	Yes	No	No	Low
Szesz <i>et al.</i> (2017)	Yes	Partial yes	Yes	Yes	No	No	Yes	Partial yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Low
Restoration support material																	
De Assis <i>et al.</i> (2020)	Yes	Yes	No	Yes	Yes	Yes	Yes	Partial yes	Yes	No	Yes	No	No	Yes	No	Yes	Critically low
Lins <i>et al.</i> (2020)	Yes	Yes	Yes	Yes	Yes	Yes	No	Partial yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Mara de Paula <i>et al.</i> (2019)	Yes	Yes	No	Yes	Yes	Yes	Yes	Partial yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate
Sousa Pamplona da Silva <i>et al.</i> (2018)	Yes	Partial yes	Yes	Yes	No	No	No	Partial yes	Yes	No	Yes	No	No	No	No	Yes	Critically low
Schroeder <i>et al.</i> (2017)	Yes	Partial yes	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate
Moraes Coelho	Yes	No	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	No	Yes	Yes	No	No	No	No	Critically low

Author (year)	*PIC O	Protocol prior to review and report deviations	Justify primary study design for inclusion	Comprehensive literature search	Duplicate screening	Duplicate data extraction	List of excluded studies	Detailed characteristics of primary studies	Method for assessment of bias	Source of funding for primary studies	*Methods for meta-analyses	*Discussed heterogeneity	*Meta-analysis and risk of bias in analyses	*Risk of bias in discussion of results	Publication bias (search, measure [10 sources], and GRADE)	Conflicts of interest and funding	Overall quality rating of review
Santos <i>et al.</i> (2014)																	
Chee <i>et al.</i> (2012)	Yes	Partial yes	Yes	Yes	No	No	Partial yes	Partial yes	Yes	No	No meta-analyses	Yes	No meta-analyses	Yes	No meta-analyses	No	Moderate
Restoration technique																	
Rocha <i>et al.</i> 2018	Yes	Yes	Yes	Yes	Yes	No	Yes	Partial yes	Yes	No	Yes	Yes	No	No	No	No	Critically low
Szesz <i>et al.</i> (2016)	Yes	Partial yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Schroeder <i>et al.</i> (2015)	Yes	Partial yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate
Qin <i>et al.</i> (2014)	Yes	No	No	Yes	Yes	Yes	Partial yes	Partial yes	Yes	No	Yes	Yes	No	No	No	Yes	Critically low

* Critical flaw

Appendix M: GRADE assessment for each review

Author (year)	Primary study design included	Overall quality rating of review	Study design	Adequate randomisation	Adequate blinding of outcome ascertainment	Heterogeneity	Adequate sample size for each outcome	AMSTAR quality rating	GRADE score: taking account of downgrades	Overall GRADE or quality of evidence
Primary dentition										
Non-cavitated caries										
Non-invasive treatment										
Ancira-González <i>et al.</i> (2018)	9 randomised or quasi-randomised controlled trials	Low	0	1	0	1	0	1	4	Low
Microinvasive treatment										
Lam <i>et al.</i> (2020)	2 randomised or quasi-randomised controlled trials	Low	0	1	1	1	0	1	3	Low
Cavitated caries										
Non-invasive treatment										
Tolba <i>et al.</i> (2019)	2 randomised clinical trials	Low	0	0	0	1	0	1	5	Moderate
Trieu <i>et al.</i> (2019)	2 randomised controlled trials	Moderate	0	0	1	0	0	0	6	Moderate
Direct restoration material										
Dias <i>et al.</i> (2018)	10 randomised controlled trials	Moderate	0	1	1	0	0	0	5	Moderate
Weber Pires <i>et al.</i> (2018)	17 randomised clinical trials	Critically low	0	1	1	0	0	2	3	Low
Raggio <i>et al.</i> (2016)	8 randomised clinical trials	Low	0	0	1	0	0	1	5	Moderate
Santos <i>et al.</i> (2016)	11 randomised or non-randomised trials	Low	1	1	1	0	0	1	3	Low
Indirect restoration material										

Author (year)	Primary study design included	Overall quality rating of review	Study design	Adequate randomisation	Adequate blinding of outcome ascertainment	Heterogeneity	Adequate sample size for each outcome	AMSTAR quality rating	GRADE score: taking account of downgrades	Overall GRADE or quality of evidence
Badar <i>et al.</i> (2019)	2 randomised controlled trials, 1 quasi-experimental study, 1 retrospective analysis study, and 1 retrospective charts review	Critically low	1	1	1	0		2	2	Very low
Innes <i>et al.</i> (2015)	5 randomised controlled trials	Low	0	0	1		0.5	1	4.5	Low
Comparison direct and indirect restoration material										
Chisini <i>et al.</i> (2018)	21 randomised controlled trials and 10 observational studies	Moderate	1	1	1	1	0	0	3	Low
Aiem <i>et al.</i> (2017)	5 randomised controlled trials	Moderate	0	0	1	1	1	0	4	Low
Restoration support material										
Schwendicke <i>et al.</i> (2015)	3 randomised clinical trials	Low	0	0	1	0	2	1	3	Low
Restoration technique										
Aiem <i>et al.</i> (2020)	8 randomised controlled trials	Moderate	0	1	0	0	0.5	0	5.5	Moderate or low
Pedrotti <i>et al.</i> (2019)	4 randomised controlled trials	Moderate	0	1	1	0	0	0	5	Moderate
Aparecida Silva Martins <i>et al.</i> (2018)	6 clinical studies	Low	1	0	1	0	0.5	1	3.5	Low
Deng <i>et al.</i> (2018)	10 randomised controlled trials and 3 prospective controlled clinical trials	Critically low	1	0	0	1	0.5	2	2.5	Low or very low
Restoration material and technique										
Tedesco <i>et al.</i> (2018)	14 randomised controlled trials and 1 non-	Critically low	1	1	1	0.5	0.5	2	1	Very low

Author (year)	Primary study design included	Overall quality rating of review	Study design	Adequate randomisation	Adequate blinding of outcome ascertainment	Heterogeneity	Adequate sample size for each outcome	AMSTAR quality rating	GRADE score: taking account of downgrades	Overall GRADE or quality of evidence
	randomised observational study									
Premanent dentition										
Non-cavitated caries										
Non-invasive treatment										
Oliveira <i>et al.</i> (2018)	3 randomised controlled trials	Critically low	0	0	0	0.5	0	2	4.5	Moderate or low
Tao <i>et al.</i> (2018)	10 randomised controlled trials	Low	0	1	0	0.5	0.5	1	4	Low
Hendre <i>et al.</i> (2017)	3 randomised controlled trials	Low	0	0	0	1	0	1	5	Moderate
Wierichs and Meyer-Lueckel (2015)	29 randomised controlled trials and 1 non-randomised trial	Critically low	1	1	0	0	0.5	2	2.5	Low
Non-cavitated caries and cavitated										
Comparison of non-invasive, microinvasive, and minimally invasive treatment										
Schwendicke <i>et al.</i> (2015a)	10 randomised controlled trials and 4 non-randomised trials	Low	1	1	1	0.5	0	1	2.5	Very low
Cavitated caries										
Direct restoration material										
Medeiros Maran <i>et al.</i> (2020)	19 randomised clinical trials	Moderate	0	1	0	1	0.5	0	4.5	Moderate or low
Raiane Mamede Veloso <i>et al.</i> (2019)	10 randomised controlled trials	Moderate	0	1	0	0	0	0	6	Moderate

Author (year)	Primary study design included	Overall quality rating of review	Study design	Adequate randomisation	Adequate blinding of outcome ascertainment	Heterogeneity	Adequate sample size for each outcome	AMSTAR quality rating	GRADE score: taking account of downgrades	Overall GRADE or quality of evidence
CADTH (2018)	8 randomised controlled trials (2 parallel and 6 split mouth)	Moderate	0	1	1	1	0	0	4	Low
de Castro Kruly <i>et al.</i> 2018	21 randomised trials	Low	0	1	1	0	0	1	4	Low
Monsarrat <i>et al.</i> (2017)	8 clinical trials	low	1	0	1	0	0.5	1	3.5	Low
Hayes <i>et al.</i> (2016)	5 randomised controlled trials or non-randomised controlled trials	Moderate	1	1	1	1	0	0	3	Low
Moraschini <i>et al.</i> (2015)	5 prospective studies, 1 retrospective cohort study, and 2 randomised controlled trials	Critically low	1	1	0	1	0	2	2	Very low
Rasines Alcaraz <i>et al.</i> (2014)	7 randomised controlled trials (2 parallel and 5 split mouth)	Low	0	1	1	1	0	1	3	Low
Sharif <i>et al.</i> (2014a)	No trials met the inclusion criteria	Empty review							No evidence	No evidence
Sharif <i>et al.</i> (2014b)	No trials met the inclusion criteria	Empty review							No evidence	No evidence
Indirect restoration material										
Bustamante-Hernández <i>et al.</i> (2020)	17 clinical trials and 12 cohort studies	Critically low	1	1	1	0	0	2	2	Very low
Becker Rodrigues <i>et al.</i> (2019)	11 randomised controlled trials and 3 prospective cohort studies	Critically low	1	0	0	0	0	2	4	Low
Sampaio <i>et al.</i> (2019)	8 retrospective cohort studies, 4 prospective cohort studies, and 1 randomised controlled trial	Moderate	1	1	1	0.5	0	0	3.5	Low

Author (year)	Primary study design included	Overall quality rating of review	Study design	Adequate randomisation	Adequate blinding of outcome ascertainment	Heterogeneity	Adequate sample size for each outcome	AMSTAR quality rating	GRADE score: taking account of downgrades	Overall GRADE or quality of evidence
Vagropoulou <i>et al.</i> (2018)	9 cohort studies	Moderate	1	1	1	1	0	0	3	Low
Morimoto <i>et al.</i> (2016)	11 retrospective studies, 2 prospective cohort studies, and 1 randomised controlled trial	Critically low	1	1	1	0	0	2	2	Very low
Grivas <i>et al.</i> (2014)	8 randomised controlled trials and 6 controlled clinical trials	Moderate	1	1	1	1	0	0	3	Low
Fron Chabouis <i>et al.</i> (2013)	2 randomised controlled trials	Critically low	0	1	1	0	0	2	3	Low
Comparison direct and indirect restoration material										
Vetromilla <i>et al.</i> (2020)	13 randomised controlled trials, 15 prospective cohort studies, and 15 retrospective cohort studies	Critically low	1	1	1	1	0.5	2	0.5	Very low
Angeletaki <i>et al.</i> (2016)	3 randomised controlled trials	Low	0	1	1	0	1	1	3	Low
Antonelli da Veiga <i>et al.</i> (2016)	9 randomised clinical trials	Moderate	0	1	0	0	0	0	6	Moderate
Restoration support material										
Schenkel <i>et al.</i> (2019)	8 randomised controlled trials	Low	0	1	1	0	0	1	4	Low
Reis <i>et al.</i> (2015)	29 randomised clinical trials	Moderate	0	0	0	0	0	0	7	High
Restoration technique										
Arcanjo Frota Barros <i>et al.</i> (2020)	4 randomised controlled trials and 1 non-randomised trial	Critically low	1	0	1	1	0	2	2	Very low

Author (year)	Primary study design included	Overall quality rating of review	Study design	Adequate randomisation	Adequate blinding of outcome ascertainment	Heterogeneity	Adequate sample size for each outcome	AMSTAR quality rating	GRADE score: taking account of downgrades	Overall GRADE or quality of evidence
Göstemeyer <i>et al.</i> (2019)	3 randomised controlled trials	Critically low	0	0	0	0	0	2	5	Moderate
Solon de Mello <i>et al.</i> (2019)	2 randomised controlled trials	High	0	0	0	0	2	0	5	Moderate
Deng <i>et al.</i> (2016)	5 randomised controlled trials	Critically low	0	1	1	0	0	2	3	Low
Mixed dentition										
Non-cavitated caries										
Non-invasive treatment										
Khijmatgar <i>et al.</i> (2020)	1 randomised controlled trial	Moderate	0	1	0	0	2	0	4	Low
Ma <i>et al.</i> (2019)	2 randomised controlled trials of interest	Moderate	0	0	1	0	1	0	5	Moderate
Chong <i>et al.</i> (2018)	1 randomised controlled trial	High	0	0	0	0	2	0	4	Low
Paula <i>et al.</i> (2017)	13 randomised controlled trials	Moderate	0	0	1	1	0	0	5	Moderate or low
Gao <i>et al.</i> (2016)	17 randomised controlled trials	Critically low	0	1	1	0.5	0	2	2.5	Low or very low
Lenzi <i>et al.</i> (2016)	5 randomised clinical trials	Low	0	1	1	1	1	1	2	Very low
Li <i>et al.</i> (2014)	2 randomised clinical trials and 1 controlled clinical trial of interest	Moderate	1	1	0	1	0	0	4	Low
Microinvasive treatment										
Chen <i>et al.</i> (2021)	17 randomised controlled trials	Low	0	0	0	0.5	0.5	1	5	Moderate or low
Elrashid <i>et al.</i> (2019)	7 randomised controlled trials	Moderate	0	0	0	0	0.5	1	5.5	Moderate
Faghihian <i>et al.</i> (2019)	8 randomised controlled trials	Critically low	0	0	0	0	0	2	5	Moderate

Author (year)	Primary study design included	Overall quality rating of review	Study design	Adequate randomisation	Adequate blinding of outcome ascertainment	Heterogeneity	Adequate sample size for each outcome	AMSTAR quality rating	GRADE score: taking account of downgrades	Overall GRADE or quality of evidence
Chatzimarkou <i>et al.</i> (2018)	9 randomised controlled trials	Low	0	0	0	0.5	0	1	5.5	Moderate
Krois <i>et al.</i> (2018)	13 randomised controlled trials	Low	0	0	1	0	0	1	5	Moderate
Liang <i>et al.</i> (2018)	6 randomised controlled trials and 1 non-randomised trial	Low	1	0	0	0	1	0	5	Moderate or low
Dorri <i>et al.</i> (2015)	8 randomised controlled trials	Low	0	0	0	0	0	1	6	Moderate
Ammari <i>et al.</i> (2014)	8 randomised controlled trials and 2 non-randomised trials	Moderate	1	0	0	0	1	0	5	Moderate
Non-cavitated caries and cavitated										
Non-invasive treatment										
Marcilio Santos <i>et al.</i> (2020)	12 randomised controlled trials	Low	0	1	1	1	1	1	2	Low or very low
Chibinski <i>et al.</i> (2017)	11 randomised controlled trials	Low	0	1	0	0	0	1	5	Moderate
Gao <i>et al.</i> (2016b)	19 prospective clinical studies	Critically low	1	1	1	0	0.5	2	1.5	Very low
Microinvasive and invasive treatment										
de Amorim <i>et al.</i> (2018)	34 clinical trials	Critically low	1	1	1	0.5	0.5	2	1	Very low
Non-invasive and microinvasive treatment										
Urquhart <i>et al.</i> (2019)	43 randomised controlled trials	Low	0	1	1	0.5	0	1	3.5	Low or very low
Microinvasive and restorative treatment										

Author (year)	Primary study design included	Overall quality rating of review	Study design	Adequate randomisation	Adequate blinding of outcome ascertainment	Heterogeneity	Adequate sample size for each outcome	AMSTAR quality rating	GRADE score: taking account of downgrades	Overall GRADE or quality of evidence
Marzouk <i>et al.</i> (2019)	7 prospective clinical studies	Moderate	1	1	1	1	0	0	3.5	Low
Paula <i>et al.</i> (2019)	16 randomised controlled trials, 3 prospective cohort studies, and 1 case-control studies	Critically low	1	1	0	0	0	2	3	Low
Treatment technique										
Wang <i>et al.</i> (2016)	4 randomised controlled trials	High	0	0	1	0	2	0	4	Low
Cavitated caries										
Direct restoration material										
Arbildo-Vega <i>et al.</i> (2020)	16 randomised controlled studies	Critically low	0	0	0	1	0	2	4	Low
Kielbassa <i>et al.</i> (2016 and 2017)	3 trials with quality assessment completed	Critically low	0	1	1	0	0	2	3	Low
Restoration support material										
Elkady <i>et al.</i> 2020	4 randomised controlled trials	Moderate	0	1	0	0.5	0.5	0	5	Moderate
Da Rosa <i>et al.</i> (2019)	14 randomised controlled trials and 1 retrospective study	Critically low	1	0	1	0	0.5	2	2.5	Low or very low
Göstemeyer and Schwendicke (2016)	10 randomised controlled trials	Low	0	1	1	0	1	1	3	Low
Schwendicke <i>et al.</i> (2015b)	11 randomised controlled trials and 3 non-randomised trials	Critically low	1	1	0	0	0	2	3	Low
Pereira-Cenci <i>et al.</i> (2013)	No trials met the inclusion criteria	Empty review							No evidence	No evidence
Restoration material and support material										

Author (year)	Primary study design included	Overall quality rating of review	Study design	Adequate randomisation	Adequate blinding of outcome ascertainment	Heterogeneity	Adequate sample size for each outcome	AMSTAR quality rating	GRADE score: taking account of downgrades	Overall GRADE or quality of evidence
Schwendicke <i>et al.</i> (2016)	72 randomised controlled trials	Low	0	1	1	0	0	1	4	Low
Restoration technique										
Cardoso <i>et al.</i> (2020)	37 controlled trials	Low	1	1	1	1	0	1	2	Very low
Zhang <i>et al.</i> (2020)	13 randomised or quasi-randomised trials	Critically low	1	1	1	1	0	2	1	Very low
Li <i>et al.</i> (2019)	7 randomised controlled trials	Moderate	0	1	1	0.5	0.5	0	4	Low
Cianetti <i>et al.</i> (2017)	2 non-randomised controlled clinical trials	Moderate	1	1	1	1	1	0	2	Very low
Dorri <i>et al.</i> (2017)	15 randomised controlled trials	Low	0	1	1	0	0.5	1	3.5	Low
Tao <i>et al.</i> (2017)	14 trials with a variety of designs comprising randomised controlled trials, quasi-randomised controlled trials, or controlled clinical trials	Moderate	1	1	0	0.5		0	4.5	Moderate or low
Montedori <i>et al.</i> (2016)	9 randomised controlled trials	Low	0	1	1	0	1	1	3	Low or very low
Hamama <i>et al.</i> (2015)	19 randomised clinical trials	Critically low	0	1	1	1	0	2	2	Very low
Schwendicke <i>et al.</i> (2015)	19 randomised controlled trials and 9 non-randomised controlled trials	Low	1	1	1	0	0	1	3	Low
Li <i>et al.</i> (2014)	6 randomised controlled trials	Moderate	0	0	1	0.5	0.5	0	5	Moderate
Schwendicke <i>et al.</i> (2013)	10 randomised controlled trials	Low	0	1	1	0	0	1	4	Low
Permanent dentition										
Non-carious cervical lesions										

Author (year)	Primary study design included	Overall quality rating of review	Study design	Adequate randomisation	Adequate blinding of outcome ascertainment	Heterogeneity	Adequate sample size for each outcome	AMSTAR quality rating	GRADE score: taking account of downgrades	Overall GRADE or quality of evidence
Factors influencing direct restoration material										
de Oliveira Correia <i>et al.</i> (2020)	24 randomised clinical trials	Moderate	0	1	1	1	0	0	4	Low
Direct restoration material										
Bezerra <i>et al.</i> (2020)	10 randomised and 5 non-randomised controlled trials	Low	1	1	0	1	0	1	3	Low
Boing <i>et al.</i> (2018)	15 randomised controlled trials	Low	0	1	0	0.5	0	1	4.5	Moderate or low
Szesz <i>et al.</i> (2017)	8 randomised controlled trials	Low	0	1	1	0	0	1	4	Low
Restoration support material										
De Assis <i>et al.</i> (2020)	5 randomised clinical trials	Critically low	0	0	0	0	0	2	5	Moderate
Lins <i>et al.</i> (2020)	27 randomised controlled clinical trials	Moderate	0	0	1	0.5	0.5	0	5	Moderate
Mara de Paula <i>et al.</i> (2019)	4 randomised controlled trials	Moderate	0	1	1	0.5	0.5	0	4	Low
Sousa Pamplona da Silva <i>et al.</i> (2018)	22 randomised controlled trials	Critically low	0	1	1	0	0	2	3	Low
Schroeder <i>et al.</i> (2017)	42 randomised controlled trials	Moderate	0	1	0	0	1	0	5	Moderate
Moraes Coelho Santos <i>et al.</i> (2014)	27 randomised clinical studies	Critically low	0	1	1	0	0	2	3	Low
Chee <i>et al.</i> (2012)	26 randomised controlled trials	Moderate	0	1	1	1	0	0	4	Low
Restoration technique										
Rocha <i>et al.</i> 2018 ¹³¹	7 randomised clinical trials	Critically low	0	0	1	0	0	2	4	Low

Author (year)	Primary study design included	Overall quality rating of review	Study design	Adequate randomisation	Adequate blinding of outcome ascertainment	Heterogeneity	Adequate sample size for each outcome	AMSTAR quality rating	GRADE score: taking account of downgrades	Overall GRADE or quality of evidence
Szesz <i>et al.</i> (2016)	10 randomised controlled trials	Moderate	0	0	0	0.5	1	0	5.5	Moderate
Schroeder <i>et al.</i> (2015)	4 randomised controlled trials	Moderate	0	1	0	0	1	0	5	Moderate
Qin <i>et al.</i> (2014)	8 randomised controlled trials	Critically low	0	0	0	0.5	0.5	2	4	Low

Appendix N: Characteristics of each included systematic review

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Primary dentition													
Non-cavitated caries													
Non-invasive treatment													
Ancira-González et al. (2018)	Compared the effectiveness of fluoride varnishes, gels, casein phosphopeptide-amorphous calcium phosphate, and other remineralisation agents with each other in the management of white spot lesions in children's primary teeth.	White spot lesions in children's primary teeth	The Netherlands, Sweden, Thailand, and the USA	5,115 children	Aged 1–8 years	Not reported	Fluoride varnishes, gels, casein phosphopeptide-amorphous calcium phosphate, and other remineralisation agents	Each other	Effectiveness (remineralisation)	3–48 months	9 randomised or quasi-randomised controlled trials	2001–2016	Not reported
Microinvasive treatment													

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Lam <i>et al.</i> (2020)	Evaluated the effectiveness of different types of pit-and-fissure sealants, as compared with no treatment measures among children and adolescents, to arrest of pit-and-fissure occlusal caries.	Pit-and-fissure occlusal caries in primary molars of children and adolescents	Greenland and Kuwait	197 participants (with 667 primary molars)	Aged 4–7 years	Not reported	Different types of pit-and-fissure sealants	No treatment, professional topical fluoride application alone, or new sealant	Caries arrest	12 and 34 months	2 randomised or quasi-randomised controlled trials	1998–2015	Not reported
Cavitated caries													
Non-invasive treatment													
Tolba <i>et al.</i> (2019)	Evaluated the effectiveness (in arresting caries) of the application of 12% silver diamine fluoride compared with 38% silver diamine fluoride in cavitated	Cavitated dentine caries in children's primary teeth	Not reported	1,864 children	Mean age range 3.8–5.2 years	Not reported	12% silver diamine fluoride	38% silver diamine fluoride	Arresting caries	24 and 30 months	2 randomised clinical trials	2009–2018	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	dentine caries in children's primary teeth.												
Trieu <i>et al.</i> (2019)	Evaluated dentine caries arrest capabilities of silver diamine fluoride compared with those of sodium fluoride in the carious teeth of children aged 12 years and under.	Carious [primary] teeth of children aged 12 years and under	China	679 children	3.4 years and 4.0 years	56–60% male	Silver diamine fluoride	Sodium fluoride	Dentine caries arrest	18 and 30 months	2 randomised controlled trials published in 6 papers	2001–2018	Not reported
Direct restoration material													
Dias <i>et al.</i> (2018)	Compared failure and clinical performance of glass ionomer cement with composite resin in Class II restorations in primary teeth.	Class II restorations in primary teeth	Not reported	592 children (with their 1,425 restorations)	Aged 3–11 years	Not reported	Glass ionomer cement	Composite resin	Failure and clinical performance	6–48 months	10 randomised controlled trials	1992–2016	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Weber Pires <i>et al.</i> (2018)	Evaluated the clinical performance of different conventional restorative materials placed in posterior primary teeth.	Posterior primary teeth (41% were Class I and II restorations)	Brazil, Greece, India, Japan, Sweden, the Netherlands, Turkey, the UK, and the USA	863 participants (2,867 restorations)	Aged 3–11 years	Not reported	Conventional restorative materials (amalgam, conventional glass ionomer cement, resin-modified glass ionomer cement, high-viscosity glass ionomer cement, compomer, and composite resin)	Each other	Failure and clinical performance	12 and 60 months	17 randomised clinical trials	1980–2016	Not reported
Raggio <i>et al.</i> (2016)	Compared glass ionomer cements with other restorative materials (amalgam, resin composite, or polyacid-modified resin composite) to prevent adjacent (secondary) carious lesions in the margins	Margins of occlusal and occlusoproximal restorations in primary teeth	Not reported	1,644 children	Aged 5–8 years	Not reported	Glass ionomer cements	Other restorative materials (amalgam, resin composite, or polyacid-modified resin composite)	Adjacent (secondary) carious lesions	36 months	8 randomised clinical trials	1999–2014	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	of occlusal and occlusoproximal restorations in primary teeth.												
Santos <i>et al.</i> (2016)	Compared glass ionomer cements, composite resins, and compomers, known as adhesive restorations, in order to determine which is superior in terms of restoration survival in the primary (molar) teeth of children.	Class I and II restorations in primary (molar) teeth	Brazil, Germany, Norway, Pakistan, Sweden, Turkey, the UK, and the USA	483 children	Aged 3–10 years	Not reported	Glass ionomer cements, composite resins, and compomers	Each other	Restoration survival and clinical performance	24–48 months	11 randomised or non-randomised trials	1999–2015	Not reported
Indirect restoration material													

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Badar <i>et al.</i> (2019)	Assessed the outcomes (retention and absence of pulpal symptoms) of placement of a crown using the Hall technique on primary carious molars in children and compared it with conventional dental restorations or stainless steel crowns.	Primary carious molars in children	Germany, New Zealand, Scotland, and the USA.	1,775 restorations	Not reported	Not reported	Placement of a crown using the Hall technique	Conventional dental restorations or stainless steel crowns	Retention and absence of pulpal symptoms	15 months to 5 years.	2 randomised controlled trials, 1 quasi-experimental study, 1 retrospective analysis study, and 1 retrospective charts review	2006–2018	Not reported
Innes <i>et al.</i> (2015)	Compared the effectiveness and safety of all types of preformed crowns (using the Hall technique) with conventional filling materials for restoring primary molar	Restoring primary molar teeth in children	Germany, Israel, Saudi Arabia, the UK, and the USA	438 children (and 693 primary molar teeth)	Aged 2.6–10 years	56% male	Preformed crowns (using the Hall technique)	Conventional filling materials	Effectiveness (failure, pain, discomfort and bleeding) and safety	12–48 months	5 randomised controlled trials	2003–2014	Yes, 2 studies

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	teeth in children.												
Comparison on direct and indirect restoration material													
Chisini <i>et al.</i> (2018)	Investigated the longevity of posterior restorations in primary teeth and the reasons for failure.	Posterior (Class I, Class II, and crown) restorations in primary teeth	Australia, Brazil, Egypt, Germany, Greece, India, Ireland, Norway, the Netherlands, Sweden, Syria, Turkey, the UK, and the USA	12,047 posterior restorations in children	Aged 1–13 years	Not reported	Restorations in primary teeth (amalgam, compomers, composite resin, conventional glass ionomer cement, modified resin glass ionomer cement, resin-modified glass ionomer cement, and steel crowns)	Each other	Longevity (or survival) and reasons for failure	12–48 months	21 randomised controlled trials and 10 observational studies	1996–2016	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Aiem <i>et al.</i> (2017)	Evaluated the clinical effectiveness (success or failure of restorations based on five criteria) of all types of aesthetic preformed crowns for restoring primary teeth, compared with conventional filling materials or other types of crowns.	Restoring carious primary teeth	Ireland, Israel, Turkey, and the United Arab Emirates	172 children and 568 teeth	Aged 2–9 years	Not reported	Aesthetic preformed crowns	Conventional filling materials or other types of crowns	Success or failure of restorations based on five criteria	6 months to 4 years	5 randomised controlled trials	2003–2014	Not reported
Restoration support material													
Schwendicke <i>et al.</i> (2015)	Evaluated the risk of restoration failure (proportion of teeth requiring retreatment) following restoration due to dentine	Primary molars in children with dentine caries requiring restoration	Brazil	62 participants and 130 restorations	Aged 4–8 years	44% male	Cavity liner following restoration	No cavity liner	Failure of restorations	12 months or more	3 randomised controlled trials	2002–2010	Not fully reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	caries in primary molar teeth, comparing restorations with cavity lining to restorations without cavity lining. The follow-up was 1 or more years after restoration.												
Restoration technique													
Aiem et al. (2020)	Compared the efficacy (measured by pulp exposure and absence of pulpal or periodontal complications or restorative failures) of three caries removal techniques – complete caries removal, selective caries	Deep carious lesions in vital (absence of irreversible pulpitis or pulpal necrosis) primary teeth	Brazil, Germany, Scandinavia, Thailand, and Turkey	669 children (and 824 teeth)	Aged 3–15 years	Not reported	Three caries removal techniques – complete caries removal, selective caries removal, and stepwise caries removal	Each other	Efficacy (measured by pulp exposure and absence of pulpal or periodontal complications or restorative failures)	1–24 months	8 randomised controlled trials	1977–2018	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	removal, and stepwise caries removal – for deep carious lesions in vital (absence of irreversible pulpitis or pulpal necrosis) primary teeth.												
Pedrotti <i>et al.</i> (2019)	Evaluated whether selective carious tissue removal of soft dentine from deep cavitated lesions in primary teeth increases the risk of experiencing restoration failure compared with complete carious tissue removal.	Deep cavitated lesions in primary teeth	Brazil, Scotland, and Thailand (one study)	312 children	Aged 3–11 years	Not reported	Selective carious tissue removal of soft dentine from deep cavitated lesions	Complete carious tissue removal	Restoration failure	12–24 months	4 randomised controlled trials	1999–2015.	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Aparecida Silva Martins <i>et al.</i> (2018)	Evaluated the clinical evidence of partial caries removal in the primary dentition, regardless of liner and restorer materials, measuring the longevity of the restorative treatment and clinical and radiographic success.	Primary dentition	Not reported	423 participants	Aged 3–11 years	Not reported	Partial caries removal in the primary dentition	No comparator	Longevity of the restorative treatment and clinical and radiographic success	12–24 months	6 clinical studies	2004–2015	Not reported
Deng <i>et al.</i> (2018)	Compared the efficiency (operation time, bacterial count, and restoration survival) and efficacy (acceptability and preference) of chemomechanical caries removal (Papacarie) in primary molar	Primary molar caries in children and adolescents	Brazil, Egypt, and India	438 adolescent and child patients with 1033 primary molar caries	Aged 3–12 years	Not reported	Chemomechanical caries removal (Papacarie)	Conventional drilling method	Operation time, bacterial count, restoration survival, acceptability and preference	Immediately after the caries removal treatment and then 1, 6, and 18 months later.	10 randomised controlled trials and 3 prospective controlled clinical trials	2009–2016	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	caries in children and adolescents with the conventional drilling method (controls).												
Resatoration material and technique													

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Tedesco <i>et al.</i> (2018)	Determined the best treatment for dentine carious lesion arrestment and the success rate of different treatments of the dentine carious lesions of primary teeth. The purpose of the review was to bridge a gap in the evidence by considering whether lesions of different depths and the number of surfaces involved affect treatment outcomes.	Dentine carious lesions of primary teeth	Brazil, China, Germany, Indonesia, Kuwait, South Africa, Syria, Turkey, and the UK	3,226 participants	Aged 2–10 years	Not reported	Different treatments: non-invasive, minimally invasive, and invasive treatments (stainless steel crown; non-restorative caries treatment; ultraconservative treatment; the Hall technique; interim restorative treatment; silver diamine fluoride; sodium fluoride; resin sealant; low-viscosity glass ionomer cement; high-viscosity glass ionomer cement; resin-modified glass ionomer	Each other, and rotary drill with restorative materials, compared with atraumatic restorative treatment with restorative materials; and non-invasive treatments, compared with atraumatic restorative treatment with restorative materials	Arrestment and the success rate by depth and number of surfaces	At least 12 months	14 randomised controlled trials and 1 non-randomised observational study	2002–2016	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
							cement; resin composite; and amalgam)						
Permanent dentition													
Non-cavitated caries													
Non-invasive treatment													
Oliveira <i>et al.</i> (2018)	Assessed the effect of professionally applied silver	Exposed root surfaces of permanent	China	895 older adults	72–79 years	Not reported	Professionally applied silver diamine fluoride	No, placebo, or other active intervention	Preventing and arresting caries	12, 24, or 30 months or more	3 randomised	2010–2017	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	diamine fluoride (SDF) compared with no, placebo, or other active intervention in preventing and arresting caries in exposed root surfaces of adults.	teeth in adults									controlled trials		
Tao et al. (2018)	Evaluated the efficacy of combining casein phosphopeptide-amorphous calcium phosphate and fluorides compared to fluorides monotherapy on patients with early carious lesions in permanent teeth.	Early carious lesions in permanent teeth	Not reported	559 patients	Young adults	Mainly female	Combined casein phosphopeptide-amorphous calcium phosphate with fluorides	Fluorides monotherapy	Decrease in size of early carious lesions	3–24 weeks	10 randomised controlled trials	2007–2016	Not reported
Hendre et al. (2017)	Evaluated the effectiveness (preventing, arresting, or	Root caries in permanent teeth of	Hong Kong, China	655 participants	Aged over 60 years	Not reported	Silver diamine fluoride	Other preventive agents (fluoride, chlorhexidine) or placebo	Arresting, or remineralising root caries	30–36 months	3 randomised	2010–2016	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	remineralising) of silver diamine fluoride in the management of root caries in older adults.	older adults									controlled trials		
Wierichs and Meyer-Lueckel (2015)	Evaluated results of clinical studies investigating chemical agents to reduce initiation of root carious lesions or inactivate existing ones (arrest root carious lesions).	Root carious lesions in permanent teeth of mainly older adults	Brazil, Canada, China, Denmark, Germany, Hungary, Israel, Spain, Sweden, Switzerland, the Netherlands, the UK, and the USA	10,136 patients	Aged 20–101 years	Not reported	Chemical agents: fluoride compounds, chlorhexidine, ozone treatment, etc. in different delivery systems (dentifrice, mouth rinse, and varnish)	Each other (positive interventions) and to negative intervention (placebo treatment) or standard therapy	Arrest root carious lesions	Time frame varied by study	29 randomised controlled trials and 1 non-randomised trial	1988–2013	Yes, 19 studies
Non-cavitated caries and cavitated													
Comparison of non-invasive, microinvasive, and minimally													

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
invasive treatment													
Schwendicke <i>et al.</i> (2015a)	Compared non-invasive, microinvasive, and minimally invasive treatments with each other, with no active treatment or a placebo treatment, or with standard oral home care for treating pit-and-fissure lesions in permanent posterior teeth in adults.	Pit-and-fissure lesions in permanent posterior teeth in adults	Albania, Brazil, Canada, China, Denmark, the USA, and Zimbabwe	1,440 patients with 3,551 treated lesions	Aged 5–68 years	Not reported	Non-invasive, microinvasive, and minimally invasive treatments	Each other and with no active treatment or a placebo treatment, or with standard oral home care	Avoidance of retreatment (progression of the lesion, sealant loss, secondary caries or fracture of restorations, pulpal complications)	6 months or over	10 randomised controlled trials and 4 non-randomised trials	1976–2012	Not reported
Cavitated caries													
Direct restoration material													

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Medeiros Maran <i>et al.</i> (2020)	Evaluated survival or clinical performance (two primary outcomes: colour match and surface texture and 6 secondary outcomes) of nanofilled/nano hybrid restorations compared with hybrid composite restorations in patients with direct posterior restorations.	Patients with direct posterior restorations	Not reported	1,142 participants	13–82 years	More females were included than males	Nanofilled/nano hybrid restorations	Hybrid composite restorations	Survival or clinical performance (two primary outcomes: colour match and surface texture and 6 secondary outcomes)	12–72 months	19 randomised clinical trials	2006–2016	Not reported
Raiane Mamede Veloso <i>et al.</i> (2019)	Evaluated whether the clinical performance (failure measured by eight criteria) of bulk-fill resin composites is comparable to that of	Restored permanent posterior (molars and premolars) teeth	Not reported	459 patients and 1,076 restorations	7–87 years	Not reported	Bulk-fill resin composites	Conventional composites	Clinical performance (failure measured by eight criteria)	12–72 months	10 randomised controlled trials	2010–2017	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	conventional composites in restored permanent posterior (molars and premolars) teeth.												
CADTH (2018)	Evaluated the comparative efficacy of direct dental restorations made of composite resin compared with amalgam for the treatment of dental caries in posterior permanent teeth.	Posterior permanent teeth of children and adults	One cross-country trial in Europe, and individual country trials in Portugal, Turkey, the UK, and the USA	3,290 composite restorations and 1960 amalgam restorations	Age data not clear	Not reported	Direct composite resin restoration	Amalgam	Effectiveness (failure rate at 3 years or over, fracture, secondary caries rate) and safety (adverse events)	At least 36 months	8 randomised controlled trials (2 parallel and 6 split mouth)	1986–2016 and 2007–2016	Yes, 3 studies at least

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
de Castro Kruly <i>et al.</i> 2018	Compared the clinical behaviour (marginal integrity/adaptation, marginal discolouration, recurrent caries, retention of composite restorations, and post-operative sensitivity) of restorations performed with low polymerisation shrinkage resin composite (bulk fill) resins in comparison with methacrylates-based (conventional) resin composite (in humans with Class I or II restorations in the permanent dentition).	Humans with Class I or II restorations in the permanent dentition	Austria, Belgium, Brazil, Canada, Denmark, Egypt, Spain, Sweden, Turkey, and the USA	1,724 restorations	Not reported	Not reported	Low polymerisation shrinkage resin composite (bulk fill)	Methacrylates-based (conventional) resin composite	Clinical performance which indicates success or failure of restorations: Marginal integrity/adaptation, marginal discolouration, recurrent caries, retention of composite restorations, and post-operative sensitivity	12 and 24 months	21 randomised trials	2006–2016.	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Monsarrat <i>et al.</i> (2017)	Evaluated the clinical performance (such as survival rates or quality of restorations) of the first generation of ormocer-based fillings against those of conventional composite restorations and glass ionomer restorations; and (2) explored the influence of different clinical factors and the impact of the quality of studies on published results.	Adults permanent teeth	Belgium, Denmark, Egypt, Germany, Italy, Sweden, and Turkey	363 participants	20–53 years	27–54% Male	First generation of ormocer-based fillings	Conventional composite restorations and glass ionomer restorations	Survival rates or quality of restorations	0.5–8 years	8 clinical trials	2006–2015	Yes, 2 trials
Hayes <i>et al.</i> (2016)	Compared the clinical performance of restorative materials for the treatment	Root caries in the permanent teeth of adult patients	Belgium, Canada, China, and the USA	269 adults (629 restorations)	Aged over 18 years: mainly middle-aged	40% male	Restorative materials: Glass ionomer cement, resin-modified glass ionomer	Each other	Failure rate and secondary caries rate	12 and 24 months	5 randomised controlled trials or non-	1990–2011	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	of root caries in the permanent teeth of adult patients.				and older		cement, resin composite, and amalgam. Three of the studies also prescribed sodium fluoride gel.				randomised controlled trials		
Moraschini <i>et al.</i> (2015)	Compared the failure rates of amalgam and composite resin in occlusal and occlusoproximal restorations in posterior permanent teeth.	Occlusal and occlusoproximal restorations in posterior permanent teeth	Not reported	27 to 472 participants in each study	Mean age 21.6 years	Not reported	Composite resin	Amalgam	Failure rate, longevity, fracture, and secondary caries	At least 12 months	5 prospective studies, 1 retrospective cohort study, and 2 randomised controlled trials	1992–2013	Not reported
Rasines Alcaraz <i>et al.</i> (2014)	Compared the restoration failure of direct composite resin fillings with amalgam fillings for permanent posterior teeth.	Posterior permanent teeth of children and adults	One cross-country trial in Europe, and individual country trials in Portugal, the UK,	3,265 composite restorations and 1,935 amalgam restorations	Age data not clear	Not reported	Direct composite resin restoration	Amalgam	Effectiveness (failure rate at 3 years or over, fracture, secondary caries rate) and safety (adverse events)	At least 36 months	7 randomised controlled trials (2 parallel and 5 split mouth)	1986–2007	Yes, 3 studies

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
			and the USA										

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Sharif <i>et al.</i> (2014a)	Compared the effects of replacing resin composite with repairing it (with resin composite) in the management of defective resin composite dental restorations in permanent molar and premolar teeth.	Defective resin composite dental restorations in permanent molar and premolar teeth	No trials met the inclusion criteria	No trials met the inclusion criteria	No trials met the inclusion criteria	No trials met the inclusion criteria	Replacing resin composite	Repairing resin composite	Failure of restoration Presence of clinical symptoms (pain, swelling, diagnosis of pulpitis, abscess formation). Extraction of tooth due to caries. Perioperative or post-operative pain or discomfort. Patient satisfaction as measured by aesthetic scales.	Time frame not predetermined	No trials met the inclusion criteria	No trials met the inclusion criteria	No trials met the inclusion criteria

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Sharif <i>et al.</i> (2014b)	Compared the effects (retention, survival) of replacing (with amalgam) compared with repair (with amalgam) in the management of defective amalgam dental restorations in permanent molar and premolar teeth.	Defective amalgam dental restorations in permanent molar and premolar teeth	No trials met the inclusion criteria	No trials met the inclusion criteria	No trials met the inclusion criteria	No trials met the inclusion criteria	Replacing amalgam	Repairing amalgam	Success or failure of restoration; Extraction of tooth due to decay.	Time frame not predetermined, but results to be presented in subgroups: under 5 years and 5 years or over	No trials met the inclusion criteria	No trials met the inclusion criteria	No trials met the inclusion criteria
Indirect restoration material													
Bustamante-Hernández <i>et al.</i> (2020)	Evaluated the clinical behaviour (survival) and the possible complications of posterior region onlays in adults' permanent posterior teeth by the type of material used for the onlay	Posterior region onlays in adults' permanent posterior teeth	Not reported	Sample sizes ranged from 14 to 231 restorations	Not reported	Not reported	Type of material used for the onlay restoration: Feldspathic ceramic reinforced with lithium disilicate, conventional feldspathic ceramic or feldspathic ceramic	Each other	Clinical behaviour (survival) and complications	2–15 years	17 clinical trials and 12 cohort studies	2000–2019	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	restoration 1 year or more after restoration intervention.						reinforced with leucite, hybrid materials, and resin composite.						
Becker Rodrigues <i>et al.</i> (2019)	Evaluated the difference in longevity of tooth-supported ceramic prostheses designed by a computer-aided design/computer-aided manufacturing system compared with a conventional manufacturing (milling) system.	Anterior and/or posterior tooth-supported single crown or multiple-unit or partial crowns	Not reported	1,209 restorations placed in 957 patients	Not reported	Not reported	Tooth-supported ceramic prostheses designed by a computer-aided design/computer-aided manufacturing system	Tooth-supported ceramic prostheses designed by conventional manufacturing (milling) system	Difference in longevity, Longevity of manufactured restorations measured as failure	24–84 months	11 randomised controlled trials and 3 prospective cohort studies	1999–2017	Yes, 7 studies

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Sampaio <i>et al.</i> (2019)	Evaluate the survival rate of indirect composite and ceramic inlays, onlays, and overlays following different manufacturing methods in children and adults teeth.	Children and adults teeth	Australia, Germany, Iran, Italy, Japan, Portugal, Sweden, and Switzerland	2,184 participants	Aged 12–79 years	Not reported	Indirect composite and ceramic inlays, onlays, and overlays following different manufacturing methods	Each other	Survival rate	5–18 years	8 retrospective cohort studies, 4 prospective cohort studies, and 1 randomised controlled trial	1998–2016	Not reported
Vagropoulou <i>et al.</i> (2018)	Investigated whether different types of indirect restorations (inlay, onlay, both inlay and onlay, and crown) used for single permanent anterior, premolar, or molar teeth had different biological or technical complications,	Single permanent anterior, premolar, or molar teeth	Not reported	775 participants	Aged 18–91 years	More females than males participated in four of these five studies	Different types of indirect restorations (inlay, onlay, both inlay and onlay, and crown): More than 50% gold, metal ceramic, all ceramic, and zirconia crowns.	Each other	Difference in survival rates, and biological or technical complications	At 5 years	9 cohort studies	2003–2015	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	or different survival rates.												
Morimoto <i>et al.</i> (2016)	Evaluated the survival rate of resin and ceramic inlays, onlays, and overlays at 5 years and 10 years in permanent teeth (deduced from reported age range and intervention), and identified the types of complications associated with the main negative clinical outcomes.	In permanent teeth (deduced from reported age range and intervention)	Austria, Germany, Italy, Japan, Sweden, and Switzerland	2,080 participants and 7,427 posterior teeth	Aged 12–79 years	Not reported	Resin and ceramic inlays, onlays, and overlays	Each other	Survival rate at 5 years and 10 years, and of complications associated with the main negative clinical outcomes	At 5 years and 10 years	11 retrospective studies, 2 prospective cohort studies, and 1 randomised controlled trial	1997–2012	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Grivas <i>et al.</i> (2014)	Evaluated clinical performance (longevity, colour match, and post-operative sensitivity) at 12 months or longer of indirect composite inlays compared with direct composite restorations as well as with ceramic and gold inlays in adults with permanent vital teeth restorations.	Adults with permanent vital teeth restorations	Not reported	507 participants with 1,326 restorations	Not reported	Not reported	Indirect composite inlays	Direct composite restorations as well as with ceramic and gold inlays	Clinical performance (longevity, colour match, and post-operative sensitivity)	3.5–11 years	8 randomised controlled trials and 6 controlled clinical trials	1995–2013	Not reported
Fron Chabouis <i>et al.</i> (2013)	Compared performance of composite inlays and onlays with ceramic inlays or onlays for restoring posterior	Restoring posterior permanent teeth in adults	Not reported	138 inlays (no onlays were evaluated) in 80 patients	Not reported	Not reported	Composite inlays and onlays	Ceramic inlays or onlays	Failure, colour match, anatomical form, occlusal marginal adaption, and surface finish	3 years	2 randomised controlled trials	1994–2006	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	permanent teeth in adults.												
Comparison on direct and indirect restoration material													
Vetromilla <i>et al.</i> (2020)	Evaluated restorative treatment types and materials for large tooth cavity restorations in permanent posterior teeth in adults with respect to tooth or restoration longevity, and ranked them from best to worst.	Large tooth cavity restorations in permanent posterior teeth in adults (from two-surface restorations up to full crowns)	Brazil, Canada, Germany, the Republic of Korea, Sweden, the Netherlands, the UK, and Uruguay. In addition, there was one multi-regional study.	Trials: 1,621 participants (with 4,063 teeth). Cohort: Over 904 participants (with 216,996 teeth)	Aged 15–55 years	Trials: 40% male. Cohorts 46% male	Restorative treatment types and materials: Amalgam, direct resin, feldspathic ceramic, glass ceramic, glass ionomer, gold, indirect resin, metal ceramic, resin sandwich, and zirconia-based ceramic.	Each other	Longevity, and ranked them from best to worst	5–50 years	13 randomised controlled trials, 15 prospective cohort studies, and 15 retrospective cohort studies	1989–2019	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Angeletaki <i>et al.</i> (2016)	Evaluated the clinical parameters of longevity (secondary caries, post-operative sensitivity, marginal discolouration, and colour match) for direct and indirect composite restorations in posterior (molar or premolar) teeth at follow-ups of 3 years or over.	Posterior (molar or premolar) permanent teeth	Denmark, the Netherlands, and Turkey	239 participants (with 424 posterior teeth)	Aged 20–81 years	45% male	Direct composite restorations	Indirect composite restorations (inlays/onlays)	Clinical parameters (secondary caries, post-operative sensitivity, marginal discolouration, and colour match) and longevity	5–11 years	3 randomised controlled trials	2003–2014	Not reported
Antonelli da Veiga <i>et al.</i> (2016)	Compared the differences in clinical performance and longevity of direct and indirect resin composite restorations in Class I and Class II cavities in	Class I and Class II cavities in permanent molar and premolar teeth	Not reported	207 plus participants and 439 restorations	Aged 20–81 years	51% male	Direct resin composite restorations	Indirect resin composite restorations	Clinical performance and longevity	2–11 years	9 randomised clinical trials	1998–2014	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	permanent molar and premolar teeth, with at least 2 years of follow-up												
Restoration support material													
Schenkel <i>et al.</i> (2019)	Compared the effects of using dental cavity liners with those of not using liners in the placement of Class I and Class II resin-based composite posterior restorations in permanent teeth in children and adults.	Class I and Class II resin-based composite posterior restorations in permanent teeth in children and adults	Germany, Saudi Arabia, Thailand, Turkey, and the USA	762 participants	Aged 15–52 years	Not reported	Dental cavity liner	No cavity liner	Pain or hypersensitivity at 1 week; Cold response; and Longevity at 1 or 2 years.	Longevity at 1 year	8 randomised controlled trials	2001–2013	Not known

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Reis <i>et al.</i> (2015)	Compared the effects of posterior resin composite restorations that were bonded using self-etching with posterior resin composite restorations that were bonded using etch-and-rinse adhesives on the risk and intensity of post-operative sensitivity in permanent dentition (posterior restorations) of adult patients.	Restoration of posterior teeth in permanent dentition of adult patients	Germany, Japan, Liechtenstein, and the USA	799 plus participants	Aged 23–57 years	28–60% male	Posterior resin composite restorations that were bonded using self-etching	Posterior resin composite restorations that were bonded using etch-and-rinse adhesives	Risk and intensity of post-operative sensitivity	Immediate	29 randomised clinical trials	1998–2013	Not reported
Restoration technique													

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Arcanjo Frota Barros <i>et al.</i> (2020)	Evaluated the risk or benefit (pulp exposure, dentine deposition, microbiological examination, quality of the restoration, and success of maintaining pulpal health) of selective caries removal for the treatment of dentinal caries in permanent teeth compared with non-selective (complete) or stepwise caries removal.	Dentinal caries in permanent teeth	Brazil, Indonesia, and Turkey	1,021 people (with 1,294 affected teeth)	Aged 4 to 53 years	45% male	Selective caries removal	Non-selective (complete) and stepwise (two-stage) caries removal	Risk or benefit (pulp exposure, dentine deposition, microbiological examination, quality of the restoration, and success of maintaining pulpal health) of selective caries removal	1–60 months	4 randomised controlled trials and 1 non-randomised trial	2008–2018	Not reported
Göstemeier <i>et al.</i> (2019)	Evaluated the efficacy of atraumatic restorative treatment compared with conventional restorative	Root carious lesions in permanent teeth of older adults	Colombia, Hong Kong, and Ireland	277 participants (with 636 lesions)	Aged 60–101 years	Not reported	Atraumatic restorative treatment	Conventional restorative treatment	Restoration failure and possible reasons for failure	6–24 months	3 randomised controlled trials	2006–2016	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	treatment for restoring root carious lesions in older adults.												
Solon de Mello <i>et al.</i> (2019)	Evaluated whether the survival rates of indirect restorations cemented with self-adhesive resin cement in permanent teeth are influenced by the presence or absence of selective enamel etching.	Permanent teeth	Not reported	65 participants	Aged 18–59 years	Not reported	Indirect restorations cemented with self-adhesive resin cement are influenced by the presence of selective enamel etching	Absence of selective enamel etching	Survival rate	48 and 78 months	2 randomised controlled trials	2012 and 2016	No response to queries
Deng <i>et al.</i> (2016)	Evaluated the effects of laser treatment of direct pulp capping in patients who required this treatment for their deep carious lesions on the success of restorations.	Deep carious lesions in permanent teeth	Not reported	534 participants	Aged 19–74 years	Not reported	Laser treatment of direct pulp capping in patients who required this treatment	Pulpectomy or pulpotomy	Success of restorations	6 months to 4 years	5 randomised controlled trials	1998–2016	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Mixed dentition													
Non-cavitated caries													
Non-invasive treatment													
Khijmatgar <i>et al.</i> (2020)	Evaluated the remineralisation potential of NovaMin compared with placebo or no intervention in humans with evidence of demineralisation (white spot lesions and/or cavitation) on teeth.	Treatment of (white spot lesions and/or cavitation) in human teeth	Not reported	48 participants	Not reported	Not reported	NovaMin	Placebo or no intervention (actually crest toothpaste)	Remineralisation potential	6 months	1 randomised controlled trial	2015	Yes 1 out of 1
Ma <i>et al.</i> (2019)	Evaluated the efficacy of casein phosphopeptide-amorphous calcium phosphate compared with no intervention or placebo for the	Humans with early enamel carious lesions or white spot lesions. Type of dentition not specified.	Denmark and Thailand	129 participants	Aged 2.5–18 years	45% and 54% male	Casein phosphopeptide-amorphous calcium phosphate	No intervention or placebo	Remineralisation	4 weeks–12 months	2 randomised controlled trials of interest	2014	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	remineralisation of white spot lesions.												
Chong <i>et al.</i> (2018)	Compared the retention, effectiveness, and safety of different types of slow-release fluoride devices on preventing, arresting, or reversing the progression of carious lesions on all surface types of primary (deciduous) and permanent teeth at 12 months following treatment.	Carious lesions on all surface types of primary and permanent teeth	UK	174 children	Mean age 8.8 years	Not reported	Slow-release fluoride devices	Placebo beads	Retention, effectiveness (preventing, arresting, or reversing), and safety	At 12 months	1 randomised controlled trial	2005	No

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Paula et al. (2017)	Compared different remineralisation agents (fluoride products, casein phosphopeptide-amorphous calcium phosphate, and ICON plc. resin) and techniques with each other for the treatment of white spot lesions in both permanent and primary teeth. There was no age cut-off, and both permanent and primary teeth were included.	Patients with white spot lesions in both permanent and primary teeth	Not reported	1,187 participants	Not reported	Not reported	Different remineralisation agents (fluoride products, casein phosphopeptide-amorphous calcium phosphate, and ICON plc. resin) and techniques	Each other	Remineralisation	1–20 months	13 randomised controlled trials	2006–2015	Not reported
Gao et al. (2016)	Compared professionally applied fluoride therapy with other active treatments, with placebo, or with no	Enamel carious lesions in primary and permanent teeth in children	Not reported	2,060 children	Not reported	Not reported	Professionally applied fluoride therapy	Other active treatments, with placebo, or with no intervention	Remineralising and arresting dental caries	1–36 months	17 randomised controlled trials	2001–2014	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	intervention in remineralising and arresting dental caries in primary and permanent teeth in children.												
Lenzi <i>et al.</i> (2016)	Evaluated the effectiveness of professional topical fluoride application (gels or varnishes) on the reversal of incipient enamel carious lesions in primary or permanent dentition in children.	Incipient enamel carious lesions in primary or permanent dentition in children	Brazil, Albania, and the USA	274 children	Mean age 3.4–11.7 years	Not reported	Professional topical fluoride application (gels or varnishes)	No intervention, or a placebo	Reversal of incipient enamel carious lesions	1–9 months	5 randomised clinical trials	2001–2015	Not reported
Li <i>et al.</i> (2014)	Compared the use of casein phosphopeptide-amorphous calcium phosphate in any modality with the use of fluoride toothpastes or	Early carious lesions in Adolescent s' teeth. Type of dentition not specified.	Not reported	2,367 participants	Aged 3.5–15 years	Not reported	Casein phosphopeptide-amorphous calcium phosphate in any modality	Fluoride toothpastes or mouthwashes, placebos, topical creams, and chewing gum	Remineralising effect on early carious lesions	6–24 months	2 randomised clinical trials and 1 controlled clinical trial of interest	2008–2012	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	mouthwashes, placebos, topical creams, and chewing gum in order to assess their long-term (>3 months) remineralising effect on early carious lesions.												
Microinvasive treatment													
Chen <i>et al.</i> (2021)	Evaluated the caries-arresting effectiveness of infiltration and sealing for proximal non-cavitated carious lesions and beyond, including different dentition types and caries risk levels in humans.	Proximal non-cavitated carious lesions and beyond, including different dentition types and caries risk levels in humans	Not reported	869 participants with 2,241 non-cavitated carious lesions	5–26 years	Not reported	Infiltration and sealing (mainly resin-based infiltration and sealants, one glass ionomer sealant)	Each other and with non-invasive treatments (placebo or no treatment)	Caries-arrest	12–84 months	17 randomised controlled trials	2005–2020	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Elrashid <i>et al.</i> (2019)	Evaluated the efficacy (clinical performance) of resin infiltration (compared with placebo or control material) on non-cavitated proximal carious lesions in primary and permanent teeth in humans.	Non-cavitated proximal carious lesions in primary and permanent teeth in humans	Not reported	263 participants (with more than 735 lesions)	Aged 5–41 years	Not reported	Resin infiltration	Placebo or control material: Fluoridated toothpaste and dental floss (1 primary study), fluoride varnish (1 primary study), or no treatment (3 primary studies)	Arrest and remineralisation	12–36 months	7 randomised controlled trials	2010–2017.	Not reported
Faghihian <i>et al.</i> (2019)	Evaluated the efficacy (clinical performance) of the resin infiltration technique in arresting initial caries progression in both primary and permanent teeth compared with control groups such as placebo, fluoride therapy, and	Early caries in primary and permanent teeth	Not reported	408 participants (238 children with 476 lesions and 170 adults with 684 lesions, or a total of 1,160 lesions)	Aged 5–41 years	Not reported	Resin infiltration technique	Placebo, fluoride therapy, and oral health instruction	Clinical performance (arresting initial caries progression)	12–24 months	8 randomised controlled trials	2010–2017	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	oral health instruction.												
Chatzimarkou <i>et al.</i> (2018)	The objective of this review was to provide a comprehensive synthesis of resin infiltration effects, in vivo, on early proximal carious lesions in primary and permanent teeth.	Early proximal carious lesions in primary and permanent teeth	Brazil, Colombia, Denmark, Germany, India, and the USA	291 participants and 997 lesions	Children's mean age 6–11 years; Adults mean age 21–25 years	25%–60% male	Resin infiltration	Other microinvasive treatment technique or non-invasive methods (control) such as dental floss, fluoride	Lesion progression	3–36 months	9 randomised controlled trials	2010–2018	Yes, 2 out of 9
Krois <i>et al.</i> (2018)	Evaluated microinvasive treatments compared with each other, non-invasive treatments, placebo or no	Early non-cavitated proximal carious lesions in primary and permanent	Brazil, Chile, Colombia, Denmark, Germany, Greenland, New	486 participants	Mean age 15 years	Not reported	Microinvasive treatments: (sealing and infiltration using resins or glass ionomer cements)	Each other, non-invasive treatments (e.g. fluoride), placebo or no treatment	Arrest caries progression	12–43 months	13 randomised controlled trials	2010–2017	Yes, 7 out of 13

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	treatment to arrest early non-cavitated proximal carious lesions in primary and permanent teeth of children, adolescents, and young adults.	teeth of children, adolescents, and young adults	Zealand, and Thailand										
Liang et al. (2018)	Compared the effectiveness of microinvasive interventions with non-invasive measures (e.g. fluoride), a placebo, or no treatment in arresting non-cavitated proximal carious lesions and analysed their effectiveness in acting on carious lesions	Non-cavitated proximal carious lesions of different depths ??	Not reported	303 participants	Aged 6.5–39 years	Not reported	Microinvasive interventions: resin sealant (which included adhesives and pit-and-fissure sealant), glass ionomer cement, and polyurethane tape	Non-invasive measures (e.g. fluoride), a placebo, or no treatment	Arresting non-cavitated proximal carious lesions, and the effectiveness of different interventions in acting on carious lesions of different depths	12–36 months	6 randomised controlled trials and 1 non-randomised trial	2005–2016	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	of different depths.												
Dorri et al. (2015)	Compared microinvasive treatments with non-invasive measures, invasive measures, no intervention, or a placebo for managing proximal carious lesions in primary and permanent dentition in children and adults.	Proximal carious lesions in primary and permanent dentition in children and adults	Brazil, Chile, Denmark, Germany, Greenland, and Thailand.	365 participants	Aged 4–39 years	Not reported	Microinvasive treatments: sealing and resin infiltration	Non-invasive measures, invasive measures, no intervention, or a placebo	Arrest of non-cavitated enamel and initial dentinal lesions at least 6 months following treatment, adverse events	6 months or over	8 randomised controlled trials	2005–2011	Yes, 4 out of 8

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Ammari et al. (2014)	Evaluated effectiveness (caries arrest and control) of sealing and/or infiltration compared with placebo or other materials or techniques to treat non-cavitated proximal lesions in primary and permanent teeth.	Children and adults with non-cavitated proximal caries, either in primary molar or posterior permanent teeth	Brazil, Chile, China, Colombia, Germany, Greenland, and the USA	451 participants (1,114 lesions)	Aged 4–39 years	Not reported	Sealing and/or infiltration: fissure sealants	Placebo in four studies, fluoride in three studies, and flossing in three studies	Caries arrest or progression	1–5 years	8 randomised controlled trials and 2 non-randomised trials	2005–2012	Not reported
Non-cavitated caries and cavitated													
Non-invasive treatment													
Marcelio Santos et al. (2020)	Evaluated the effectiveness (antimicrobial effect and lesion progression or regression) and safety (adverse events) of ozone therapy	Cavitated and non-cavitated dental caries in participants of any age	Germany, India, Saudi Arabia, Serbia, Sweden, Switzerland, Turkey,	696 participants with 1,284 lesions	5–82 years	49–65% male	Ozone therapy	No treatment, sham, or any other antibacterial intervention (including pharmacological and non-pharmacological treatments)	Antimicrobial effect, lesion progression or regression, adverse events	0–18 months	12 randomised controlled trials	2003–2020	Yes 1 out of 12

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	compared with no treatment, sham, or any other antibacterial intervention (including pharmacological and non-pharmacological treatments) for treating cavitated and non-cavitated dental caries in participants of any age.		and the UK										
Chibinski <i>et al.</i> (2017)	Evaluated the efficacy of silver diamine fluoride in controlling (arresting) caries progression in children's primary or permanent teeth when compared with active treatments	Children's primary (eight studies), mixed (two studies), or permanent (one study) molar dentition with caries	Not reported	4,328 children	3–15 years	Not reported	Different percentages of silver diamine fluoride (38%, 30%, and 12%) application at various frequencies (once-off, every 6 months, every year)	Active treatments (different doses of silver diamine fluoride, fluoride varnish, sealant, atraumatic restorative technique) or placebos (water or saline)	Arresting caries progression	12–36 months	11 randomised controlled trials	2002–2016	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	(different doses of silver diamine fluoride, fluoride varnish, sealant, atraumatic restorative technique) or placebos (water or saline).												
Gao <i>et al.</i> (2016b)	Evaluated the effectiveness of silver diamine fluoride in arresting dental caries in primary or permanent teeth in children, using prospective clinical studies.	Non-cavitated and cavitated carious lesions in primary or permanent teeth in children	Not reported	13,603 participants	Not reported	Not reported	Silver diamine fluoride: Various strengths of silver diamine fluoride were used in the retrieved literature: 14 studies used 38% silver diamine fluoride, 3 used 30% silver diamine fluoride, and 2 used 10% silver diamine fluoride	A negative control (no treatment) or a placebo (treatment with water)	Arresting dental caries	3–48 months	19 prospective clinical studies	1969–2016	Not reported
Microinvasive and													

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
invasive treatment													
de Amorim <i>et al.</i> (2018)	The authors evaluated the survival rate of atraumatic restorative treatment glass ionomer restorations and atraumatic restorative treatment sealants in primary and permanent posterior teeth.	Non-cavitated and cavitated carious lesions in primary and permanent posterior teeth	Argentina, Brazil, China, Ecuador, Egypt, Hong Kong, India, Iraq, Kuwait, Latvia, Malaysia, Mexico, Nigeria, Panama, Pakistan, South Africa, Suriname, Syria, Tanzania, Turkey, Uruguay, and Zimbabwe	Not reported	Aged 2–39 years	Not reported	Atraumatic restorative treatment with glass ionomer restorations and atraumatic restorative treatment using sealants	No comparator	Survival of single-surface and multiple-surface atraumatic restorative treatment restorations	1–3 years	34 clinical trials	1999–2017	Not reported
Non-invasive and microinva													

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
sive treatment													
Urquhart <i>et al.</i> (2019)	Compared non-restorative treatments with other active intervention(s), or with no treatment or a placebo, for the arrest or reversal of non-cavitated and cavitated carious lesions in primary and permanent teeth in children and adults.	Non-cavitated and cavitated carious lesions in primary and permanent teeth in children and adults	Australia, Brazil, Canada, Chile, China, Colombia, Cuba, Denmark, Estonia, Germany, Greenland, Hong Kong, India, Kuwait, Nepal, the Netherlands, Poland, Spain, Sweden, Thailand, the UK, and the USA	7,378 participants	Aged 2–83 years	Not reported	Non-restorative treatments: Sodium fluoride, stannous fluoride toothpaste or gel, acidulated phosphate fluoride, difluorsilane, ammonium fluoride, polyols, chlorhexidine, calcium phosphate, amorphous calcium phosphate (ACP), casein phosphopeptide-ACP (CPP-ACP), nano hydroxyapatite, tricalcium phosphate, prebiotics and/or 1.5%	Other active intervention(s), or with no treatment or a placebo	Arrest or reversal	Varied by outcome	43 randomised controlled trials	1984–2018	Yes, 9 out of 43

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
							arginine, probiotics, silver diamine fluoride, silver nitrate, lasers, resin infiltration, sealants, sodium bicarbonate, calcium hydroxide, and carbamide peroxide						
Microinvasive and restorative treatment													

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Marzouk <i>et al.</i> (2019)	Evaluated bisphenol A exposure in humans from resin-based dental sealants and restorations which contain bisphenol A glycidyl methacrylate by retrieving all clinical studies that measured urinary BPA (uBPA) concentrations in patients before and after resin-based dental treatments. In addition, the authors explored the degree to which baseline bisphenol A concentrations were associated with prior resin-	Humans	Brazil, Republic of Korea (South), and the USA.	348 participants	4 were of children ; and 1 study included adolescents and adults	Not reported	Resin-based dental sealants and restorations which contain bisphenol A glycidyl methacrylate	Before and after	Urinary bisphenol A (uBPA) concentrations	24 hours after treatment to 1 month	7 prospective clinical studies	2005–2017	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	based dental treatments.												
Paula et al. (2019)	Estimated the release of bisphenol A, after the use of composite resins and/or dental sealants, to determine if the increase is higher than the acceptable daily exposure and may cause harmful effects to the health of children, adolescents, and pregnant adults. However, harmful effects were not examined.	Children, adolescents, and pregnant adults who were prescribed these interventions	Not reported	4 to 1,001 patients, with a mean of 171.6 participants (and ± 268.19 standard deviations)	Children to adults aged 55 years	Not reported	Release of bisphenol A following the use of composite resins and/or dental sealants	No comparator	Estimated the release of bisphenol A compared to acceptable daily exposure and adverse or harmful events (no data)	From treatment to 1 week	16 randomised controlled trials, 3 prospective cohort studies, and 1 case-control studies	1996–2018	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Treatment technique													
Wang et al. (2016)	Compared the effects (survival and failure) of rubber dam isolation compared with other types of isolation (cotton roll) used for direct and indirect restorative treatments in children's molars.	Direct and indirect restorative treatments in children's primary or permanent molars or premolars	Brazil, China, Germany, and Kenya	1,270 participants	Aged 5.9 to 16.9 years	60% male	Rubber dam isolation	Other types of isolation (cotton roll)	Survival and failure rates and adverse events	6 and 24 months	4 randomised controlled trials	2010–2013	Yes, not clear how many
Cavitated caries													
Direct restoration material													
Arbildo-Vega et al. (2020)	Evaluated the clinical performance (based on 11 parameters) of bulk-fill direct resin composites used in direct restorations in	Direct restorations in human teeth	Brazil, Denmark, Germany, Saudi Arabia, Sweden, and Turkey	764 participants and 1,915 teeth	Mean age ranged 7.4–55.3 years	47% male	Bulk-fill direct resin composites	Conventional direct resin composites	Clinical performance (based on 11 parameters)	6 months to 10 years	16 randomised controlled studies	2010–2020	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	human teeth and compared them with conventional direct resin composites.												
Kielbassa <i>et al.</i> (2016 and 2017)	Compared the clinical performance of high-viscosity glass ionomer cement covered with a resinous coating with the use of amalgam (no studies), resin composite, or other glass ionomer cements in Class I and Class II restorations of posterior primary or permanent teeth.	Class I and Class II restorations of posterior primary or permanent teeth	Not reported	784 participants and 1,395 teeth	Not reported	Not reported	High-viscosity glass ionomer cement covered with a resinous coating	Amalgam (no studies), resin composite, or other glass ionomer cements	Clinical performance: Colour match and success at	3 or 4 years	3 trials with quality assessment completed	2014–2016	Yes, 2 out of 3
Restoration support material													

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Elkady <i>et al.</i> 2020	Evaluated the effect of chlorhexidine as a cavity pretreatment or mix-in on the survival of atraumatic restorative treatments in primary or permanent teeth with occlusal or occlusoproximal cavities.	Primary or permanent teeth with occlusal or occlusoproximal cavities	Egypt and Brazil	261 patients and 467 treated teeth	Mean age ranged 3.84–14.6 years	Not reported	Chlorhexidine as a cavity pretreatment or mix-in on the survival of atraumatic restorative treatments	No treatment	Survival	1 year	4 randomised controlled trials	2009–2019	Not reported
Da Rosa <i>et al.</i> (2019)	Evaluated the role of calcium hydroxide liner in the treatment of deep carious lesions in primary or permanent teeth with respect to restoration failure.	Deep carious lesions in primary or permanent teeth	Not reported	567 subjects and 1,036 teeth	Aged 3–12 years	Not reported	Calcium hydroxide liner	No liner	Restoration failure	3–60 months	14 randomised controlled trials and 1 retrospective study	2002–2017	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Göstemeier and Schwendicke (2016)	Evaluated the risk of retention loss and failure of adhesively placed resin-based restorations after degradation inhibitory cavity pretreatment with chlorhexidine, ethanol wet-bonding, or quaternary ammonium compounds compared with no treatment, placebo, or alternative pretreatments.	Primary or permanent teeth receiving adhesively placed resin-based restoration	Brazil, Iran, Mexico, and Turkey	209 adults and children and 709 teeth	Aged 8–9 years	Not reported	Adhesively placed resin-based restorations after degradation inhibitory cavity pretreatment with chlorhexidine, or ethanol wet-bonding, or quaternary ammonium compounds	No treatment, placebo, or alternative pretreatments	Risk of retention loss and failure	6–36 months	10 randomised controlled trials	2005–2015	Not reported
Schwendicke <i>et al.</i> (2015b)	Compared the antibacterial effects of different cavity liners with each other, a placebo, or no liner.	There was no age limit and any type of teeth could be included.	Not reported	457 participants and 500 treated carious lesions	Aged 4–67 years	Not reported	Different cavity liners: calcium hydroxide, mineral trioxide aggregate, antibiotic/disinfectant, calcium phosphates, zinc oxide	Each other, a placebo, or no liner	Number of and reduction in positive bacterial dentine samples remaining in a cavity	1 day–24 months	11 randomised controlled trials and 3 non-randomised trials	1998–2013	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
							eugenol, black copper cement, and glass ionomer cement liners						
Pereira-Cenci <i>et al.</i> (2013)	Compared antibacterial agents incorporated into composite restorations with composite restorations containing no antibacterial agents for the prevention of negative clinical outcomes.	Adults and adolescents in any age group with restorations in the permanent dentition, and children with restorations in the primary dentition	No trials met the inclusion criteria	No trials met the inclusion criteria	No trials met the inclusion criteria	No trials met the inclusion criteria	Composite restorations consist of two major components: a resin composite for filling and the bonding systems to be applied to the cavity before the placement of filling materials. The incorporation of antibacterial substances in these two components would have different roles relating to the prevention of the harmful	Composite restorations and bonding agent containing no antibacterial agents	Longevity of restorations (failure or success); post-operative sensitivity, marginal adaptation, anatomic form, and other clinical outcomes (tooth vitality and pulpitis); patient satisfaction	Not predetermined	No trials met the inclusion criteria	No trials met the inclusion criteria	No trials met the inclusion criteria

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
							effects caused by bacteria within the biofilm covering the tooth/restoration interface						
Restoration material and support material													

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Schwendicke <i>et al.</i> (2016)	Compared the survival of combinations of adhesive and restorative materials placed in one of two types of cavitated lesions (cervical cavitated lesions or load-bearing posterior cavitated lesions) with each other in permanent and primary teeth. The lesions may or may not be due to caries.	Adults and children with cervical cavitated lesions and load-bearing posterior cavitated lesions in permanent and primary teeth	Not reported	3,633 patients and 11,070 restorations (5,330 cervical and 5,740 load bearing)	Not reported	Not reported	Combinations of adhesive ((1) Four- or three-step etch-and-rinse, (2) two-step etch-and-rinse, (3) two-step self-etch, (4) one-step self-etch, and (5) no adhesive used) and restorative materials((1) conventional composite resin (nanofilled, microfilled, and hybrid) (2) ormocer, (3) bulk fill (flowable and packable), (4) siloranes. (5) compomer, (6) amalgam, and (7) glass ionomer cements or resin-modified glass ionomer	Each other	Survival and annual failure rates	12 months–13 years	72 randomised controlled trials	2005–2015	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
							cements were assessed).						
Restoration technique													
Cardoso et al. (2020)	Evaluated the efficiency (time for treatment, caries removal, anaesthesia, and colony-forming units count) of alternative methods (chemomechanical methods, laser, and air-	Primary and permanent decayed teeth with dentine lesions in humans	Not reported	1,600 patients	Aged 3–84 years	Not reported	Alternative methods (chemomechanical methods, laser, and air-and/or sono-abrasion) for caries removal	Conventional mechanical method (rotary or hand instruments) and each other	Time for treatment, caries removal, anaesthesia, and colony-forming units count	Not reported	37 controlled trials	2000–2020	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	and/or sono-abrasion) for caries removal, compared with the conventional mechanical method (rotary or hand instruments), for removing dental caries from primary and permanent decayed teeth.												
Zhang <i>et al.</i> (2020)	Evaluated the extent of microleakage from tooth cavities in humans prepared by Er,Cr:YSGG lasers compared with microleakage from cavities prepared by traditional burs, and the effectiveness of acid etching on	Tooth cavities in primary and permanent teeth prepared for restoration	Brazil, Germany, Iran, Spain, and Turkey	1243 teeth	Not reported	Not reported	1.Er,Cr:YSGG lasers; 2. Acid etching when using the Er,Cr:YSGG laser	1. Traditional burs; 2. No acid etching when using the Er,Cr:YSGG laser	Microleakage	Not reported	13 randomised or quasi-randomised trials	2001–2018	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	the adhesive potential of self-etch and etch-and-rinse adhesives after laser preparation compared with no etching.												
Li <i>et al.</i> (2019)	Evaluated the clinical efficacy (operation time, pain, and long-term outcomes) of the Er:YAG laser for caries removal and cavity preparation in children compared with that of the conventional mechanical method.	Caries removal and cavity preparation in children	Not reported	327 participants	Aged 3–16 years	Not reported	Er:YAG laser	Conventional mechanical method	Operation time, pain, and long-term outcomes	Immediate for some outcomes, but unclear for longer-term outcomes	7 randomised controlled trials	2006–2016	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Cianetti <i>et al.</i> (2017)	Evaluated the effectiveness (treatment time, need for anaesthesia, clinical performance and pulpal complications) and degree of acceptance (pain, discomfort, and fear) by children and adolescents of the use of Sonic and ultrasonic devices with oscillating tips compared with conventional rotating drills to remove carious tissue from primary or permanent teeth.	Carious tissue removal from primary or permanent teeth in children and adults	China and Poland	103 children	Aged 2–12 years	Not reported	Sonic and ultrasonic devices with oscillating tips	Conventional rotating drills	Dental caries removal, dental anxiety, pain, discomfort, patients' preference, duration of treatment, and durability of restoration	Immediate for some outcomes, 6 months for longer-term outcomes	2 non-randomised controlled clinical trials	2004 and 2010	No response to queries

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Dorri et al. (2017)	Compared atraumatic restorative treatment with conventional treatment (the drill and fill approach) for managing dental carious lesions in the primary and permanent teeth of children and adults.	Dental carious lesions in the primary and permanent teeth of children and adults	Brazil, China, Colombia, Indonesia, Ireland, Suriname, Tanzania, and Turkey	3,760 participants	Aged 3–101 years	48% male	Atraumatic restorative treatment	Conventional treatment (the drill and fill approach)	Restoration failure, pain during and around procedure, and adverse events	6–24 months	15 randomised controlled trials	2003–2016	Yes, 4 out of 15
Tao et al. (2017)	Evaluated the comparative clinical success (restoration loss, pulpal vitality, and post-operative sensitivity) and efficacy (procedure time, requirement for anaesthesia and acceptability) of erbium laser, compared with	Individuals with carious lesions	Bulgaria, China, Germany, India, Taiwan, Turkey, the UK, and the USA	1,646 teeth	Aged 3–84 years	45% male.	Erbium laser	Traditional drilling	Restoration loss, pulpal vitality, post-operative sensitivity, procedure time, requirement for anaesthesia and acceptability	Immediate for some outcomes, 3 months to 2 years for longer-term outcomes	14 trials with a variety of designs comprising randomised controlled trials, quasi-randomised controlled trials, or	1997–2015	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	traditional drilling, in individuals with carious lesions.										controlled clinical trials		
Montedori <i>et al.</i> (2016)	Compared laser-based methods with conventional mechanical methods for removing dental caries in deciduous and permanent teeth measuring the outcomes pain, anaesthesia, durability of restoration, pulp damage.	Cavitated deciduous and permanent teeth	Bulgaria, Germany, Taiwan, Turkey, the United Kingdom (UK), and the USA	662 participants	Aged 3.5–84 years	22– 63% male	Laser-based methods for removing dental caries	Conventional mechanical methods: a handpiece with a bur, the chemomechanical system, the sono-abrasion system, and the air-abrasion system	Pain, anaesthesia, marginal integrity, durability of restoration, recurrent caries, pulp damage	Varied by outcome	9 randomised controlled trials	1998–2014.	Yes, 5 out of 9

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Hamama <i>et al.</i> (2015)	Compared the time required for chemomechanical (sodium hypochlorite-based agent, known as Carisolv, and enzyme-based agent, known as Papacarie) caries removal with the other conventional caries removal methods in primary and permanent teeth.	Cavitated primary and permanent molar teeth	Asia (Egypt, India, Pakistan), Europe, North America (the USA), and South America.	1,909 teeth	Not reported	Not reported	Chemomechanical (sodium hypochlorite-based agent, known as Carisolv, and enzyme-based agent, known as Papacarie) caries removal	Other conventional caries removal methods	Time required	1 week to 24 months	19 randomised clinical trials	2003–2012	Not reported
Schwendicke <i>et al.</i> (2015)	Evaluated and compared the effects (with respect to risk of complications, pain, time required for excavation, and/or number of bacteria remaining) of	Natural primary or secondary carious lesions in primary or permanent teeth with excavated caries	Not reported	1,782 patients (2,555 carious lesions)	Not reported	Not reported	Different criteria used for caries excavation: State of dentine, Method of caries removal,	Each other	Risk of complications, pain, time required for excavation, and/or number of bacteria remaining	Not predetermined	19 randomised controlled trials and 9 non-randomised controlled trials	1993–2014	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	using different criteria for caries removal in primary and permanent teeth.												
Li et al. (2014)	Evaluated CariSolv for chemomechanical caries removal from primary or permanent teeth, compared with the conventional rotary instrument, for the outcomes complete caries removal rate, the treatment time (in minutes), and the use of local anaesthesia.	Caries removal from primary or permanent teeth	Not reported	426 children and 578 teeth	Children aged 3–17 years and adults aged 18–84 years	50–55% male	Chemomechanical caries removal	Conventional rotary instrument	Complete caries removal rate, the treatment time (in minutes), and the use of local anaesthesia	Immediate for some outcomes, but unclear for longer-term outcomes	6 randomised controlled trials	1999–2009	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Schwendicke <i>et al.</i> (2013)	Compared one- or two-step incomplete removal with complete caries removal of primary or permanent teeth with primary carious lesions requiring a restoration with respect to risk of pulpal exposure, post-operative pulpal symptoms, overall failure, and caries progression.	Primary dentine caries in primary or permanent teeth	Brazil, Germany, Scandinavia, Scotland, Thailand, Turkey, and the USA	1,257 patients and 1,628 teeth	Not reported	Not reported	One- or two-step incomplete removal	Complete caries removal	Risk of pulpal exposure, post-operative pulpal symptoms, overall failure, and caries progression	6 months–10 years	10 randomised controlled trials	1977–2012	Not reported
Permanent dentition													
Non-carious cervical lesions													
Factors influencing direct restoration material													

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
de Oliveira Correia <i>et al.</i> (2020)	Evaluated how tooth- and cavity-related properties of non-carious cervical lesions in humans' permanent teeth that already had resin composite restorations affect the retention of such restorations.	Non-carious cervical lesions in humans' permanent teeth that already had resin composite restorations	Not reported	962 participants and 3,129 restorations	Aged 18–84 years	Not reported	Tooth- and cavity-related properties	Each other	Restoration retention rate	At 2 years and beyond	24 randomised clinical trials	1993–2019	Not reported
Direct restoration material													
Bezerra <i>et al.</i> (2020)	The study evaluated, through a systematic review and meta-analysis, the clinical performance/longevity of composite resin restorations and glass ionomer cements	Adults with non-carious cervical lesions	Not reported	352 participants and 1914 lesions	Not reported	Not reported	Composite resin restorations	Glass ionomer cements restorations	Clinical performance/longevity (based on seven parameters)	12–60 months	10 randomised and 5 non-randomised controlled trials	1995–2019	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	restorations used in adults with non-carious cervical lesions.												
Boing <i>et al.</i> (2018)	Compared retention and colour match of glass ionomer cement restorations with resin-based composite restorations in non-carious cervical lesions in the permanent teeth of adults.	Resin-based composite restorations in non-carious cervical lesions in the permanent teeth of adults	Not reported	321 plus and the number of restorations was 1,640	Aged 18–88 years	Vast majority were female	Glass ionomer cement restorations	Resin-based composite restorations	Retention and colour match. Other outcomes included surface texture, marginal adaptation, marginal discolouration, and secondary caries	1–10 years; more commonly 1, 2, or 3 years	15 randomised controlled trials	1988–2014	Not reported
Szesz <i>et al.</i> (2017)	Compared flowable resin composite restorations with regular (or conventional) resin composites for improving the marginal adaptation, marginal	Restorations placed in non-carious cervical lesions in permanent adult teeth	Germany, Japan, Liechtenstein, and the USA	262 participants	Aged 28–81 years	Majority were female	Flowable resin composite restorations	Conventional resin composites	Marginal adaptation, marginal discolouration, and retention rates of restorations	1–3 years	8 randomised controlled trials	2003–2012	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	discolouration, and retention rates of restorations placed in non-carious cervical lesions in permanent adult teeth.												
Restoration support material													
De Assis <i>et al.</i> (2020)	Evaluated whether there are any differences in clinical performance (including retention) between one-step self-etching and two-step self-etching adhesive systems in non-carious cervical lesions.	Adults with non-carious cervical lesions	Not reported	237 patients and 822 restorations	Mean age 45 years	Not reported	One-step self-etching adhesive systems	Two-step self-etching adhesive systems	Clinical performance (including retention)	Mean follow-up time was 18 months	5 randomised clinical trials	2005–2016	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Lins <i>et al.</i> (2020)	Assessed whether the type of solvent (acetone-based compared with alcohol-based) in dental adhesives for composite resin restorations influences the clinical performance (including survival and 10 other parameters) of composite restorations placed in adults with non-carious cervical lesions (Class V restorations).	Adults with non-carious cervical lesions (requiring Class V restorations)	Australia, Belgium, Brazil, Egypt, Germany, Italy, Japan, Sweden, Turkey, and the USA	3,959 dental restorations in 1,087 adults	Not reported	Not reported	Acetone-based solvent in dental adhesives for composite resin restorations	Alcohol-based solvent in dental adhesives for composite resin restorations	Survival and 10 other parameters	18–72 months	27 randomised controlled clinical trials	2001–2019	Not reported
Mara de Paula <i>et al.</i> (2019)	Evaluated whether the retention rates of non-carious cervical lesion restorations in adults permanent	Non-carious cervical lesion restorations in adults permanent teeth	Not reported	112 adults and 429 restorations	Aged 22–73 years	Not reported	Composite resin restoration using sandwich technique (a lining of glass ionomer cement or resin-modified	Composite resin	Retention rates	12–36 months	4 randomised controlled trials	1991–2016	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	teeth that used the sandwich technique (a lining of glass ionomer cement or resin-modified glass ionomer cement) were greater than those of composite resin only restorations.						glass ionomer cement)						
Sousa Pamplona da Silva <i>et al.</i> (2018)	Compared 2-hydroxyethyl methacrylate (HEMA)-free adhesive systems with HEMA-containing systems to treat non-carious cervical lesions in permanent teeth in adults.	Treat non-carious cervical lesions in permanent teeth in adults	Belgium, Brazil, China, Denmark, Germany, Italy, Japan, Serbia, Sweden, Turkey, and the USA	997 adults	Mean age range 46–64.7 years	Not reported	HEMA-free adhesive	HEMA-containing adhesive	Retention, marginal adaptation, marginal discolouration, secondary caries, and post-operative sensitivity	1–13 years	22 randomised controlled trials	1994–2016	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
Schroeder <i>et al.</i> (2017)	Compared composite restorations in non-carious cervical lesions in adults' permanent teeth bonded using self-etch adhesives with composite restorations bonded using etch-and-rinse adhesives for post-operative sensitivity, retention rates, and marginal discolouration.	Composite restorations in non-carious cervical lesions in adults' permanent teeth	Germany, Japan, Korea, Liechtenstein, Switzerland, and the USA	1,486 participants	Mean age range 35–61 years	33–75% male	Composite restorations bonded using self-etch adhesives	Composite restorations bonded using etch-and-rinse adhesives	Post-operative sensitivity, retention rates, and marginal discolouration	1– 8 years	42 randomised controlled trials	2003–2015	Not reported
Moraes Coelho Santos <i>et al.</i> (2014)	Assessed the effect of different adhesive systems, surface treatments, and tooth preparation techniques on the retention of tooth-coloured	Tooth-coloured restorative materials placed in non-carious cervical lesions	Not reported	1,249 adults (with 1,674 restorations)	Aged 18–88 years	Not reported	Different adhesive systems, surface treatments, and tooth preparation techniques to place tooth-coloured restorative materials	Each other	Retention	3 years or longer follow-up period	27 randomised clinical studies	1991–2013.	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	restorative materials placed in non-carious cervical lesions.												
Chee et al. (2012)	Compared simplified adhesives (two-step self-etch and one-step self-etch) with conventional adhesives (three-step etch-and-rinse and two-step etch-and-rinse) for treatment of non-carious cervical lesions in the permanent teeth of adults.	Treatment of non-carious cervical lesions in the permanent teeth of adults	Not reported	1,032 adults	Mean age range 45–61.8 years	Not reported	Simplified adhesives (two-step self-etch and one-step self-etch)	Conventional adhesives (three-step etch-and-rinse and two-step etch-and-rinse)	Restoration retention or loss, marginal adaptation, and marginal discolouration	18 months–8 years	26 randomised controlled trials	1996–2011	Not reported
Restoration technique													
Rocha et al. 2018 131	Evaluated the influence of different dentine surface treatments on the retention	Resin composite restorations in non-carious	Brazil, Chile, Turkey, and the USA.	299 participants (with 947 restorations)	Aged 20–80 years	59% male	Different dentine surface treatments prior to placing composite restorations	Each other	Retention of resin composite restoration	18 months–8 years	7 randomised clinical trials	2010–2015	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	rate of resin composite restorations in non-carious cervical lesions.	cervical lesions											
Szesz <i>et al.</i> (2016)	Compared selective etching of enamel margins with no etching to improve the retention rates and marginal discolouration of cervical composite restorations in non-carious cervical lesions in permanent teeth of adults.	Composite restorations in non-carious cervical lesions in permanent teeth of adults	Germany, Japan, Liechtenstein, and the USA	242 participants	Aged 18–78 years	27–61% male	Selective etching of enamel margins prior to placing composite restorations	No etching	Marginal adaptation, discolouration, and retention	1–5 years	10 randomised controlled trials	2005–2014	Not reported
Schroeder <i>et al.</i> (2015)	Compared enamel bevelling with no enamel bevelling to improve the retention of composite restorations in non-carious cervical lesions	Composite restorations in non-carious cervical lesions in the permanent teeth of adult patients	Germany, Liechtenstein, and the USA.	164 participants	Aged 22–59 years	Not reported	Enamel bevelling prior to placing composite restorations	No enamel bevelling	Retention of composite restorations and marginal discolouration	12–18 months	4 randomised controlled trials	2003–2013	Not reported

Author (year)	Research question	Study population (s) (dentition and tooth type)	Countries	Sample size	Ages	Gender	Study intervention(s)	Study comparator(s)	Study outcome(s)	Time frame for follow-up (actual)	Primary study design included	Primary study years	Industry funding for primary studies
	in the permanent teeth of adult patients.												
Qin et al. (2014)	Compared the clinical effectiveness (retention, marginal defects and marginal discolouration) of self-etching adhesives, with or without previous enamel bevelling and selective phosphoric acid etching, in restorations of non-carious cervical lesions in adults permanent teeth.	Restorations of non-carious cervical lesions in adults permanent teeth	Not reported	744 teeth	Not reported	Not reported	Self-etching adhesives with previous enamel bevelling and selective phosphoric acid etching	Self-etching adhesives without previous enamel bevelling and selective phosphoric acid etching in restorations	Retention, marginal defects and marginal discolouration	2–8 years	8 randomised controlled trials	1993–2011	Not reported

Appendix O: American Dental Association clinical guidelines for non-invasive treatment of non-cavitated caries and cavitated

Permanent teeth³⁰⁵


Evidence-Based Clinical Practice Guideline on Nonrestorative Treatments for Carious Lesions:
 A Report from the American Dental Association

Summary of clinical recommendations for the nonrestorative treatment of caries on permanent teeth

GRADE Certainty in the Evidence

High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect.
Low	Our confidence in the effect estimate is limited.
Very Low	We have very little confidence in the effect estimate.

GRADE Interpretation of Strength of Recommendations

Implications	Strong Recommendations	Conditional Recommendations
For Patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For Clinicians	Most individuals should receive the intervention.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences.
For Policy Makers	The recommendation can be adapted as policy in most situations.	Policy making will require substantial debate and involvement of various stakeholders.

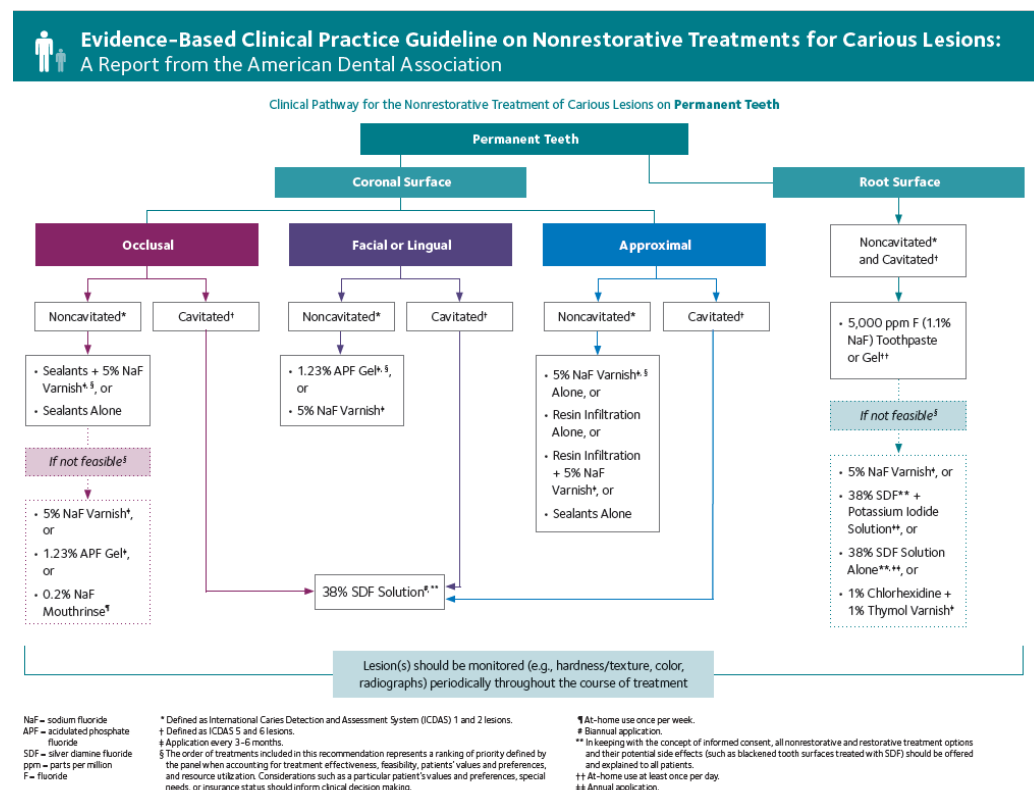



Expert Panel Recommendation	Certainty in the Evidence	Strength of Recommendation
To arrest advanced cavitated carious lesions on any coronal surface of permanent teeth, the expert panel suggests clinicians* prioritize the use of 38% silver diamine fluoride (SDF) solution (biannual application) over 5% sodium fluoride varnish (application once per week for 3 weeks).†	Low	Conditional
To arrest or reverse noncavitated carious lesions on occlusal surfaces of permanent teeth, the expert panel recommends clinicians* prioritize the use of sealants + 5% sodium fluoride varnish (application every 3–6 months) or sealants alone over 5% sodium fluoride varnish alone (application every 3–6 months), 1.23% acidulated phosphate fluoride gel (application every 3–6 months), or 0.2% sodium fluoride mouthrinse (once per week).‡	Moderate	Strong
To arrest or reverse noncavitated carious lesions on facial or lingual surfaces of permanent teeth, the expert panel suggests clinicians* use 1.23% acidulated phosphate fluoride gel (application every 3–6 months) or 5% sodium fluoride varnish (application every 3–6 months).‡	Moderate to Low	Conditional
To arrest or reverse noncavitated carious lesions on approximal surfaces of permanent teeth, the expert panel suggests clinicians* use 5% sodium fluoride varnish (application every 3–6 months), resin infiltration alone, resin infiltration + 5% sodium fluoride varnish (application every 3–6 months), or sealants alone.‡	Low to Very Low	Conditional
To arrest or reverse noncavitated and cavitated carious lesions on root surfaces of permanent teeth, the expert panel suggests clinicians* prioritize the use of 5,000 ppm fluoride (1.1% sodium fluoride) toothpaste or gel (at least once per day) over 5% sodium fluoride varnish (application every 3–6 months), 38% SDF + potassium iodide solution (annual application), 38% SDF solution (annual application), or 1% chlorhexidine + 1% thymol varnish (application every 3–6 months).‡,§	Low	Conditional
To arrest or reverse noncavitated carious lesions on coronal surfaces of permanent teeth, the expert panel suggests clinicians* do not use 10% casein phosphopeptide-amorphous calcium phosphate paste if other fluoride interventions, sealants, or resin infiltration is accessible.	Low	Conditional

SDF = silver diamine fluoride
ppm = parts per million
* Clinicians refers to the target audience for this guideline, but only those authorized/trained to perform the specified interventions should do so.
† In keeping with the concept of informed consent, all nonrestorative and restorative treatment options and their potential side effects (such as blackened tooth surfaces treated with silver diamine fluoride) should be offered and explained to all patients.
‡ The order of treatments included in this recommendation represents a ranking of priority defined by the panel when accounting for treatment effectiveness, feasibility, patients' values and preferences, and resource utilization. Considerations such as a particular patient's values and preferences, special needs, or insurance status should inform clinical decision making.

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ADA Center for Evidence-Based Dentistry™



Source: American Dental Association³⁰⁵



Evidence-Based Clinical Practice Guideline on Nonrestorative Treatments for Carious Lesions: A Report from the American Dental Association

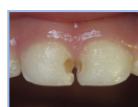
Summary of clinical recommendations for the nonrestorative treatment of caries on **primary teeth**

GRADE Certainty in the Evidence

High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect.
Low	Our confidence in the effect estimate is limited.
Very Low	We have very little confidence in the effect estimate.

GRADE Interpretation of Strength of Recommendations

Implications	Strong Recommendations	Conditional Recommendations
For Patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For Clinicians	Most individuals should receive the intervention.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences.
For Policy Makers	The recommendation can be adapted as policy in most situations.	Policy making will require substantial debate and involvement of various stakeholders.



Expert Panel Recommendation

To arrest advanced cavitated carious lesions on any coronal surface of primary teeth, the expert panel recommends clinicians* prioritize the use of 38% silver diamine fluoride (SDF) solution (biannual application) over 5% sodium fluoride varnish (application once per week for 3 weeks).†

Certainty in the Evidence

Strength of Recommendation

To arrest or reverse noncavitated carious lesions on occlusal surfaces of primary teeth, the expert panel recommends clinicians* prioritize the use of sealants + 5% sodium fluoride varnish (application every 3–6 months) or sealants alone over 5% sodium fluoride varnish alone (application every 3–6 months), 1.23% acidulated phosphate fluoride gel (application every 3–6 months), resin infiltration + 5% sodium fluoride varnish (application every 3–6 months), or 0.2% sodium fluoride mouthrinse (once per week).‡

Certainty in the Evidence

Strength of Recommendation

To arrest or reverse noncavitated carious lesions on facial or lingual surfaces of primary teeth, the expert panel suggests clinicians* use 1.23% acidulated phosphate fluoride gel (application every 3–6 months) or 5% sodium fluoride varnish (application every 3–6 months).‡

Certainty in the Evidence

Strength of Recommendation

To arrest or reverse noncavitated carious lesions on approximal surfaces of primary teeth, the expert panel suggests clinicians* use 5% sodium fluoride varnish (application every 3–6 months), resin infiltration alone, resin infiltration + 5% sodium fluoride varnish (application every 3–6 months), or sealants alone.‡

Certainty in the Evidence

Strength of Recommendation

To arrest or reverse noncavitated carious lesions on coronal surfaces of primary teeth, the expert panel suggests clinicians* do not use 10% casein phosphopeptide-amorphous calcium phosphate paste if other fluoride interventions, sealants, or resin infiltration is accessible.

Certainty in the Evidence

Strength of Recommendation

SDF = silver diamine fluoride

Clinicians refers to the target audience for this guideline, but only those authorized/trained to perform the specified interventions should do so.

†In keeping with the concept of informed consent, all nonrestorative and restorative treatment options and their potential side effects (such as blackened tooth surfaces treated with silver diamine fluoride) should be offered and explained to all patients.

‡The order of treatments included in this recommendation represents a ranking of priority defined by the panel when accounting for treatment effectiveness, feasibility, patients' values and preferences, and resource utilization. Considerations such as a particular patient's values and preferences, special needs, or insurance status should inform clinical decision making.

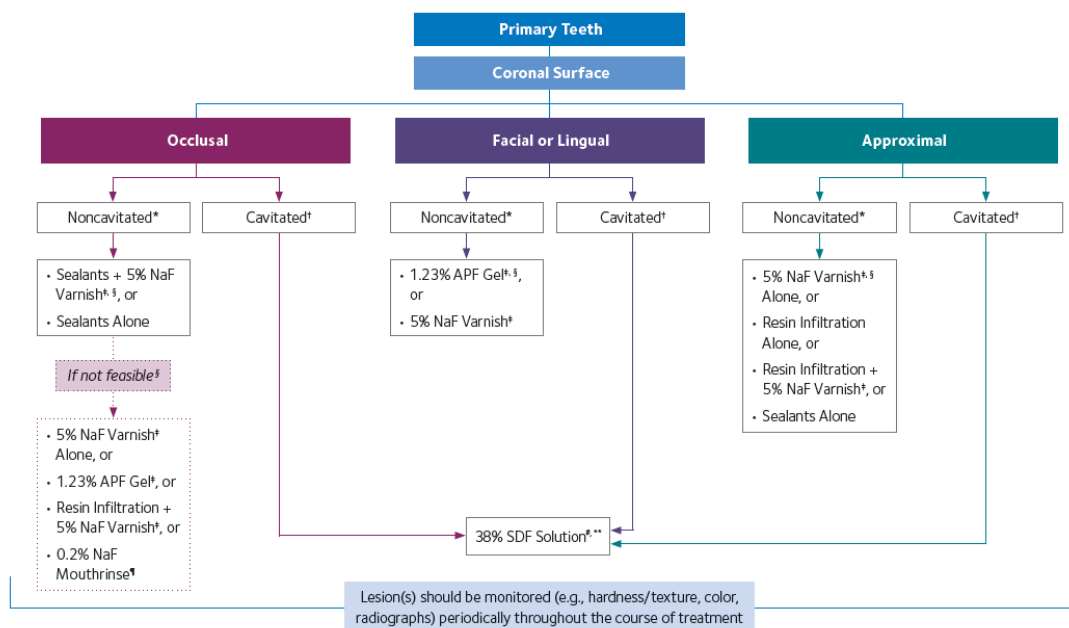
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Evidence-Based Clinical Practice Guideline on Nonrestorative Treatments for Carious Lesions: A Report from the American Dental Association

Clinical Pathway for the Nonrestorative Treatment of Carious Lesions on **Primary Teeth**



NaF = sodium fluoride
APF = acidulated phosphate fluoride
SDF = silver diamine fluoride

* Defined as International Caries Detection and Assessment System (ICDAS) 1 and 2 lesions.

† Defined as ICDAS 5 and 6 lesions.

‡ Application every 3–6 months.

§ The order of treatments included in this recommendation represents a ranking of priority defined by the panel when accounting for treatment effectiveness, feasibility, patients' values and preferences, and resource utilization. Considerations such as a particular patient's values and preferences, special needs, or insurance status should inform clinical decision making.

¶ At-home use once per week.

• Biannual application.

**In keeping with the concept of informed consent, all nonrestorative and restorative treatment options and their potential side effects (such as blackened tooth surfaces treated with SDF) should be offered and explained to all patients.

