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# Impact assesment of the All-Ireland Cooperative Oncology Research Group

**Final report**

## **Impact assessment of ICORG**

Final report

technopolis |group|, March, 2012

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# Executive summary

## Introduction

The All-Ireland Cooperative Oncology Research Group (ICORG) was set up in 1996 to create more research opportunities for clinical trials in the field of oncology. Up until 2011, ICORG has received €36.5 million to build capacity for cancer clinical trials in Ireland from the Health Research Board (HRB). Besides funding from HRB, ICORG also receives funding from the Irish Cancer Society. ICORG is based on the co-operative group model, with a large number of hospitals participating in the HRB funded programme. ICORG is coordinated by its group central office (GCO), which also received a grant to develop its capacity.

The HRB asked Technopolis to perform an impact assessment of ICORG and get a better understanding of the environment that ICORG operates in. This assessment should provide information for an internal funding decision and whether or not the HRB's strategic objectives of ICORG funding should be revised or extrapolated in any way after 2012.

The specific objectives of the impact assessment are:

- To assess the impact of ICORG on cancer clinical research in Ireland.
- To capture impacts of ICORG to date on cancer care and clinical practice.
- To identify, capture and analyse some defined indicators concerning the economic impact of ICORG and cancer clinical trials.
- To engage with cancer care policymakers and clinical practice leaders in order to identify strategic opportunities by which any future HRB funding of ICORG may have an impact on cancer care policy and practice in Ireland.

The following methods were used during the impact assessment:

1. Desk research and logical framework analysis.
2. Data collection. Data was gathered amongst the various stakeholders by carrying out interviews and sending out two types of surveys. Furthermore, a bibliometric analysis was performed.
3. Analysis and reporting. For the final phase, all the collected data (from desk research, interviews, survey, bibliometric study) were analysed and described to provide answers to the evaluation questions proposed by HRB.

An indicator framework was developed to measure ICORG's impacts making a division between outputs, outcomes and impacts.

A number of the expected outputs of ICORG's activities include the increased quantity of clinical cancer studies in Ireland; an increased number of professionals working in hospitals on clinical cancer research; an increased training opportunities for cancer clinical studies in Ireland; an increased number of (high-impact) publications and (international) presentations based on cancer clinical studies in Ireland and an increased number of (and rate) patients participating in clinical studies in Ireland.

Some of the expected outcomes of ICORG's efforts are an increased number of new/improved treatments and/or diagnostics introduced into the clinical practice in Ireland; an increased income generated by industry-sponsored studies; an increased leveraged funding for cancer clinical trials in Ireland over the years from public and private sources (non-exchequer); developed guidelines and standards for clinical cancer research in Ireland

Expected, longer-term impacts of ICORG's efforts are increased quality of the clinical cancer research in Ireland; improved standards of clinical care in Ireland; improved

benefits for cancer patients in Ireland; increased attractiveness of Ireland for cancer clinical research (for industry and world-class physicians). A full table of indicators is provided in the report.

### Impact on cancer clinical research

In general, ICORG's impact on clinical research in oncology in Ireland has been high, both in terms of quantity and quality. In terms of **quantity**, the HRB funding has allowed ICORG to grow from a small organisation focusing mainly on breast cancer to a large cooperative group that runs trials in several disease areas. The total number of studies open during a year has risen over the years from 11 in 2006 to 41 in 2010, although this trend has reversed recently. There is a consensus that without ICORG the number of studies that are done in Ireland would be a fraction of the current number. ICORG is the **one and only** major cooperative research group in Ireland, not just in oncology. This pattern of **quantitative growth** corresponds with an increase in ICORG funded staff (from 8 FTE in 2002 to 80 FTE in 2011) and the number of members (from 235 in 2005 to 435 in 2011). All relevant hospitals had joined ICORG by 2009.

Through the HRB funding ICORG has been able to create the necessary infrastructure to perform clinical research. This infrastructure appears to be suitable for in-house studies and local studies as well as collaborative and industry studies. While at the start ICORG was mainly focussing on breast cancer, they now perform clinical trials in many disease areas. The pattern of distribution of phases is quite pronounced, with a strong focus on phase III studies and increasingly phase II studies, whereas phase I and IV are marginal in number. The low number of phase I studies does suggest that ICORG's main purpose is not purely scientific excellence, although there are a few outstanding examples such as the *Herceptin* study.

ICORG's impact on **quality** of clinical research is high. By providing training for research staff, ICORG ensures that they are qualified to perform clinical research and that they are up to date on current regulations and guidelines. ICORG training activities have enhanced capacities in hospitals through maximising the number of medical and nursing staff able to participate in cancer clinical trials. From 2006-2011 128 **training** sessions have been organised by ICORG. Fifty-five percent of these trainings were on Good Clinical Practice (GCP).

By virtue of its coordinating function, its audit and quality assurance activities, ICORG has contributed strongly in improving and harmonizing clinical trial **guidelines** throughout the participating hospitals. Because of a joint responsibility for the general quality in a study, ICORG support and 'peer-pressure' assure that all **minimum standards** are adhered to.

ICORG's quality is also shown from the **publications** association with its clinical trials. Since 2006, ICORG studies have led to 47 (co)-publications. ICORG papers score strongly above average for citations scores, with a C-index of 3.28. The number of publications and their citations scores also shows a growing trend over the years. ICORG researchers have held **presentations** at major international oncology conferences, but not enough data was consistently captured to put this into perspective. ICORG's contribution to quality can also be assessed by the level of satisfaction of industry and external groups, which are all very positive about ICORG's reliability, dedication and data quality. ICORG has developed **a strong international reputation**, mainly in North America, where it is considered 'one of the best' oncology research groups in certain disease subgroups like breast cancer.

Although part of its original objectives, ICORG has not been able to set up or facilitate the creation of **national key resources** for clinical research, such as **cancer biobanks** and disease-specific cohorts, although ICORG's presence has contributed to raising the profile of this issue among policy makers.

### Impact on cancer care and clinical practice



When looking at the effect of ICORG on clinical care, it has definitely increased the **clinical participation rate of Irish patients**. Between 2006 and 2011, ICORG recruited 4553 patients in their trials, of which more than half breast-cancer patients. Other big disease groups are genito-urinary and gastrointestinal cancer. For breast cancer, the participation rate lays around 16%, which is quite high internationally. The total average accrual percentage, however, is only around 4%. This low rate is an international problem, and not specific to ICORG. Another activity related to patient care is stakeholder **communication**. Although internal communication seems to be adequately arranged, policy makers feel that ICORG is weak on external communication. There is currently no structural communication towards patients around clinical trials, and the extent to which ICORG should play a direct or indirect role is debated.

When considering the impact on **new treatments, diagnostics and prognostics**, it became apparent that ICORG over the past 10 years was able to deliver some very effective new treatments to patients during the trials. ICORG played a leading role in some major international studies that resulted in very successful new treatments. Because of their participation in clinical trials, successful treatments were faster implemented in hospitals that participated. There is also evidence of new diagnostics and prognostics, although these are more limited in scope and number. The ICORG process also ensures the presence and updating of standards of practise and **guidelines**. However, ICORG does not seem to go beyond the minimum standards required for participation in clinical trials, and the function of ICORG as a diffusion network of new treatments and care protocols is limited. On a more indirect level, virtually all stakeholders agree that ICORG has had a large effect in vitalizing the oncology groups in Ireland, resulting in better-qualified staff with more motivation and recent knowledge. Hospitals are proud to participate in international trials, as they yield 'status, honour and glory'. These more subtle and qualitative effects are likely to have improved care for patients as well, although this may be limited by the distance between standard care and clinical trial departments.

The direct effect of providing care for patients while on trial results in **direct benefits for patients**. Especially in breast cancer, a large number of patients directly benefitted from receiving superior treatments through ICORG trials. The benefit accruing to participants in general, regardless of treatment, is more difficult to measure, and at this point there is no conclusive evidence that patients receive consistently better than standard care while being on trial. Looking at **long-term benefits, such as better outcomes and quality of life**, is perhaps even more difficult. It is clear that ICORG has had at least some positive effect on outcomes by providing some successful new treatments in trials and early adaptation of subsequent commercialized drugs, but it is impossible to quantify this effect. There is some qualitative evidence that ICORG's capacity building in breast cancer care and research has helped Ireland to make full use of internationally developing treatments and diagnostics that resulted in a 10% improvement in 5-year survival rate.

### **Economic and financial impacts**

Although ICORG does not have a specific **economic** mandate, some impacts on economy have been analysed. Data provided by ICORG and HRB show that over the last six years, about 20-30% of the ICORG studies were **sponsored by industry**, and an increasing share of the total number of ICORG studies was sourced by the industry. € 1.2 million was invested by industry in ICORG in the last three years up to 2011. On top of this, the industry has provided **free-of-charge drugs**, scans and other in-kind contributions to ICORG, with a stable annual estimated value is of € 3 to 4 million over the last six years. From other sources ICORG says to have **leveraged** about € 2 million (of which about € 1.7 from collaborative studies and the rest from charities and other sources) and this amount is increasing every year.

It seems that the number of companies with which ICORG collaborates increased significantly over the years, showing the positive stance of ICORG. ICORG closely cooperates with almost all pharmaceutical companies based in Europe, and they have

an intense relationship with some of the largest pharmaceutical companies in the world such as GSK and Pfizer. The **industry values the collaboration** with ICORG as very positive and beneficial. They consider ICORG as professional and well organised with the ability to manage complex trials with high accrual rates and good quality data. For some of them, ICORG is the **reason to be active in Ireland** in oncology research and they strongly recommend the development of ICORG-like organisations in other clinical fields as well.

### Challenges and opportunities for the future

One of the objectives of the impact assessment was to engage with cancer care policy-makers (e.g. NCCP, Department of Health) and clinical practice leaders in order to identify strategic opportunities by which any future HRB funding of ICORG may have an impact on cancer care policy and practice in Ireland. It was found that partial implementation of the National Cancer Strategy had been achieved, with most progress having been made in improving access to clinical trials for patients. Interviewees felt that ICORG has helped with the implementation of the NCCP, mainly in the breast-cancer area, but interaction between NCCP and ICORG could be intensified. Many opportunities for future collaboration with NCCP have been identified.

Cancer will remain high on the agenda; therefore ICORG faces many scientific opportunities in the future, with specific attention to translational research. However, the organisation could increase its cooperation with other disease areas and work with a clinical research support centre. An opportunity is to increase cooperation with NCCP and organise a more structural interface with NCCP.

ICORG will need to deal with the fact that Ireland is a small country and economic developments are not very promising on the short term. HRB funding is decreasing, and general health care budget cuts are a huge threat. ICORG will need to further diversify its sources of income and focus on efficiency to remain strong and on the competitive edge with other countries. An important threat is the high work pressure for the oncology professionals which prevents them to explore possibilities to source new cutting-edge studies (and phase I studies) and the closure of hospitals is putting the research opportunities under pressure. ICORG envisages for the group and increasing expertise in the area of early phase clinical development.

In a number of different areas the ICORG expects to continue to accrue strongly and contribute to a range of the most interesting research questions. The organisation itself could however further professionalise, and develop a clear long-term strategy in order to sustain the high level of research and accrued number of patients in the trials in different disease areas. Finally, the organisation could increase its financial and organisational transparency and appoint a 'liaison officer' to deal with the communication with other players in the field.

### Recommendations

- Cancer will remain high on the agenda; therefore ICORG faces many scientific opportunities in the future, with specific attention to translational research. However, the organisation could increase its cooperation with other disease areas and work with any national clinical research support centre. It could make more efficient use of resources by for instance working with the Irish Cancer Society and develop a stronger interface with the NCCP.
- Our analysis shows that ICORG has had significant impact on the quantity and quality of clinical research in Ireland. This has had some effects already on clinical practice and patient care. However, ICORG currently has no explicit strategy to improve patient care and contribute to the development of clinical standards in oncology across the board. Policy makers however seem eager to use the unique opportunity that the ICORG network offers to also work more explicitly on jointly raising the quality of cancer care in general. We recommend to ICORG therefore to

develop an explicit strategy by, for instance, strengthening the cooperation with the NCCP and other care stakeholders.

- Moreover, ICORG could better monitor and map its added value for patient care and the healthcare system in order to convince decision-makers to continuously support collaborative oncology research in Ireland.
- ICORG will need to deal with the fact that Ireland is a small country and economic developments are not very promising on the short term. HRB funding is decreasing, and general health care budget cuts are a huge threat. ICORG will need to further diversify its sources of income and focus on efficiency to remain strong and on the competitive edge with other countries.
- An important threat is the high work pressure for the oncology professionals which prevents them to explore possibilities to source new cutting-edge studies (and phase I studies) and general budget cuts in the healthcare system are putting research opportunities under pressure. In the past, ICORG has built its (international) reputation by managing a broad base of high-quality studies while also pursuing a select number of exceptionally innovative studies. Given the limited time and resources for the clinical researchers to pursue many of these innovative studies, ICORG should proactively foster those studies where international (scientific) impact is highest and disseminate the results broadly.
- ICORG could improve its organisational data management and monitoring systems in order to increase transparency to its funders and its internal management.

## 1. Introduction

### 1.1 Background of the study and objectives

Established in 1986, the Health Research Board (HRB) is the leading agency in Ireland supporting and funding health research. By supporting excellent research it facilitates the generation of knowledge and its application in policy development and medical practice. Largely funded by the Department of Health and Children, it has an annual budget of around €37 million (2009) to achieve its goals.

The All-Ireland Cooperative Oncology Research Group (ICORG) was set up in 1996 to create more research opportunities for clinical trials in the field of oncology. More than 95% of cancer treating consultants in the Republic of Ireland and in Northern Ireland are members of ICORG. The HRB has funded ICORG since 2002 as part of the National Cancer Strategy and the Cancer Consortium. Up until 2011, ICORG has received €36.5 million to build capacity for cancer clinical trials in Ireland. Besides funding from HRB, ICORG also receives funding from the Irish Cancer Society.

ICORG is based on the co-operative group model, with a large number of hospitals participating in the HRB funded programme. ICORG is coordinated by its group central office (GCO), which also received a grant to develop its capacity.

The HRB asked Technopolis to perform an impact assessment of ICORG and get a better understanding of the environment that ICORG operates in. The current three-year ICORG contract with HRB will expire in June 2012 and there have been several changes in the health care system in Ireland. As quoted in the terms of reference *“The main driver for the overall review of ICORG is to inform an internal funding decision and whether or not the HRB’s strategic objectives of ICORG funding should be revised or extrapolated in any way”*.

Although ICORG exists since 1996, it receives funding from HRB since 2002, therefore the assessment will focus on the impact achieved since 2002.

The specific objectives of the impact assessment are:

- To assess the impact of ICORG on cancer clinical research in Ireland.
- To capture impacts of ICORG to date on cancer care and clinical practice.
- To identify, capture and analyse some defined indicators concerning the economic impact of ICORG and cancer clinical trials.
- To engage with cancer care policymakers and clinical practice leaders in order to identify strategic opportunities by which any future HRB funding of ICORG may have an impact on cancer care policy and practice in Ireland.

The HRB has proposed several key questions for each of these specific objectives, which can be found in Appendix A.

### 1.2 Approach and methodology

The evaluation questions defined by the HRB were leading in the development of an approach. This approach was discussed and approved by the HRB.

The following methods were used during the impact assessment:

4. **Desk research and logical framework analysis.** Desk research was done to perform a ‘logical framework analysis’ (LFA). The LFA reconstructs the intervention logic of ICORG and describes the needs (or problems) ICORG addresses, the rationale, its objectives and activities. It also gives an overview of

expected outputs, outcomes and impacts and their translation into ‘evaluation indicators’. These indicators were used to assess the impact of ICORG and were largely aligned with the key evaluation questions as provided by the HRB. This LFA and a list of indicators are presented in this final report.

5. **Data collection.** Data was gathered amongst the various stakeholders by performing interviews and sending out two types of surveys. Appendix B shows the names and organisations of the interviewees. Among the 18 interviewees were internal stakeholders (GCO, ICORG chairs and principle investigators (PI’s)), policy stakeholders, external experts and representatives from collaborating industry. Technopolis discussed the preliminary findings as described in the interim report (January 2012) in a group interview with the members of the ICORG peer review panel. The surveys were developed (with support of Technopolis), executed and analysed by the HRB. Two surveys were developed: one for the principal investigators and team leaders of ICORG participating hospitals (11) and one for a selection of collaborating industry (7 companies were selected by the GCO out of a total of 46 companies that have collaborated with ICORG since 2002). The response rate was 91 percent for the hospital survey (10 responses) and 71 percent for the industry survey (5 responses).

Furthermore, a bibliometric analysis was performed. HRB analysed the publications associated with ICORG research and Thomson Reuters was asked to provide an analysis of the citation impact of the ICORG papers. The results of the surveys, interviews and bibliometric analysis are integrated in this final report

6. **Analysis and reporting.** For the final phase, all the collected data (from desk research, interviews, survey, bibliometric study) were analysed and described to provide answers to the evaluation questions proposed by HRB.

## 2. Measuring the impact of the All-Ireland Cooperative Oncology Research Group

ICORG is a not-for-profit registered charity and a cooperative clinical trials group modelled on similar groups from the USA. ICORG was established in 1996 by a group of PI's and cancer consultants to promote, design, conduct and facilitate clinical cancer research on the island of Ireland. Clinical cancer research is taken to mean the investigation of methods of prevention, diagnosis, management and treatment of patients with cancer.

The Group consists of clinicians and researchers involved in clinical cancer research. Today, about 95% of all oncologists in Ireland are members (including haematologists (47), medical (55), surgical (80), radiation (35) and translational (23) oncologists) as well as 195 research specialists: in 2011<sup>1</sup> it counted 435 members, six affiliated universities and 16 (10 funded by HRB) major affiliated hospitals, which together treat more than 19,000 new cases of cancer annually in Ireland. As is stated by ICORG in its latest interim report, this figure is set to grow to nearly 30,000 by 2020<sup>2</sup>. Coordination activities are split between a GCO in the Republic of Ireland and a Statistics and Data Management Office (SDMO) within the Clinical Research Support Centre (CRSC) in Northern Ireland.

ICORG received funding from HRB from 2002. On an annual basis the Group reports on its activities and progress related to its objectives.

In Appendix E an extensive overview is given of ICORG's intervention logic based on a 'logical framework analysis (LFA)' conducted by Technopolis. It described the needs (or problems) the programme addresses, the rationale, its strategic and operational objectives and activities. It also gives an overview of expected outputs, outcomes and impacts and their translation into 'evaluation indicators'. All objectives and activities focus on the island of Ireland, unless otherwise stated. Here we will briefly summarise the main objectives and performance indicators that we have used for the impact assessment as further described in the appendix.

### 2.1 ICORG's mission and key objectives

ICORG's mission is to foster the growth of clinical trials activity and scientific research, in the domain of cancer, on the island of Ireland".<sup>3</sup> It aims to:

- create more research opportunities for patients
- make Ireland more attractive as a location to international cancer research groups and the pharmaceutical industry.

The main objectives for ICORG are:

1. To improve the quantity and quality of clinical research<sup>4</sup>;
2. To provide access to newest treatment regimens for patients;
3. To make Ireland more attractive as a location to international cancer research groups and the pharmaceutical industry.

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<sup>1</sup> GCO and SDMO interim report HRB -2011 Final report V1.

<sup>2</sup> GCO and SDMO interim report HRB -2011 Final report V1

<sup>3</sup> Progress Report, Group Central Office and Statistics & Data Management Office, 1 July 2010 – 30 June 2011

<sup>4</sup> the balance has shifted in the last few years towards improving patient and clinical care.



The GCO and the SDMO are responsible for many of the tasks involved in order to pursue the organisation's mission and objectives. The GCO has a role in project management, pharmacovigilance (PhV), on-site monitoring, group meetings and international collaborations. The GCO has also employed experienced data management and statistics professionals. The GCO also coordinates the activities of the Disease Specific Sub-Groups (DSSGs) through which the scientific development of ICORG is directed and monitored. It provides local expertise in regulatory and ethics processes in Ireland, the UK and Europe. The GCO is also responsible for drug distribution, accountability and labelling. The SDMO, which has been funded in full by the HRB since April 2010, is tasked with responsibility for all quantitative aspects of cooperative group activity, and with contributing to the overall management of the Group. In this impact assessment no distinction is made between GCO and SDMO, they are both called 'ICORG' here.

## 2.2 Outputs, outcomes, impacts

A number of the expected outputs of ICORG's activities are the increased quantity of clinical cancer studies in Ireland; an increased number of professionals working in hospitals on clinical cancer research; an increased training opportunities for cancer clinical studies in Ireland; an increased number of (high-impact) publications and (international) presentations based on cancer clinical studies in Ireland and an increased number of (and rate) patients participating in clinical studies in Ireland (improved trial entry).

Some of the expected outcomes of ICORG's efforts are an increased number of new/improved treatments and/or diagnostics introduced into the clinical practice in Ireland; increased income generated by industry-sponsored studies; increased leveraged funding for cancer clinical trials in Ireland over the years from public and private sources (non-exchequer); developed guidelines and standards for clinical cancer research in Ireland

Expected, longer-term impacts of ICORG's efforts are increased quality of the clinical cancer research in Ireland; improved standards of clinical care in Ireland; improved benefits for cancer patients in Ireland; increased attractiveness of Ireland for cancer clinical research (for industry and world-class physicians)

## 2.3 Indicators to assess ICORG's impact

The following matrix contains an extensive list of indicators that could be used for the impact assessment of ICORG. Not all indicators were measured within the scope of this project since data was not available for some indicators. Where this was the case, we collected as much as possible 'soft data' in the interviews (e.g. opinions and stories) that provided at least anecdotal evidence of achieved outputs, outcomes and impacts.

Figure 1 Indicators to measure outputs, outcomes and impacts

Indicator Type	To improve quantity and quality of clinical research	To provide access to newest treatment regimens for patients	To make Ireland more attractive as a location to international cancer research groups and the pharmaceutical industry.
Output	# of sponsored studies (increase in time), % of studies financed by ICORG	# Patients accrued in ICORG funded clinical studies  % Of total patients in disease area in Ireland reached by ICORG research	# Industry sponsored studies ICORG participated in

	# Training sessions organised	# Patient education and outreach programmes developed by ICORG or funded by ICORG	# Collaborations with international groups in ICORG studies
	# Professionals working in hospitals on clinical studies in Ireland	Satisfaction about information delivery by ICORG amongst stakeholders  # People that accessed the ICORG website  # Downloaded ICORG apps	
<b>Outcome</b>	# Publications  Average impact score of publications  # Presentations in international conferences	# New/improved treatments  # New/improved diagnostics	# Euro investment in biobanks, cohorts developed with contribution of ICORG
	# Participants in training sessions  Satisfaction about training and quality improvement amongst professionals	Knowledge and understanding amongst patients about clinical research and the newest treatment regimes	Income generated by industry sponsored studies in Ireland
	Interaction with ICORG and professionals about ethics and regulatory processes	# Contact hours with specialist before and during trial for patients	Leveraged funding for ICORG by charities, international research groups, other funders, etc over the years
	New/improved guidelines and standards for clinical cancer research in Ireland		Value of drugs provided free-of-charge by industry for cancer clinical trials
	Perception of (reduction of) barriers to involve in clinical research in Ireland for professionals and industry		Satisfaction of industry and international research groups about cooperation with ICORG
<b>Impacts</b>	Satisfaction about the quality of clinical cancer research in Ireland	Satisfaction of policy makers responsible for clinical care about the Irish standards of care	# (return) requests/proposals for studies by industry to ICORG
	Changed research policies in Irish governments and industry in relation to clinical research because of ICORG actions	Satisfaction of patients about Irish standards of care	Retention and attraction of high-level staff (brain drain/ brain gain)
		% Patients with survival (defined as 'still alive > five years after 'diagnosis cancer-free') with or without participation in ICORG clinical trial	Reduction of barriers perceived by industry to involve in trials in Ireland
		Awareness of importance of clinical (cancer) research in Ireland	(Inter) national reputation of clinical research in Ireland

Technopolis Analysis



### 3. ICORG's impact on cancer clinical research

The main objective of this study was to assess the impact of ICORG on cancer clinical research in Ireland. The initial idea behind funding ICORG for HRB was to develop the capacity and infrastructure in Ireland for the conduct of high-quality cancer clinical research, including translational research. Therefore, the assessment primarily focused on ICORG's success in meeting this objective.

As was already described in the previous chapters, ICORG specifically aims to improve the quantity and quality of cancer clinical research by facilitating clinical trials, providing training, building capacity and infrastructure in the hospitals and developing strong links with cancer research groups. To achieve this they undertake several activities.

This chapter describes the output, outcomes and impacts that ICORG has had on cancer clinical research in the period 2002-2011. First, the clinical research activities of ICORG are being described, and an overview is given of the number of trials executed over the years in the different phases and disease areas. An overview is also given of the education and training activities, and the way capacity and infrastructure has been built for clinical trials. In addition an overview is given of the existing collaboration and links with leading cancer research groups. Second, the impacts of ICORG on the quality and standard setting for cancer clinical trials in Ireland are described, as well as its impact on the infrastructure for cancer clinical trials.

#### 3.1 Facilitating cancer clinical trials

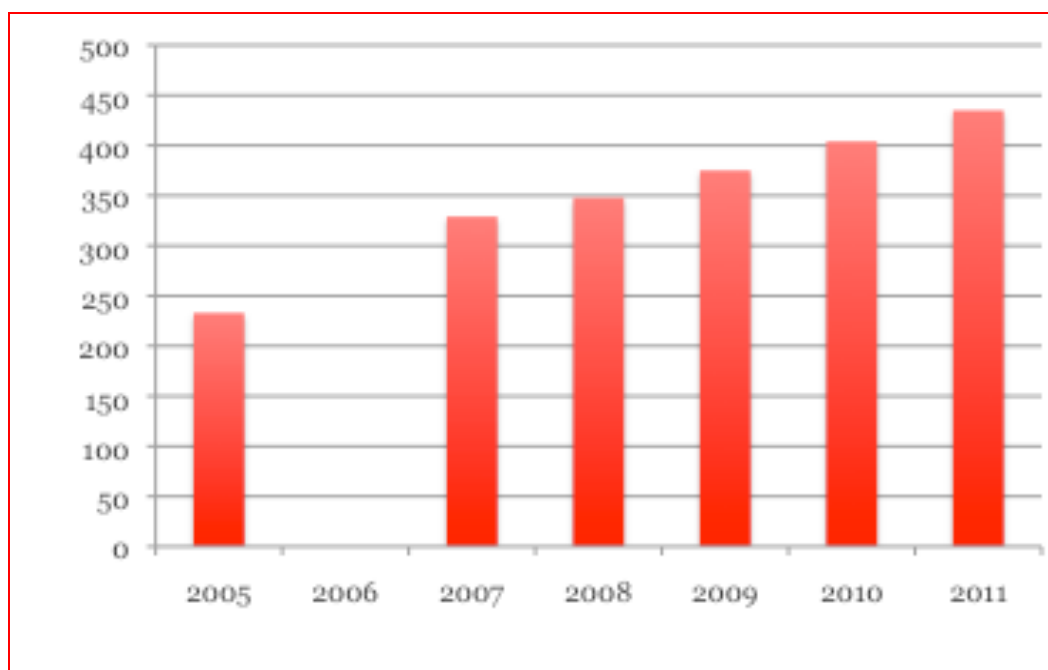
##### 3.1.1 ICORG as a collaborative group

ICORG is a collaborative group and is thus dependent on the involvement of their members. Membership of ICORG is open to oncology professionals in the fields of:

- Medical oncology;
- Radiation oncology;
- Surgical oncology;
- Haematological oncology;
- Research Specialists (i.e. Research Nurse, Research Coordinator, Research Manager, Data Manager, Research Registrar, Research Pharmacists, Clinical Scientists etc.)

Since 2005 the number of members has slowly increased (see Figure 2). According to the ICORG website more than 95% of Ireland's cancer treating consultants are ICORG members. The increasing numbers indicate an increase in the number of oncology professionals in Ireland, and not necessarily a poorer coverage in the early ICORG years.

Figure 2 ICORG members 2005-2011<sup>5</sup>



Source: ICORG interim progress reports.

The high percentage of Ireland's consultants who are a member of ICORG shows that ICORG has succeeded in forming an inclusive cooperative group which truly represents the oncology field, and that it offers added value to medical professionals.

ICORG's clinical trials are executed in clinical trial sites in hospitals in Ireland. Currently there are 16 affiliated hospitals<sup>6</sup>, although the activity report 2011 only mentions 15 hospital sites involved with ICORG (listed in **Error! Reference source not found.** below). Currently, eleven of these hospitals receive direct funding from the HRB. The number of sites has grown steadily since 2002, with the highest growth in 2007 when three sites joined ICORG. Since 2009 no new sites joined ICORG. The current group of hospitals includes all eight designated adult and the one paediatric cancer centres under the National Cancer Control Programme.

Figure 3 ICORG hospital sites

Abbreviation	Name hospital
AMNCH	Adelaide and Meath incorporating the National Children's Hospital, Tallaght, Dublin
BCH	Belfast City Hospital
BH	Beaumont Hospital, Dublin*
CUH	Cork University Hospital*
GUH	Galway University Hospital*
LGH	Letterkenny General Hospital
MMUH	Mater Misericordiae Hospital, Dublin*

<sup>5</sup> This and most other figures are based on ICORG and HRB data, which unfortunately do mostly provide information from 2005/2006 onwards. Prior to this, little information is available.

<sup>6</sup> GCO and SMO interim report HRB -2011 Final report V1.

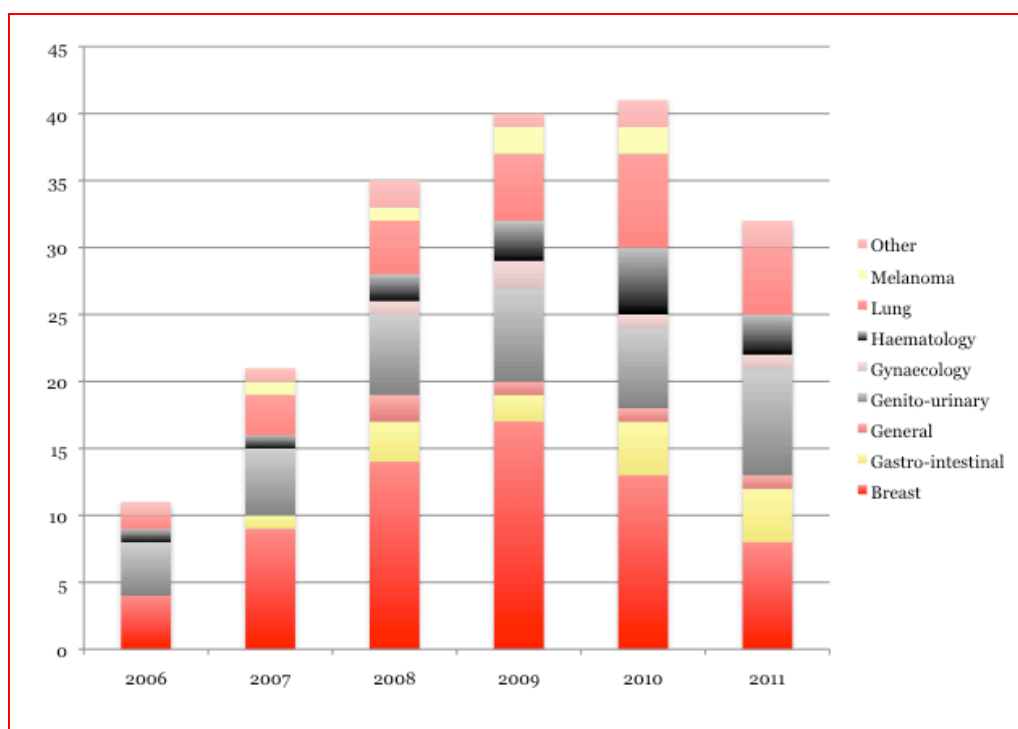
Abbreviation	Name hospital
MRHT	Midland Regional Hospital, Tullamore
MWRH	Mid Western Regional Hospital, Limerick*
OLCHC	Our Lady's Children's Hospital, Crumlin*
SGH	Sligo General Hospital
SJC	St James's Hospital, Dublin*
SLH	St Luke's Hospital, Dublin
SVUH	St Vincent's University Hospital, Dublin*
WRH	Waterford Regional Hospital

Source: ICORG activity report 2010. With \*: designated cancer centres

### 3.1.2 Development of clinical studies over the years

A key metric in defining ICORG's activities is the number of clinical trials executed by its members and under its auspices. Unfortunately, there are no data available on the number of clinical trials before 2006, but according to most interviewees, clinical research in Ireland before ICORG's foundation was very sporadic and marginal on the international level. Researchers were depending solely on a scarce and volatile supply of clinical trials sponsored by industry. All stakeholders agree that the current activities in clinical research in oncology in Ireland can almost be completely attributed to ICORG.

Figure 4 Total number of open trials per disease area per year<sup>7</sup>



Source: Grant Application 2012

<sup>7</sup> This and subsequent figures show data on ICORG trials with study status 'Open'. They should be interpreted as the number of running studies during a particular year. The sum over the years is therefore not equal to the number of unique studies, since trials usually run over several years.

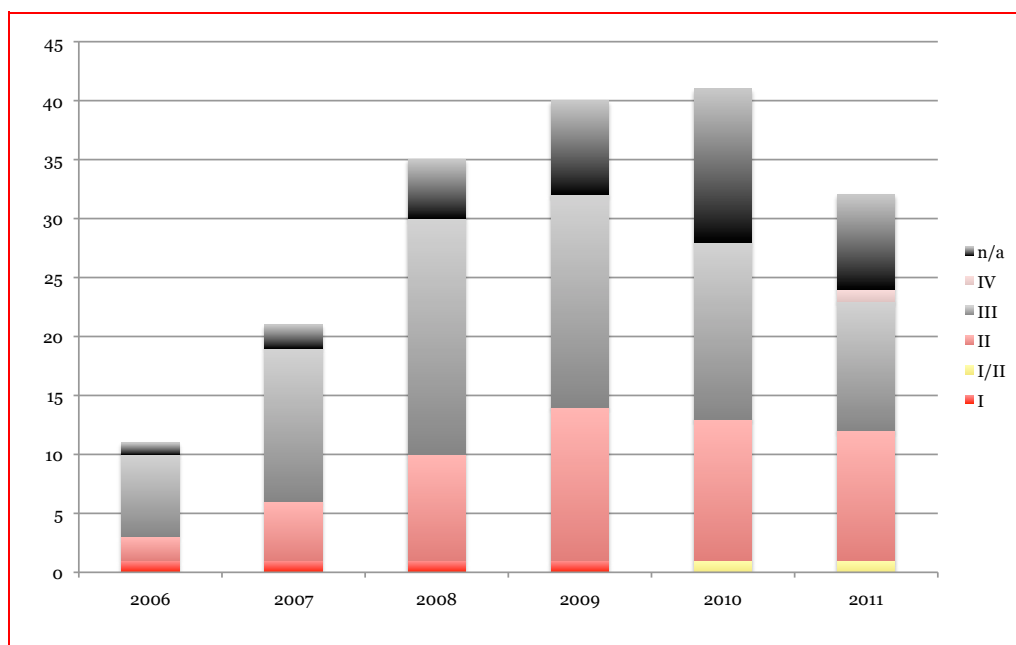
Figure 4 shows the total number of open trials per disease area per year. It can be seen that there has been an increase in the total number of trials from 2006-2009. From 2006 to 2008 the total number even trebled. From 2009-2011 the number of trials decreased. This decrease was mainly caused by a decline in trials on breast cancer. According to an external expert, the total number of clinical trials in Ireland has been going down for years, but the studies are now generally of higher quality than before. The significant drop in number of trials in 2011 is related to an international trial lifecycle issue, where many large breast cancer studies were completed in 2010. This reduction has been seen across all major international oncology study groups, according to the ICORG researchers.

In 2007 two new disease areas were added to ICORG trial portfolio, as one study on gastro-intestinal and one study on melanoma were initiated. In 2008 ICORG started its first study on gynaecology and two studies in the category 'general' were initiated. ICORG aims to have trials in all disease areas. The ICORG grant application for 2012 reports that "for each disease area, gap analysis has been performed to identify areas where there are unmet needs". This is an on-going agenda item at every DSSG meeting. Members of each DSSG review various sources to identify potential studies and suitable studies are proposed at these meetings. If there is agreement at these meetings that a study may potentially meet a "gap", further details are requested, so that the study can be formally proposed for ICORG adoption".

The trials include both clinical trials and translational studies, which is in line with ICORG's overall objectives. Translational studies are mostly in-house studies (designed and run by ICORG) and investigator-led. Some of the translational studies have been developed on the back of clinical ideas that have also come from ICORG. It is also stated that these studies are becoming increasingly important since the emphasis of oncology research has shifted to biomarker-focused research and treatments that target the specific tumour biology of a patient.

Figure 5 shows per year the number of phase I, II, II and IV trials. The pattern of distribution of phases is quite pronounced, with a strong focus on phase III studies and increasingly phase II studies, whereas phase I and IV are marginal in number. The increase in relative importance of phase II studies was part of a strategic focus by ICORG to increase the number of these studies, as they also often yield the opportunity to take on subsequent phase III studies. Until 2010 there is also an increasing number of translational studies which are included in the 'not applicable' (n/a) category.

Figure 5 Number of open trials per phase



Source: ICORG Grant Application 2012

One oncologist noted in an interview that because of Ireland's small size, Phase I and II trials will always be a niche. It was also mentioned by an interviewee that a number of institutions in Ireland are capable of doing phase I and phase II studies, but others are not. To avoid any discontent among the centres that cannot do phase I and phase II trials, there is a preference at ICORG to do more third phase trials, according to the interviewee. One external collaborator stated that phase III trials are generally less interesting because they don't yield much research experience. Being involved in early phase puts you in the driver's seat with a big chance of becoming the research leader in later phases. However, as the external collaborator put it, "*phase 3 pays the bills*". ICORG has acknowledged that its future goal is to diversify more into phase I trials.

### 3.1.3 Non-ICORG versus ICORG studies

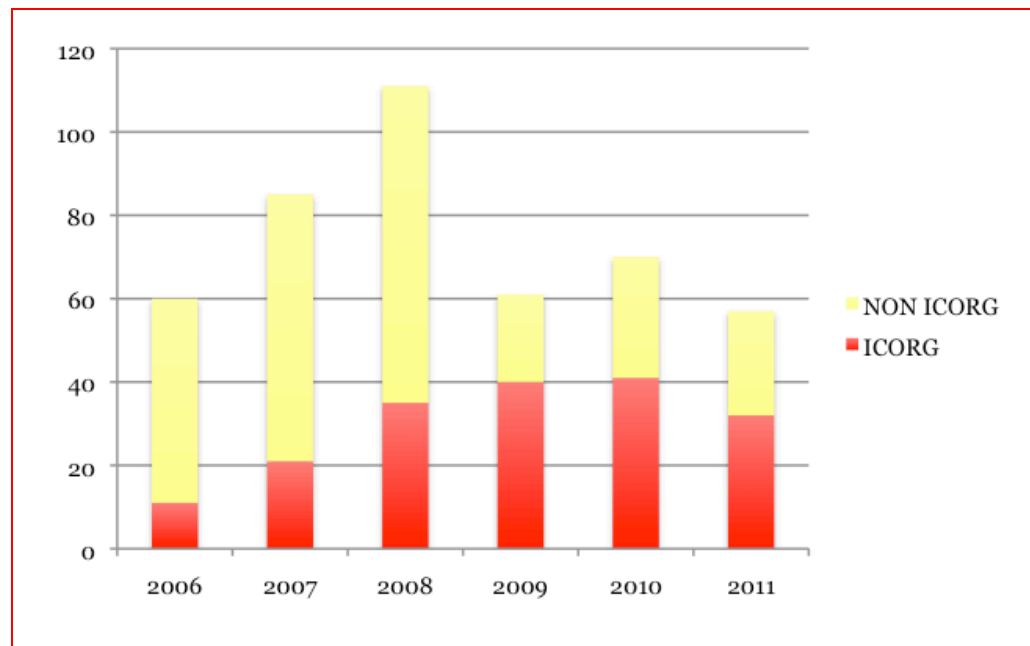
According to the HRB, ICORG hospital sites can also participate in studies that run independent of ICORG. Since ICORG studies must potentially be open across a number of sites, non-ICORG studies are often studies where an industry partner or collaborative group decides to work only with one particular site. Hospitals can make use of the ICORG-resources for non-ICORG studies (but must reimburse the cost to ICORG). The availability of ICORG-resources enables hospitals to participate in clinical trials and thereby contribute to an increase in quantity of clinical trials in Ireland. The figure below shows the number of open ICORG and non-ICORG trials per year. It shows that the share of non-ICORG decreased significantly in the last few years.

Each study undergoes a thorough selection process before it is approved and adopted as an 'ICORG-study'. Once a study has been approved the protocol development process begins (with in-house studies) or, if there is already a protocol the regulatory and ethics processes will start. The following figure shows the source of the trials per year. In line with the number of studies sourced 'in-house' increased since 2006, while the number of studies sourced by collaborative groups in which ICORG participates decreased.

Some non-ICORG researchers feel that ICORG is focusing too much on industry studies and is not doing enough investigator-led early phase studies, but the figures presented here do not suggest an overly strong focus on industry studies.

In the remainder of this chapter we will only focus on the ICORG studies.

Figure 6 Non-ICORG and ICORG studies



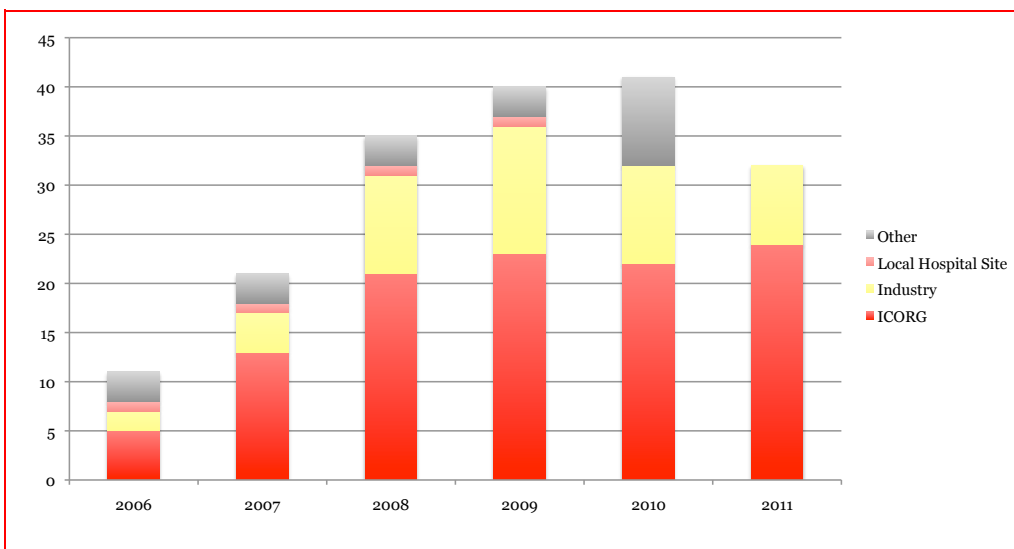
Source: ICORG Grant Application 2012

#### 3.1.4 Study sponsors and sources

All ICORG-studies are categorised by ICORG according to which organisation is acting as sponsor for the study. For this impact assessment the same categories are used:

- ICORG: this includes in-house, local and collaborative groups studies;
- Industry;
- Local Hospital Site;
- Other: if the protocol does not fall into any of the above.

Figure 7 ICORG study sponsors

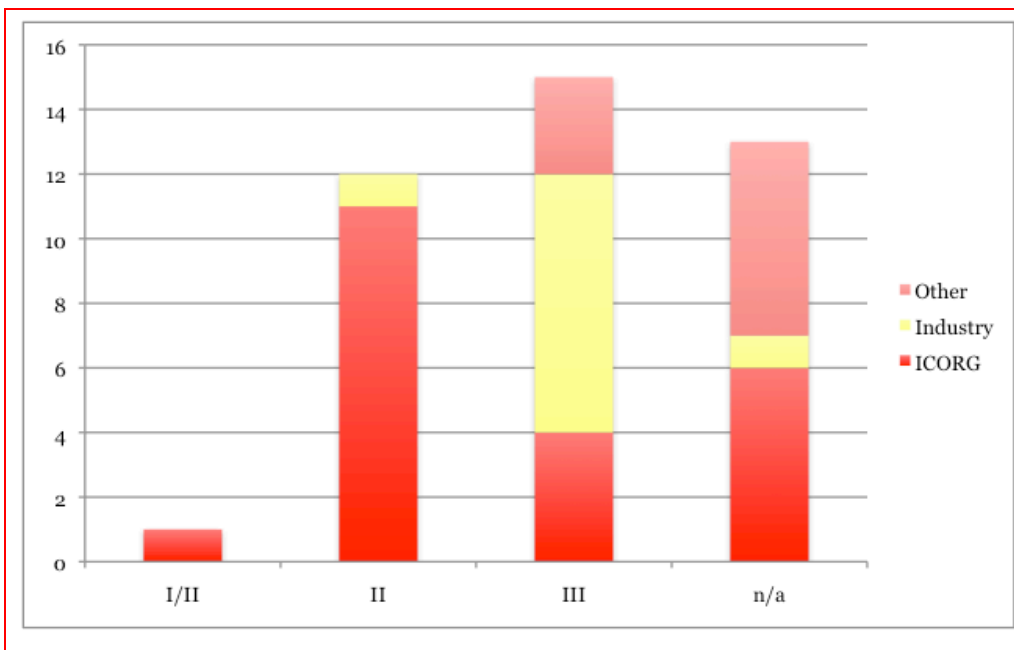


Source: ICORG Grant Application 2012

From 2006-2009 the number of industry-sponsored studies and ICORG-sponsored studies have increased, while there was one study sponsored by a local hospital site. Study sponsors in the category 'Other' are Queen Mary's Hospital (University of London) or studies with unknown sponsors. According to the GCO, the flat funding for the past years has led to a lower growth in the number of clinical trials, while also partly switching to more industry-sponsored studies. However, there is a limit to this since limited funding for research nurses has made ICORG reject 8-10 industry studies. This is in line with ICORG's contract, which states that HRB does not indirectly subsidise industry studies and ICORG need to recover full costs from industry.

The figures also show that, as expected, early phase trials are generally funded by ICORG itself, whereas phase III trials are generally sponsored by industry. These figures are for 2010, but other years show similar patterns.

Figure 8 Sponsors per trials in 2010



Technopolis Group, ICORG data

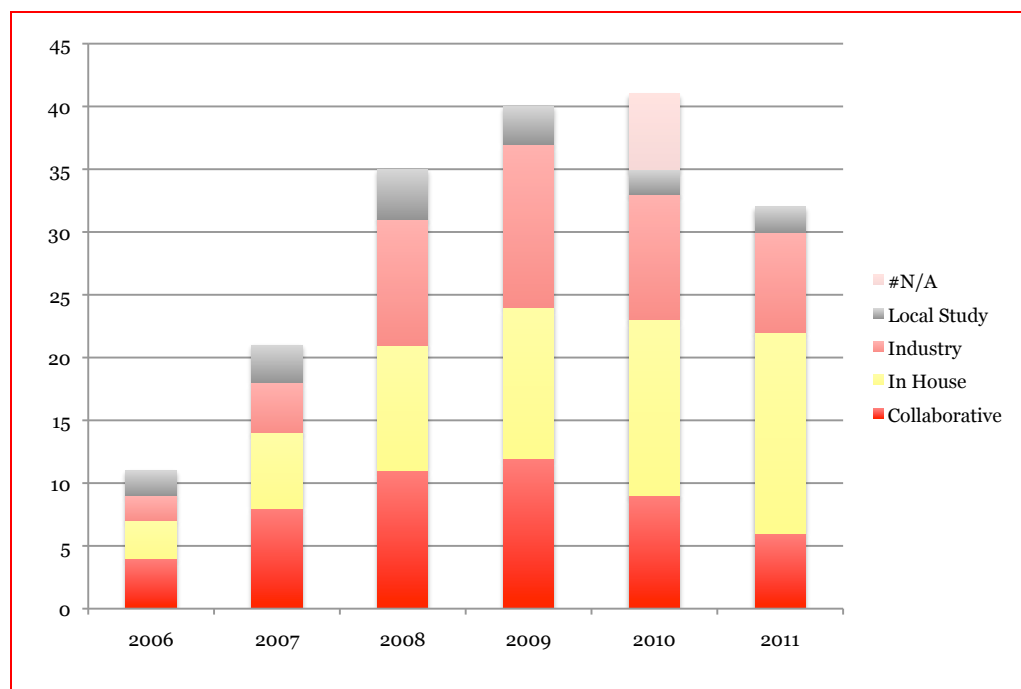
With regard to the future, ICORG reports that there are 36 collaborative group studies, 32 industry-sponsored studies and 32 ICORG in-house sponsored studies at the advanced stages of opening. In addition, there are 10 investigator-sponsored studies pending.

ICORG distinguishes furthermore four categories of study sources:

- **Industry:** in these cases a company asks ICORG to review its protocol. This protocol undergoes a selection process (described below) at ICORG. If there is agreement, the protocol becomes an ICORG study.
- **Collaborative group:** these are studies in which the protocol was developed by another research group. For example, an investigator learns through attendance at an international meeting that a particular compound/protocol might be of interest to the members of ICORG. They communicate this to the GCO who would then make enquiries with the cooperative group, which leads to a study.
- **In-house:** the protocol is conceived, designed and run by ICORG. This includes investigator-lead studies in which leaders in a disease area decide that a protocol is required for a particular subset of patients. Groups or centres outside of ICORG can participate in ICORG's in-house studies.
- **Local Study:** a protocol that has been developed independently by a site with minimal GCO or SDMO involvement

Figure 9 shows the study source of ICORG's open clinical trials. The category 'not applicable' (N/A) refers to ICORG trials of which no study source is applicable or trials with unknown study source.

Figure 9 Study source 2006-2011



Source: Grant Application 2012

### 3.2 Building capacity and infrastructure for clinical research

Building capacity (attracting professionals and providing training) in clinical research is a very important objective for ICORG. From the interviews with industry it became



clear that is very difficult to conduct clinical trials without capacity in term of the availability of professionals (such as oncologists, nurses and pharmacists) at the trial sites. By building capacity, ICORG aims to improve the quantity of available trial site staff and the quality of their services.

### 3.2.1 Staff development

Currently there are almost 90 full-time equivalents (FTE) working at ICORG clinical trial sites. Figure 10 shows the number of FTE per hospital and the origin of the funding. Some hospitals fully depend on the HRB grant, while others, such as St Vincent's University Hospital, are able to fund almost half of their FTE from other sources. These can be are charities, local hospital funds or funding from the pharmaceutical industry.

Figure 10 Number of FTE funded by HRB grant and other sources in 2012<sup>8</sup>

	AMNCH	BH	CUH	GUH	MMUH	MWRH	OLCHC	SJC	SLH	SVUH	WRH	Total
<b>Funded by HRB grant</b>	6.8	6.5	9.0	7.8	10.4	2.0	6.1	7.0	5.7	10.0	2.5	73.7
<b>Other sources</b>							0	0	2.1	4.8	1.4	14.0
<b>Total</b>	8.8	7.7	10.5	7.8	10.4	3.0	6.1	7.0	7.8	14.8	3.9	87.7

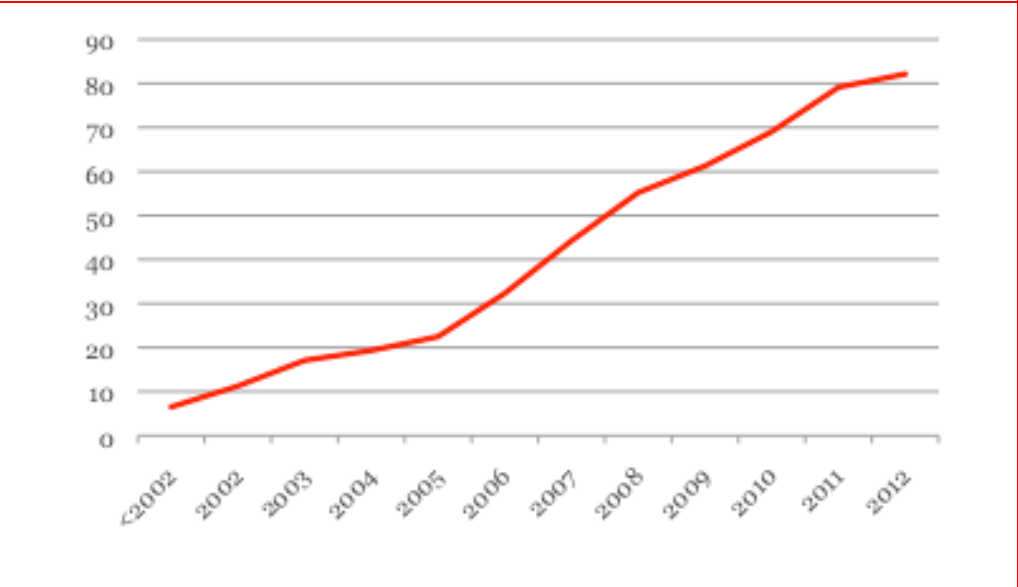
Source: Hospitals reports of ICORG Application 2012

Figure 11 shows the growth in FTE of clinical trial staff over the years. Figure 12 shows the start year of the staff working at the sites in 2012. The grant application only reports on start dates of staff working at the hospital at the time of writing. This means for example that the figures do not include the positions that became available before 2012 but were discontinued before 2012. The figures include all on-site staff, both funded through the HRB grant as well as funded through other sources. The figures does not include FTE for which no start date was reported, neither does it include Sligo General Hospital and Letterkenny General Hospital as they are currently not included in the HRB Credit System.

From both figures it appears that staff levels have been increasing, with growth accelerating since 2006.

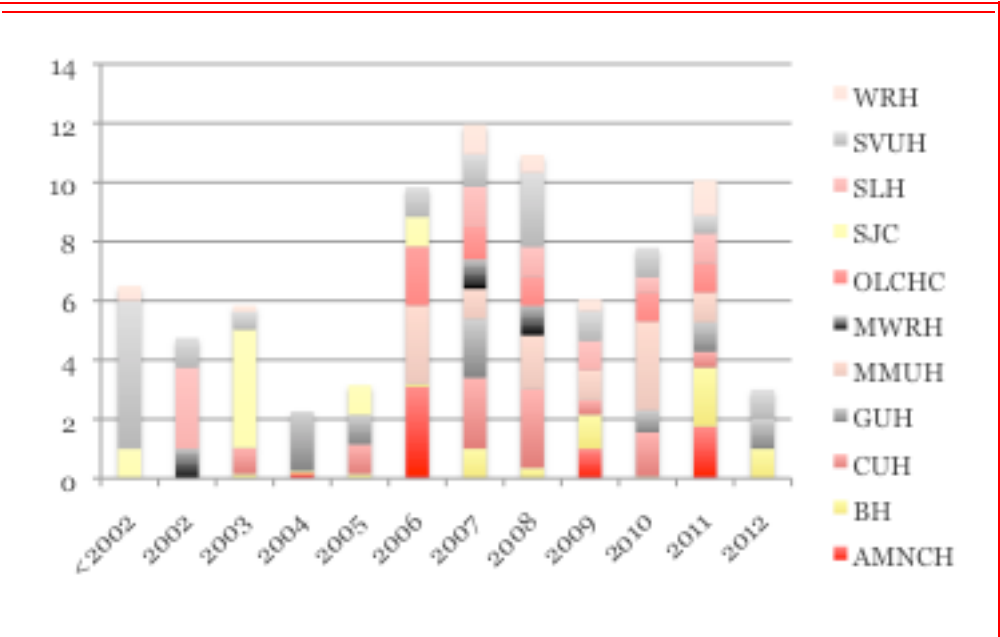
<sup>8</sup> This does not include Sligo General Hospital and Letterkenny General Hospital as they are currently not included in the HRB Credit System

Figure 11 FTE of on-site staff (2012)



Source: Hospitals reports of ICORG Application 2012

Figure 12 Number of FTE of on-site staff hired by the hospitals per year (2012)



Source: Hospitals reports of ICORG Application 2012

According to an ICORG oncologist, HRB funding has led to the ability to employ more staff, leading to a critical mass of expertise available. Another oncologist stressed the fact that Ireland had been lagging enormously behind other European countries, and that the last 10 years of funding also constitute an investment in general infrastructure and capacity for cancer clinical trials, of which the benefits will be reaped in the future.

### 3.3 Providing education and training in clinical research

ICORG organises several activities in this area with the aim to improve the quality of their services. An important activity is providing training for site staff and GCO staff.

According to ICORG, training of members and staff is a prerequisite of quality assurance. The training is facilitated by the GCO.

The development of the training programmes is done in close communication with the sites. The programmes cover a wide range of topics related to clinical research and are categorised here as follows:

- Good Clinical Practice (GCP) training: each person involved in a clinical trial should receive training in Good Clinical Practice. ICORG offers currently a two-day programme (GCP Day 1 and Day 2) and a GCP refresher course. ICORG recommends that all on-site staff attend their two-day programme within six months of starting their positions. The one-hour refresher course is held four times each year at the ICORG scientific meetings. In some cases on-site training is provided.
- Audit training: this training focuses on audit/inspection processes, common findings, audit readiness and preparation tips.
- Principal Investigator (PI) training: this training is available during the quarterly DSSG meeting days. The PIs receive training on Protocol Development and Pharmacovigilance Processes. It also involves training on several ICORG SOPs which describe the processes within the areas.
- Adverse Event Expedited Reporting System (AdEERS) training: this training supports hospitals to report safety events correctly across different regulations.
- Other: the category 'Other' includes for examples key-note speakers, time management training, grant renewal workshops and SOP training.

In chapter 3.5 the outcomes of, and satisfaction about, training and education are further analysed.

### 3.4 Developing links with other networks

ICORG aims to develop strong links with leading cancer research groups and other international research collaborative groups. Through these links ICORG can exchange knowledge and collaborate in international clinical trials.

ICORG reports on maintaining successful relationships with the following international groups:

- NSABP: National Surgical Adjuvant Breast and Bowel Project, USA;
- TORI: Translational Oncology Research International, USA;
- TRIO: Translational Research in Oncology, USA and Canada;
- ECOG: Eastern Cooperative Oncology Group, USA;
- BIG: Breast International Group, Belgium;
- EORTC: European Organisation for Research and Treatment of Cancer, Belgium;
- GELA: Groupe d'Etude des Lymphome de l'Adu, France;
- NCRN: National Cancer Research Network UK (incorporating Cancer Research UK (CRUK), Clinical Trials Research Unit (CTRU) & Medical Research Council (MRC);
- NCRI: The National Cancer Research Institute, UK;
- ACCOG: Anglo Celtic Cooperative Oncology Group;
- IBCSG: International Breast Cancer Study Group, Switzerland;
- ACOSOG: American College of Surgeons Oncology Group, USA;
- Finnish Uro-Oncological Group, Finland;

- AGO-OVAR: Arbeitsgemeinschaft Gynaekologische Onkologie, Germany;
- Ovarian Cancer Study Group;
- IAEA: International Atomic Energy Agency, Austria;
- TROG: Trans-Tasman Radiation Oncology Group, Australia;
- MRC Scottish Cancer Trials Breast Group – University of Edinburgh, UK;
- ICR: Institute of Cancer Research UK;
- ANZGOG: Australia and New Zealand Gynaecological Oncology Group;
- GCIG: Gynaecologic Cancer InterGroup, USA;
- UNCCN: University of North Carolina Cancer Network, USA;
- AIO: Arbeitsgemeinschaft Internistische Onkologie, Germany.

Some of the relationships are long lasting: the collaboration with the groups Breast International Group; (BIG), Breast Cancer International Research Group (BCIRG) and Cancer Research UK (CRUK) started in 1998 and 1999<sup>9</sup>. It was mentioned during the interviews that TRIO has carried out 14 studies over the years with ICORG. Figure 13 shows the open trials that have their origins in collaborative groups per year. The number of collaborative groups trials in which ICORG participates has increased in the years 2006-2009, but from 2009-2011 the number decreases.

Figure 13 Number of ICORG open trials per international research group

Study Source	2006	2007	2008	2009	2010	2011
ACOSOG		1	1			
ECOG		1	2	1	1	1
NCRN	3	4	4	3	3	
NSABP			1	1		
TU	1	2	2			
CTORI			1	1	1	1
IBCSG				1		
ICR				1	1	1
NSABP				1		1
TRIO				2	2	
TROG						1
UKMRC				1	1	1
Total	4	8	11	12	9	6

Source: Grant Application 2012

The fact that ICORG has contributed to hospitals in developing new collaborations or partnerships is supported by the outcomes of the survey. Respondents in the survey to the hospital sites were asked whether activities carried out as part of their ICORG studies led to any collaborations or partnerships with health agencies, charities, other

<sup>9</sup> Grant Application 2009

clinical research groups or university-based research groups that resulted in tangible outputs. Seven of the respondents stated that their ICORG studies had led to new collaborations, mostly with university-based research groups, followed by clinical research groups and, to a lesser extent, charities. Respondents were asked to give examples of new collaborations and what beneficial outcomes had arisen as a result of these. Examples were given in the following categories:

- Charities: one participant described extensive collaboration with charities for clinical research, stating that funding was provided by the Irish Cancer Society (grant funding for a PhD student), the Drogheda Cancer Research and Education Trust (€100,000), and the 'Dip in the Nip (€30,000)' charity event.
- University-based research groups: one participant described collaboration with the Karolinska Institute in Sweden for an investigator-initiated study in renal cancer. A second participant described collaboration with Professor Karen Lu in the Department of Gynaecologic Oncology and Prof. Russell Broadus in the Department of Pathology at the University of Texas M. D. Anderson Cancer Centre (USA). This collaboration led to co-authored publications, further funding and exchange of knowledge and material.
- Clinical research groups: collaborations were described with other clinical research groups both nationally and internationally. For example, one participant described a new collaboration with EUTROC, a translational organisation for ovarian cancer research in clinical trials, which led to exchange of knowledge and material.

One interviewee (external collaborator) mentioned an example of ICORG's international orientation: ICORG is now sending four PhD students to UCLA to do research in translational research.

The results from the PI-survey (Figure 21) show that participation in international cancer research consortia was strongly increased by ICORG. Also the number of collaborative cancer clinical studies has strongly increased according to the PIs who responded to the survey.

There are no comparable cancer clinical research networks or cooperative groups operative in Ireland outside of ICORG. According to the GCO, ICORG is internationally seen as a gold standard in the area of breast cancer, and increasingly so for haematology and lung. External policy stakeholders agree that ICORG has a strong international reputation, mainly in North America. Among international cooperative groups in oncology, ICORG is considered one of the best worldwide (mainly in breast cancer), and in particular Prof John Crown, an ICORG founder, is very highly regarded.

## 3.5 Outcomes and impacts

### 3.5.1 Quality of research: publications

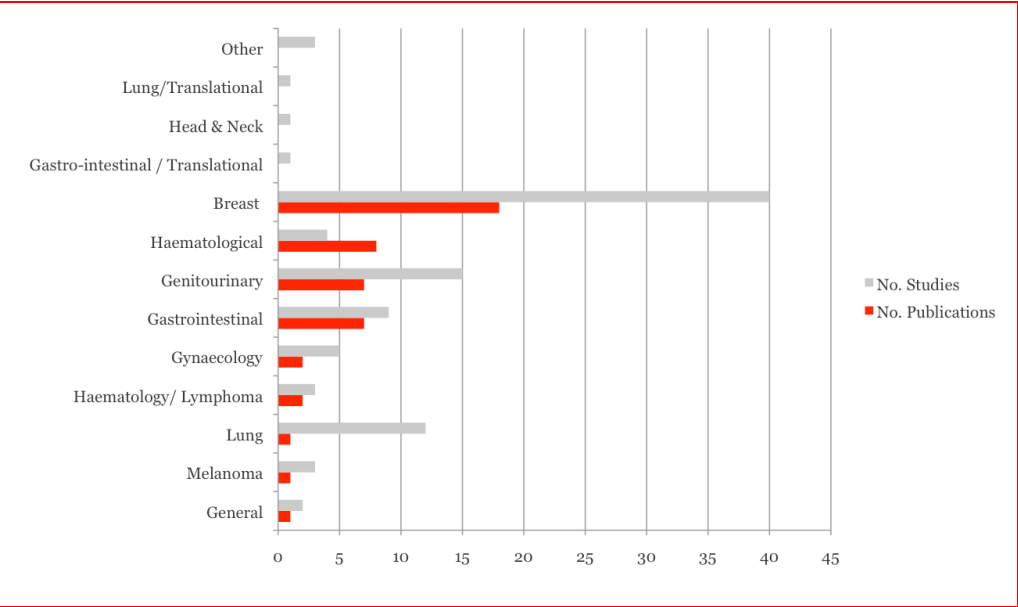
The HRB has analysed the publications associated with ICORG research as an indicator of research quantity and quality. Since 2002, ICORG has been associated with at least 47 peer-reviewed publications in the international literature.

In clinical studies, it is common practice to only reach authorship status if the organisation or researcher contributed to the study with at least 10% of the patient accrual. Of the 47 associated publications, ICORG reached authorship status in 34 cases. Since we have not performed a benchmark, it is not possible to conclude whether this is high or low compared to others.

An analysis of studies and publications since 2006 shows that, in absolute numbers, studies in breast cancer top the list with 40 studies and 18 publications (Figure 14). In relative terms however, the haematological studies led to the largest number of

papers: based on 4 studies, 8 papers were published. Translational studies (lung, gastro-intestinal) and the head and neck study have not as yet led to publications.

Figure 14 Number of publications compared to number of ICORG studies in each disease area since 2006

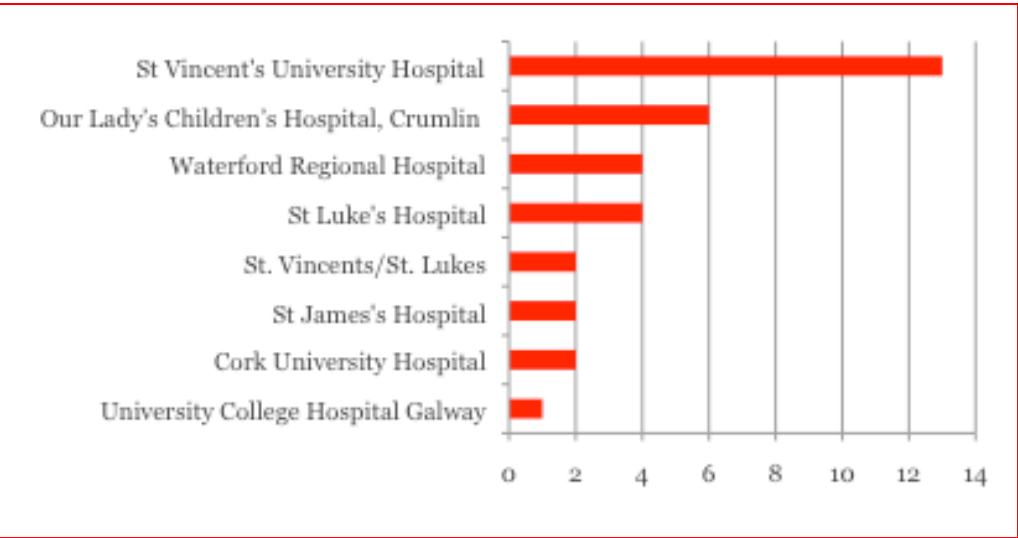


Source: HRB analysis

Most studies led to one publication, but in 5 cases the study led to 2 publications. One study led to 3 publications, and one to 5 publications.

The following figure shows the division of publications per hospital site.

Figure 15 Distribution of publications across ICORG sites (where PI was co-author)



Source: HRB analysis

Most publications are co-authored by researchers from England (15 papers), followed by the US (13), Australia (10), Spain (10). The following table shows the origin of the co-authors.

Figure 16 Country of origin of ICORG co-authors

Country	No. Papers
England	15
USA	13
Australia, Spain	10
France, Scotland	9
Germany	8
Poland, Belgium	7
Wales	6
Switzerland, Italy	5
Hungary, Canada, Austria, Sweden, Denmark, Czech Rep	4
Netherlands, Russia	3
New Zealand, Israel, Chile	2
Northern Ireland & Other countries	1

Source: HRB analysis

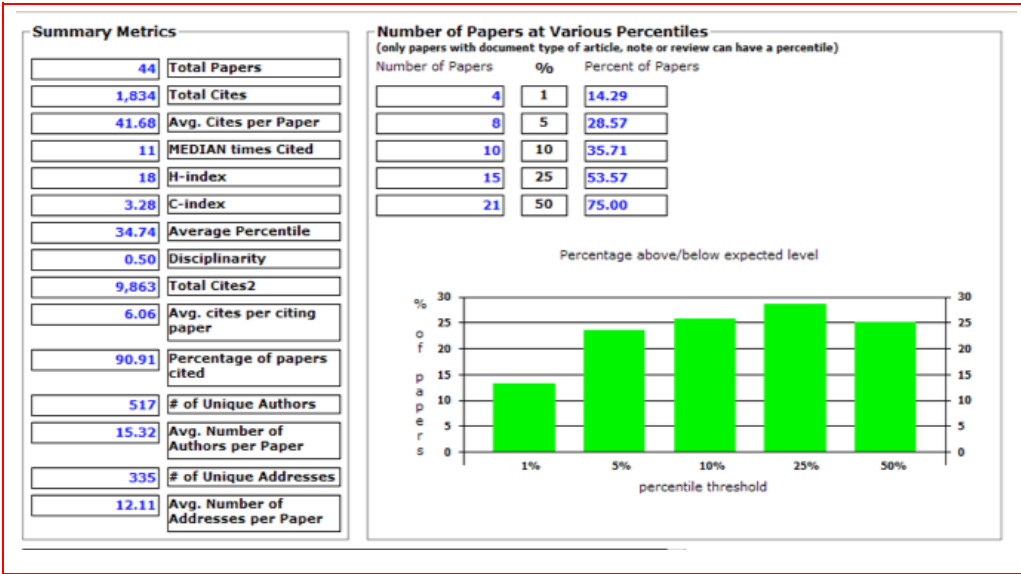
Thomson Reuters was asked to provide an analysis of the citation impact of the ICORG papers. A smaller number of papers than analysed by HRB was taken into account, namely 44. These papers were cited 1834 times, with an average of 41.68 times per paper. The H-index shows that 18 papers were cited at least 18 times. The C-index<sup>10</sup> shows that the ratio of actual to expected citations is 3.28, meaning that overall performance is good. All papers in the set received a strongly above average number of citations for their respective journal, article type and year.

The analysis also shows that these papers are written by a set of 517 unique authors, working for over 335 different organisations, with an average of 15.32 authors per paper.

One paper (Crown et al NEJM 2006) was cited 775 times, which biases the overall outcomes of this analysis. However, when excluding this paper, the C-index is still rather high, namely 2.40.

<sup>10</sup> The C-index equals the sum of all actual citations divided by the sum of all the expected citations. This indicates the ratio of actual to expected cites for a group of papers. This will tell you how a group of papers has performed overall, with each paper's impact having been normalized for its journal, year (indexed year), and article type. A C-index of 1.0 would indicate that all papers in the set received the average number of citations for their respective journal, article type, and year. The figure 20 also includes the **H-Index**. This statistic reflects the number of papers (**N**) in a given dataset having **N** or more citations. For example, an H Index of 77 indicates that in the dataset 77 papers were cited at least 77 times each.

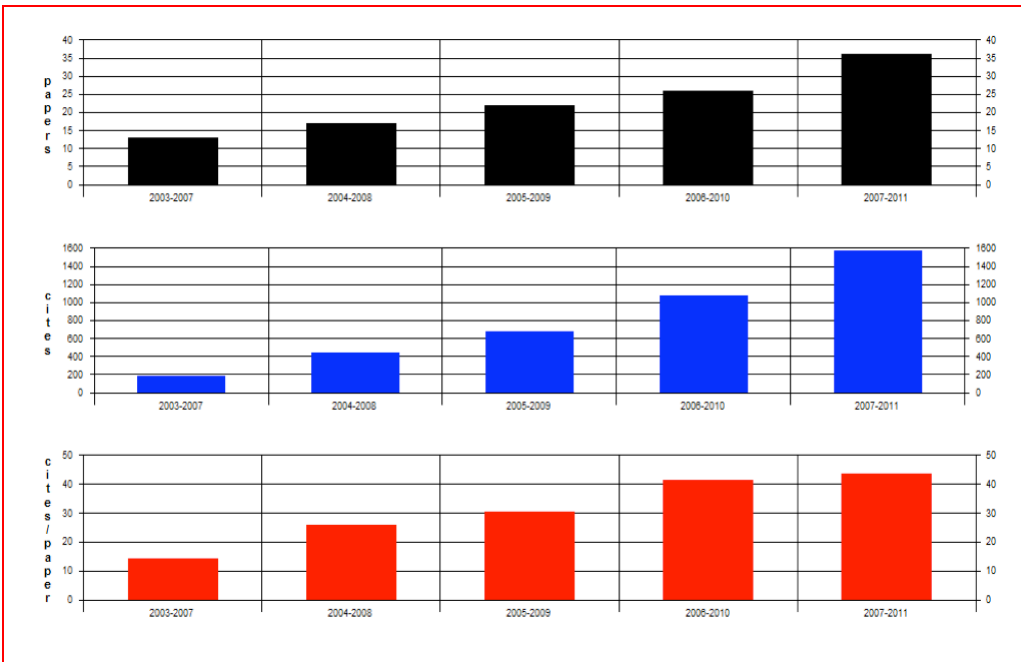
Figure 17 Thomson Reuters publication analysis



Source: Thomson Reuters

Moreover, there is an increasing trend in numbers of publications, and citations per publications over the years.

Figure 18 ICORG 5-year publication and citation trends



Source: Thomson Reuters

Finally, looking at the impact factors of the publications, one can conclude that the ICORG publications score high: 18 papers (41%) are published in journals with a very high impact factor (IF) > 15, of which four in the New England Journal of Medicine, a journal with an IF over 50. Seven papers are published in journals with IF between 5 and 10. One paper is published in a journal with IF between 10 and 15.

It is not known to what extent ICORG clinical trials have been disseminated through invited presentations and keynote speeches at major oncology conferences, as this data is not structurally collected by or made available through ICORG.



### 3.5.2 Impact on staff capacity building

#### 3.5.2.1 Training sessions and attendees

Figure 19 shows the total number of attendees that participated in ICORG training programmes and the number of times training sessions were organised per category. Figure 20 shows the distribution across these different types. According to the data from the interim progress reports, 690 people attended training related to GCP. GCP introductory, update/refresher and advanced trainings and hospital talks have been organised by ICORG since 2006, so it is very likely that the actual number of unique participants is significantly lower.

ICORG GCP trainings having been attended by a broad audience including principal investigators, sub-investigators, research nurses, pharmacists, pharmacy technicians, study administrators, data managers, radiation therapists, biostatisticians, translational scientists and ethics committee members. The participants include also personnel working in non-profit research in emergency medicine and HRB representatives. Two representatives from the Health Information and Quality Authority (HIQA) have applied to attend the first courses in 2012.

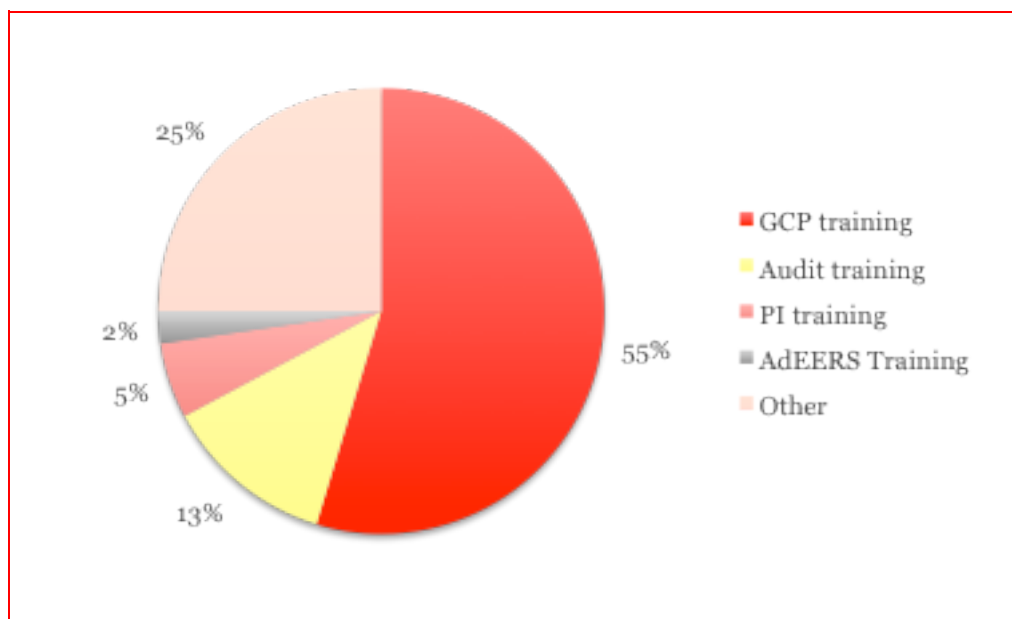
Figure 19 ICORG training 2006-2011: number of sessions and attendees

	2006		2007		2008		2009		2010		2011		Total	
	# t	# a	# t	# a	# t	# a	# t	# a	# t	# a	# t	# a	# t	# a
<b>GCP training</b>	7	149	12	141	23	190	13	98	11	87	4	25	70	690
<b>Audit training</b>	3	68	1	21	6	62	4	25	1	8	1	7	16	191
<b>PI training</b>	0	0	0	0	0	0	3	52	3	20	1	3	7	75
<b>AdEERS Training</b>	0	0	0	0	2	34	1	6	0	0	0	0	3	40
<b>Other</b>	2	56	8	95	8	156	9	131	5	50	0	0	32	488
<b>Total</b>	12	273	21	257	39	442	30	312	20	165	6	35	128	1484

Source: ICORG interim progress reports 2006-2011

# t = number of training sessions ; # a = number of attendees

Figure 20 Distribution between ICORG training types, by number of sessions, 2006-2011



Source: ICORG interim progress reports 2006-2011

Of all trainings in the category 'Other' the highest number of attendees was reached when Dr Charles Geyer (Medical Director of the NSABP) was invited as a keynote speaker (#45).

#### 3.5.2.2 Satisfaction about the training sessions

From the hospital progress reports and the interviews it can be concluded that most people feel that the training sessions respond to their needs and are of a high quality. The interviewed oncologists are also very positive about the training opportunities, and the quality is considered high. ICORG, however, does not consistently monitor the satisfaction of the attendees on the attended trainings so, unfortunately, no codified knowledge about training satisfaction is available.

When asked in the survey about training provided by ICORG, ninety percent of the hospital site respondents stated that ICORG training activities had enhanced capacities in cancer clinical research at their hospital through maximising the number of medical and nursing staff able to participate in cancer clinical trials. Also, because of ICORG-provided training on compliance with statutory regulation and audit preparation, better audit outcomes have been achieved and this has helped to increase the capacity for hospitals to host cancer clinical trials. Unfortunately there is no data available on the outcomes of audits.

Participants were also asked to identify training needs that should be met by ICORG within the next one to three years. Respondents put forward the following areas that they thought could benefit from ICORG-provided training in the future:

- Data management
- Pharmacovigilance
- Project management
- Clinical trial development
- Public relations and presentation skills
- Budget management
- Training on quality control system

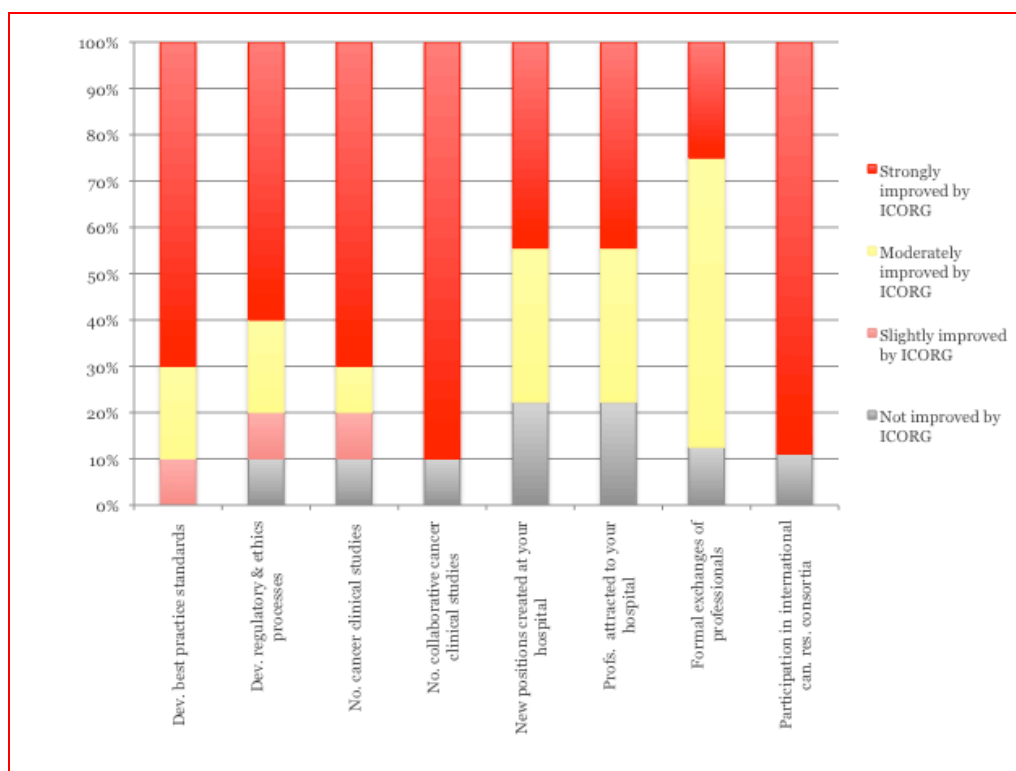
Some interviewees were less positive about the current training opportunities of ICORG. One industry representative mentioned that they do not recognize the ICORG GCP training, and that oncologists participating in their studies have to take their own course as well. According to one policy stakeholder, nurses do not yet benefit sufficiently from training.

### 3.5.3 Impacts on standard setting

According to the interviewees ICORG has had an important impact on standard setting. A policy maker indicated that ICORG has been very important in ensuring quality in clinical research as it ensures minimum standards and provides oversight. This approach “rules out individual ‘pet projects’ that are not in the general patients’ interest”. Industry representatives mention that ICORG has helped establish and disseminate guidelines through its members in the disease specific subgroups. An ICORG oncologist noted that standards that are applied in clinical trials are often later adopted hospital-wide. Another stated that standards in pharmacovigilance in particular have improved due to ICORG. There is some room for improvement in knowledge dissemination as researchers from other disciplines noted that ICORG’s standards are not disseminated to other disease groups, since there is very little interaction in this respect.

The majority of the PIs who responded to the survey (n=10) stated that ICORG has strongly improved all capacity areas at their hospital, and has had a positive effect on the number of collaborative cancer clinical studies carried out. It also improved their participation in international cancer research consortia. One hospital site (OLHSC) however was consistently less positive, which might be caused by the fact that it is less strongly integrated into the group.

Figure 21 Impact of ICORG on member hospital’s capacity to conduct cancer clinical trials.



HRB analysis

The respondents described the benefits of working within a network with strong central administration. In particular, the benefit of having support and expertise from

the GCO, which enables trials to be efficiently established and managed, was emphasised by the respondent group. For example, according to one respondent:

*“ICORG GCO staff have enormous expertise in the conduct of international trials, from EudraCT numbers to drug importing regulations which enables the smooth initiation of clinical trials”*

Respondents also stated that as the GCO is responsible for preparation of ethics and regulatory report, staff at the hospitals are able to focus on the practical work of running the clinical trial.

They also described the network and cooperation between the trial sites as a benefit of ICORG membership. This was mostly expressed in terms of increasing opportunities for networking and exchange of ideas between staff working on ICORG cancer clinical trials. One participant also described the network of sites as a benefit in the following way:

*“National network - It counts for more than 95% of the Island's cancer treating consultants among its membership ensuring that research into cancer develops at a national level across all localities. It creates more research opportunities for patients by having a formal structure that makes Ireland more attractive as a location for cancer research trials”*

Membership in ICORG was regarded as facilitating members to collaborate with international cancer research groups, illustrated by the following comment from one respondent:

*“Because the ICORG network offers industry and international co-operative groups access to numerous centres our patients get access to clinical trials as part of ICORG when individual centres would not be considered for participation”*

#### 3.5.4 Impact on research infrastructure and research policies for clinical trials in Ireland

The impact assessment did not lead to any evidence of ICORG's impact on the creation of key resources such as biobanks, data sets or cohorts. Interviewed policy makers do not think that ICORG has directly influenced the development of national (research) infrastructure for clinical trials, such as the above-mentioned biobanks, etcetera. Although this was not a core objective for ICORG, it is interesting to see whether it has had impact on the further development of it by other actors. The results from the interviews point in the direction that ICORG might not have had a direct impact on this infrastructure creation, but it did serve as an incentive for others to start working on this.

In addition, most interviewees did not think that there were any changes in research policies in Irish governments as a result of ICORG actions.

It was also asked in the Hospital site survey what other factors (i.e. in addition to ICORG) might have influenced the quality and quantity of cancer clinical research in Ireland over the last decade. Factors mentioned are:

- Recruitment, and attracting back from overseas, of more consultant medical oncologists
- The development of the National Cancer Control Strategy
- Availability of grant funding to collaborative groups
- Close collaboration, support and advice from the Irish Medicines Board
- The presence of major pharmaceutical companies in Ireland

One policy stakeholder was very positive about ICORG: *“Compared to the Canadian situation, ICORG’s clinical and translational research in Ireland is very impressive for such a small country. Ireland is punching above its weight, and ICORG has been hugely effective in scaling up clinical research.”*

Most interviewees state that without ICORG HRB funding would not have lead to similar results. As one external policy stakeholder stated: *‘ICORG is the engine [of clinical trials; ed.] and HRB funding is the fuel. You need both.’*

### 3.6 Conclusions

In the chapter above several aspects of ICORG’s activities, outcomes and impacts on cancer clinical research have been presented. In general, ICORG’s impact has been high, both in terms of quantity and quality. The total number of studies and staff has risen and ICORG is a unique organisation in Ireland. ICORG created the necessary infrastructure to perform high-quality clinical research and provided training on all levels. ICORG published and presented its results in international journals and on conferences and has built a strong international reputation. ICORG contributed to improving and harmonising guidelines for trials and to raising the national awareness for the need of putting key resources in place for clinical research, such as cancer biobanks and diseases specific cohorts.

## 4. ICORG's impact on cancer care and clinical practice

### 4.1 ICORG and clinical care

Although the conduct of clinical trials in oncology in Ireland is the direct goal and mission of ICORG, the ultimate aim of such research is to improve clinical care and clinical practice. Although it is difficult to attribute changes in clinical care and practice to individual clinical trials, a decade of ICORG activities offers an opportunity to assess any measurable impact. A number of key issues can be defined in this respect:

- Impact on clinical guidelines, new treatments, diagnostics and prognostics
- Benefits accrued while patients participate in ICORG clinical trials
- Long-term benefits, such as better outcomes and improved quality of life
- Impact on the clinical participation rate

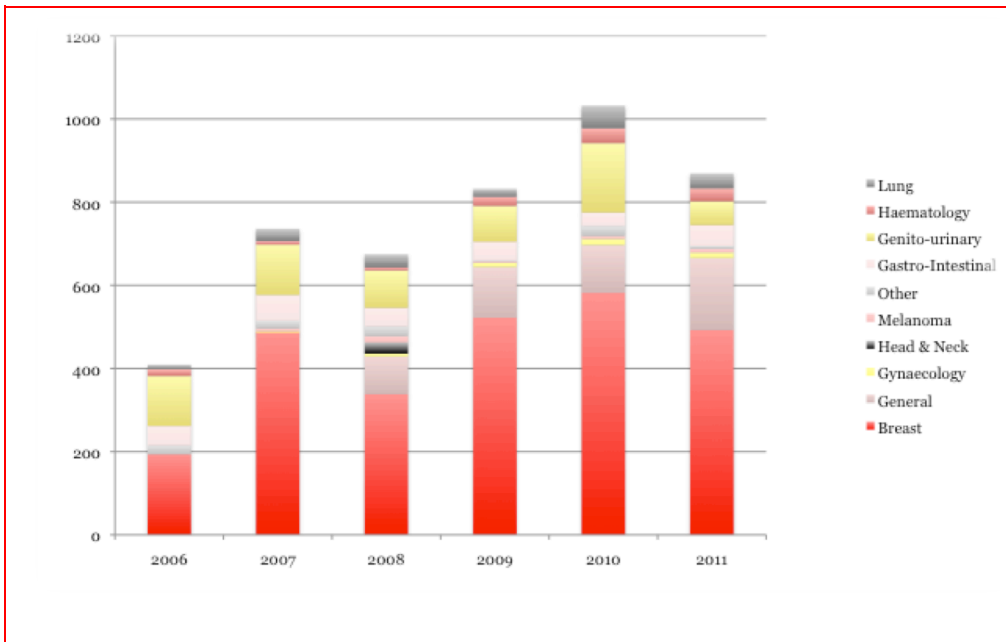
These issues and related topics will be discussed in this chapter. Following the structure of the previously described methodology, the analysis will start with a description of ICORG activities that relate to clinical care. Then, an overview will be given of direct outcomes, such as direct benefits for participating patients and newly developed treatments. After that, the more long-term and general impacts on care and clinical practice of ICORG activities and subsequent outcomes are discussed, followed by a summary conclusion.

### 4.2 Care and clinical practice activities

#### 4.2.1 Patient accrual

The most obvious activity of ICORG, related to clinical care, is the conduct of clinical trials and then recruiting patients into these trials. As can be seen in **Error! Reference source not found.**, patient accrual has increased from around 400 patients in 2006 to 850 in 2011. Data before 2006 is unfortunately not consistently captured, and has therefore not been included. It is important that the shown data and those further on, are based on the figures for ICORG studies only. Other clinical trials pursued in the Irish hospitals are not included. There has been considerable fluctuation over the years, with 2010 so far having the highest accrual with over 1000 patients recruited. What is noticeable is that breast cancer has consistently represented by far the largest group of patients in ICORG studies. As explained before, the drop in accrual in 2011 can be related to the fact that many large breast cancer studies were completed in 2010. An interesting development, also mentioned in the previous chapter, is a process of diversification throughout the years. The total number of disease groups included in ICORG studies has risen, and the patient shares between different groups have become more balanced.

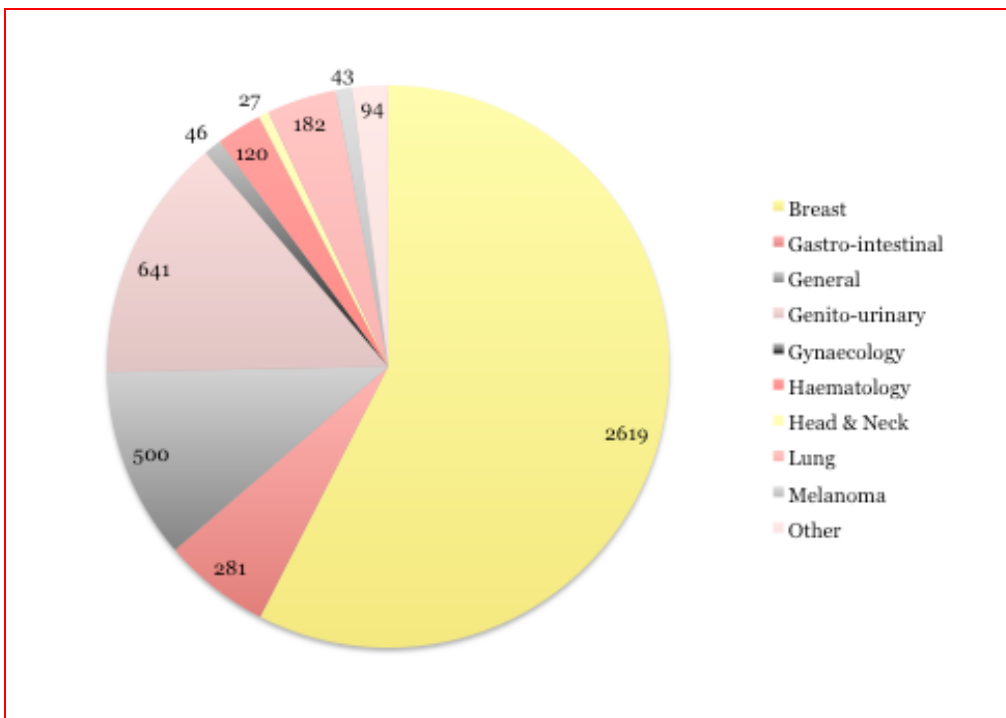
Figure 22 Patient accrual for ICORG studies



Technopolis Group, based on ICORG data

The total number of patients participating in ICORG studies over the years 2006-2011 can be found in Figure 23. The figure clearly shows that accrual to breast cancer studies represented more than half of the total accrual, with other major disease groups represented in ICORG studies being 'general', genito-urinary and haematology. General studies are those that study treatments, diagnostics or prognostics that are not disease-specific. The total number of accrued patients over this period was 4553.

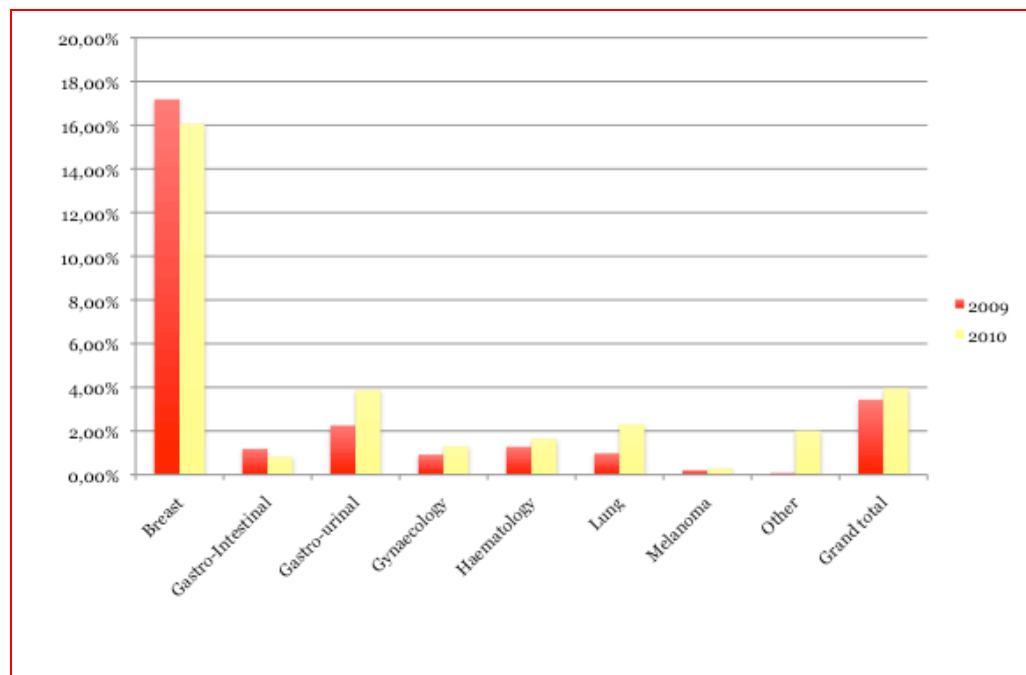
Figure 23 Total patient accrual 2006-2011



Technopolis Group, ICORG data.

In order to gauge how these figures compare to the total number of cancer patients in Ireland, Figure 24 shows the accrual percentages of ICORG studies in Ireland for 2009 and 2010. These have been calculated by dividing the number of patients on ICORG trials by the total number of patients in the Irish public hospitals where cancer clinical care is given by disease groups. These figures are estimates and could be slightly different as data on the Waterford Regional Hospital is missing and patients on 'general' trials could not be classified by disease group. The figures indicate that ICORG has a relatively high accrual percentage for breast cancer in 2009 and 2010, around 16% of all patients in Ireland. All other included disease areas stay below an accrual rate of 4%. Interestingly, there is a slight trend towards diversification noticeable, as accrual rates for the breast cancer have been dropping, most other disease areas have had increasing accrual rates. Overall, 3.95% of Irish oncology patients participated in ICORG studies in 2010. According to the international expert panel, this rather low accrual rate is an international problem, and not ICORG-specific. Because of a development towards personalised medicine and better disease aetiologies, large cohorts are much more difficult to find. Although personalised medicine and molecular stratification and subdiagnosis of diseases classically organised by their anatomical site has increased the understanding of a variety of cancers, accrual for clinical trials became more difficult, all over the world. For ICORG this effect became clear in the past few years as well and studies are often smaller and more targeted. The peers also stated that despite this international trend, the overall goal internationally remains around 10% accrual to clinical trials.

Figure 24 Accrual percentages ICORG studies



Technopolis Group, HRB and ICORG data

#### 4.2.2 Information delivery and communication to stakeholders

A key activity of ICORG as a cooperative coordination group is to share and deliver information to all relevant external stakeholders. An overview of ICORG communication instruments is given below in Figure 25. The ICORG Newsletter is an important tool for internal communication and generally well received by its members and some policy makers that receive it as well. The only communication tool for ICORG also explicitly aimed at external stakeholders is the website, which is quite well visited with around 2000 unique visitors a month. The websites was appreciated by



some policy makers, but others were critical about the fact that the website is not very interactive and that news items on the website are not up to date. There is some merit to this argument, since in mid-February 2012 the latest update stemmed from October 2011, and the new ICORG chair was not yet mentioned. Many policy makers feel that the overall communication to external stakeholders is lacking, resulting in a perception of a closed organisation with opaque activities.

Figure 25 ICORG communication instruments

Communication instrument	Goal and target group	Target group	Size of target group
<b>Website</b>	<p>The ICORG website is divided into a “public” area and “member’s only access” area.</p> <p>The “member’s only access” area provides access to the study specific information and study documents.</p> <p>The public area describes ICORG’s structure and background, a list of all ICORG members, a section with news and events, a background of clinical trials and a section on training.</p>	ICORG members and public	2000 unique visitors a month.
<b>iPhone App.</b>	<p>Recently launched. It currently mirrors the information available to members through the member’s section of the ICORG website e.g. studies per disease area that are open to accrual, protocol details, PIL documents etc. This allows the investigators at site access to this information in the clinic setting enabling them to inform their patients of their potential eligibility for suitable studies immediately</p> <p>Future developments would for example include the use of push notifications – these would be used to inform members of newly opened studies and upcoming meetings.</p>	ICORG members	Unknown
<b>ICORG Newsletter</b>	The purpose of the ICORG newsletter is to inform the Group members of progress on studies as well as keeping the members up to date on issues such as training opportunities and DSSG news. A minimum of four newsletters is issued per year, preceding the DSSG meetings.	ICORG members	At least to all ±430 members
<b>Minutes of DSSG meetings</b>	The minutes of DSSG meetings are sent to members one month after the DSSG meetings. The minutes provide information on the accrual numbers among the hospital sites. It also describes the issues and possible solutions and outline the action plan generated as a result of the discussions.	DSSG members	Dependent on disease group

Patient communication is a crucial part of conducting a successful trial, as patients always have to consent to participate. Currently this communication is mainly ad-hoc, and policy stakeholders considered that the current awareness among patients of the possibility of participating in clinical trials was quite low. Recruiting patients is currently mostly up to the individual consultant that is responsible for informing and referring patients. If the oncologist is not research-oriented or simply too busy, there is a risk that patients are not offered the possibility of participating in a study. The ICORG stakeholders confirmed in the interviews that there are no major ICORG activities for raising patient awareness.

There was some discussion among stakeholders in the interviews whether it would be beneficial to have a more explicated communication strategy towards patients. Whereas some policy makers, oncologists and patient representatives saw a general benefit in raising more awareness among patients and the general public, some medical professionals noted that due to strict eligibility criteria many patients would never qualify for participation. It could be dangerous to raise expectations too high and afterwards having to disappoint many. These oncologists would rather focus on targeting other oncologists that are not involved with research to better refer patients they are treating. One suggestion that was offered by many was to work closer with the

Irish Cancer Society, which has strong communication resources and good access to patients through their daffodil centres in hospitals.

### 4.3 Outcomes, and impacts

#### 4.3.1 Direct patient benefits

Over the past decade a significant number of patients have participated in ICORG trials. In order to assess how this has contributed to patient care, it is important to distinguish between three different levels of benefit. The first group are those patients that received access to new treatments as a part of their trial. The second group are all patients that participated in trials, including the control group that received a different treatment due to their participation. The last group of effects are indirect spillover effects by which ICORG trials have changed the standards of care for the general cancer care system in Ireland.

When looking at the direct effect for those patients receiving new treatments as a part of their participating in the trial, there is widespread agreement among research oncologists that this has been the most important impact of ICORG. Although the very nature of clinical trials and research is that there is a fundamental uncertainty regarding potential benefits of new treatments, most oncologists and external stakeholders do believe that ICORG studies have provided access to very successful new treatments. The table below, Figure 26, shows an overview of some of the most successful treatments that were delivered through ICORG studies to Irish patients. These examples resonated with virtually all stakeholders. Both in the survey, as well as in the interviews, many oncologists referred to the Herceptin study (Trastuzumab) as a particular achievement of ICORG. This study, where ICORG was internationally leading the investigation, pioneered the use of targeted drugs tailored to patients with a Her2 positive genetic expression. In total, 129 Irish patients enrolled in this study.

Figure 26 Selection of ICORG successful treatments

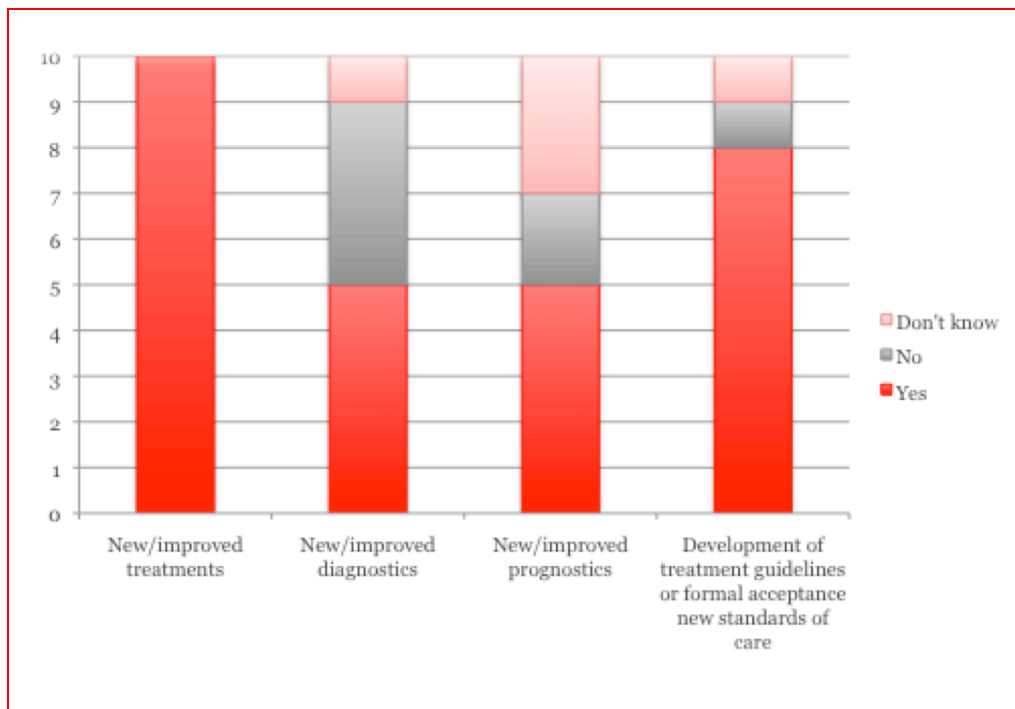
Start Year	Treatment name	Description
2001	Trastuzumab (Herceptin study)	Adjuvant breast phase III trial with Trastuzumab showed a reduction in breast cancer relapse by approximately 50%. (NEJM 2011)
2002	Glivec / Imatinib	A study into Chronic Myeloid Leukaemia (CML) which resulted in the effective drug Glivec that increases life expectancy of CML patients.
2003	Capecitabine & Oxaliplatin	The combination of capecitabine & oxaliplatin offered significantly superior Disease-free survival at 3, 4 and 5 years.
2004	Lapatinib	Lapatinib significantly improved the overall survival rate (NEJM 2006)
2005	Bortezomib	Study Reported at World Myeloma congress 2009, bortezomib shown to be effective in 2nd line myeloma
2006	Biweekly treatment for prostate cancer	Biweekly treatment shown to be better tolerated and improves survival
2008	Exemestane	Adjuvant therapy with exemestane appears to be more effective than tamoxifen in reducing disease recurrence in breast cancer patients.
2008	Abiraterone	Study reported in October 2010, abiraterone increases survival by an average of 4 months

Technopolis

Besides new treatments made accessible during ICORG trials, the survey also inquired about new or improved diagnostics and prognostics. The overall responses of this survey question can be found in Figure 27. As mentioned before, ICORG investigators are unanimous regarding new treatments, but only half were convinced that new

diagnostics and prognostics were developed. Most diagnostic and prognostic improvement is related to improvement in general infrastructure and will be discussed later on, but a good example of a prognostic direct benefit is the TAILORx (Trial Assigning Individualized Options for Treatment (Rx)) study. This study examined whether genes, that are frequently associated with risk of recurrence for women with early-stage breast cancer, can be used to assign patients to the most appropriate and effective treatment. Led by the National Cancer Institute in the US, almost 11,000 patients participated in this study. In Ireland, ICORG's TAILORx trial included 690 patients that benefitted from this new approach, according to the ICORG GCO. The resulting test has recently been approved for clinical use in Ireland by the NCCP.

Figure 27 Number of respondents who considered that ICORG studies had led to improvements in clinical practice and patient care



Source: HRB analysis

#### 4.3.2 Direct benefits for all participants

The second group of effects which ICORG could have had on patient care are those not related to receiving the treatment while being on trial, but rather on the effect of different care itself. Do patients receive better care with better outcomes, even when they receive a placebo? A significant number of oncologists do believe that patients generally receive better care due to more contact hours and more follow-up. Other oncologists confirmed the latter, but were of the view that this does not necessarily lead to better outcomes. Some interviewees also doubted whether patients receive a higher quality of care, since all care should already be up to gold standard if hospitals want to participate in clinical trials. Proponents and opponents agree that it is impossible to measure whether ICORG trials overall led to better outcomes and survival rates for participants when comparing to standard care. The selection bias in trials, since patients with multiple conditions are often excluded from trials, makes it very difficult to generate conclusive evidence on this question.

#### 4.3.3 Indirect effects and impact on standards of care

The third group of effects that can be distinguished are those that ICORG had on raising general standards of care in ICORG hospitals and on the general healthcare system. These effects are mainly side effects of having the ICORG structure operational and clinical trials taking place in Irish hospitals.

The first, and perhaps most obvious effect of ICORG, is the availability of new treatments to Irish patients after trials successfully concluded, such as those mentioned before in Figure 26. Although the drugs and treatments might have been developed without ICORG as well, ICORG's participation led to a fast-tracked implementation of new treatments for all patients in Ireland, according to both medical and industry stakeholders.

A second indirect effect, which is often recognised among stakeholders, is an improved capacity among medical professionals. When continuously involved with trials, medical staff stay up-to-date with latest treatments, diagnostics and prognostics. ICORG training further raises skill and knowledge levels among clinical consultants. Also mentioned is an improved awareness of potential side effects and complications when working with these new treatments due to earlier experience. These capacities do not just benefit trial patients, but also other patients receiving care from staff that have taken or will take part in trials. Some policy makers, however, were disappointed with the scope of this 'spillover', since trials often take place in separate departments with very little exchange in staff.

Another effect on standards of care relates to the increase in the availability of infrastructure. ICORG trials have spurred the introduction of on-site clinical diagnostics, which became available to all patients. For instance, one oncologist mentioned that hosting an ICORG clinical trial led to the introduction of KRAS/EGFR/BRAF testing. Another professional mentioned that the trials have led to greater use of MRI for patients diagnosed with spinal cord compressions.

Having an organisation like ICORG also ensures quality standards of care in multiple ways. In order to be eligible for a study, a hospital site has to continuously keep their guidelines and standards up to date. This aspect is strongly reinforced by the fact that ICORG performs internal audits of participating sites. One oncologist noted that a joint responsibility for quality standards at all sites has helped weak sites enormously to improve their standards of oncology care, by offering feedback and solutions. Policy makers were extremely positive about this of ICORG activity. One senior policy maker noted that ICORG had identified the same weak sites as they did during internal research, and ICORG resolved the situation without the need for government intervention. While acknowledging this important contribution of ICORG to ensuring minimum standards of care, some policy makers feel that ICORG could and should have gone beyond minimum standards. The exchange of best practices in treatments, care and diagnostics does not take place on a structural level. According to some policy makers, their studies still found wide discrepancies in implementation of new treatments and care protocols, leaving much room for improvement in terms of patient care. This heterogeneity was confirmed by an external medical professional, who urged to use ICORG as a way to disseminate already developed international standards and guidelines in clinical care.

It needs to be said that the NCCP has only been in existence since late 2008, and that that also explains why there is currently still a dearth of clinical guidelines in cancer care in Ireland. This is set to change over the next years as they will take a more proactive role in this respect. Due to the small number of oncologists in this country and the high coverage of ICORG, ICORG researchers are well situated to influence these guidelines. Also, one PI is the national lead for medical oncology and most other relevant people are also ICORG members.

Finally, it may be interesting to assess whether ICORG has had an overall impact on patient outcomes and survival rates. Most stakeholders arrive at an intuitive positive answer, but also point out that this is impossible to quantify and prove. Since there are

no obvious detrimental effects of ICORG and the previous paragraphs have indicated that ICORG has had various benefits to patient care, it would seem logical to conclude that ICORG has had a general positive effect. However, taking into account that in the end only 4% of Irish cancer patients participated in ICORG trials it is hard to conclusively establish that it had a substantial or even large impact on patient outcomes. However, according to some oncologists, there is some tentative evidence that ICORG's focus on breast cancer made it able to fully capture the potential improvement in survival rates. Between 1997 and 2007, the 5-year survival rate increased from 70% to 80.6%. Although this has been a global trend, many oncologists are convinced that the Irish health care system would not have been able to absorb the responsible treatments, diagnostics and prognostics without ICORG.

#### 4.4 Conclusions

ICORG has had a large impact on the number of clinical studies in Ireland, but also on the participation rate of Irish patients to these studies. Especially for breast cancer, the accrual rates are high. In the other fields, more recently developed, the accrual rates can still be improved although this seems to be an international problem and not specific to ICORG. There is an overall feeling that ICORG is weak on external communication, and this could be improved. There is currently no structural communication towards patients around clinical trials, and the extent to which ICORG should play a direct or indirect role is debated.

ICORG was able to deliver some effective and new treatments to patients. There is also evidence of new diagnostics and prognostics, although these are more limited in scope and number. The function of ICORG as a diffusion network of new treatments and care protocols is limited. ICORG however has had a large effect on vitalising the oncology groups in Ireland. Especially in breast cancer, a large number of patients directly benefitted from receiving superior treatments through ICORG trials but the general benefit accruing to patients regardless of treatment is more difficult to measure.

## 5. ICORG's impact on the economy

ICORG does not have a specific economic mandate. However, HRB requested in the terms of reference for this study to examine, at a limited level, the economic impact that ICORG might have had since 2002. This includes the leveraged funding, and any other revenues or other in-kind benefits accruing to ICORG and the economy from industry collaboration. The analyses in this chapter of the economic impacts of ICORG are based on information provided by ICORG and HRB, on interviews held with key stakeholders and on two surveys sent to the PI's of the ICORG sites and to the most important industry collaborators.

### 5.1 Activities with industry, funding and outputs

Over the years, ICORG increasingly collaborated with industry. Industry trials are important for ICORG since they bring new drugs to patients and can fill gaps in the portfolio of available trials. According to ICORG, it has collaborated since 2002 with about 46 companies, including the large companies such as Abbott, Cougar, Syndax, AstraZeneca, Astellas, Boehringer Ingelheim, Bristol Myers Squibb, GSK, Johnson & Johnson, Sanofi-Aventis, MSD, Wyeth, Pfizer, Amgen, Novartis, Roche/Genentech, Merck/Serono, Bayer. These relationships vary from first-time collaborations to close collaboration with companies that repeatedly return to ICORG.

ICORG collaborates with industry in studies ranging from the earlier phases of development of novel compounds to the larger trials in which established compounds are being used. Many of the studies are pivotal registration trials for the compounds involved. This reflects the growing reputation of the group amongst its industry partners.

The figure below shows the current collaborations of ICORG with industry.

Figure 28 Industry collaborators in 2012

Pharmaceutical company	Number of trials ICORG is participating in
<b>GSK</b>	12
<b>Pfizer</b>	5
<b>Amgen</b>	5
<b>Novartis</b>	5
<b>Bristol Myers Squibb</b>	4
<b>Celgene</b>	3
<b>Sanofi-Aventis</b>	2
<b>MSD</b>	2
<b>Roche/Genentech</b>	2

Source: ICORG Application to HRB, 2012

The figure shows that ICORG has a strong relationship with GSK: it is participating in 12 studies with the company. According to ICORG, this relationship has significantly grown in recent years with ICORG sites participating in multiple GSK sponsored trials. One of the follow-ups is that GSK now supports the development of a number of ICORG in-house investigator initiated trials. A number of the ICORG sites (SVUH,

SJH, AMNCH) are seen as ‘hub sites’ for GSK which is, according to ICORG, related to the positive accrual contribution and the quality of the data of these sites<sup>11</sup>.

A study can be both sourced or sponsored by industry. If it is sourced by industry the company asks ICORG to review a protocol. This is then circulated in ICORG and if the study is adopted by the DSSG and ICORG executive, the protocol becomes an ICORG study. An increasing number of ICORG studies was sourced from the industry, as already was shown in Figure 9.

The table below shows the percentage of the ICORG studies that was sponsored by industry from 2006.

Figure 29 Industry sponsored studies

	2006	2007	2008	2009	2010	2011
<b>Total ICORG studies</b>	24	39	54	51	59	48
<b>Industry sponsored</b>	20%	26%	30%	35%	29%	29%

## 5.2 Outcomes, impacts

The collaboration with industry has led to various outcomes and impacts. According to the GCO, collaborations with industry have helped the group to develop relationships that have aided in the funding of many of the ICORG in-house investigator led studies. This way, the collaborations help strengthening the financial position of the Group.

The five companies<sup>12</sup> that answered our question what the reasons were to collaborate with ICORG say that:

- ICORG helps them to meet their company targets;
- ICORG allows them to work with the best oncology experts in Ireland. Since the network represents almost all oncology experts in the country, it is an easy way to access them through ICORG.

Most of these respondents say to have provided medication or prognostic tests free of charge as their contribution to the ICORG trials, and in some cases a form of financial contribution. One of the respondents for instance stated that an annual 2.7 million Euro was spent by the company on oncology trials in Ireland, of which mostly through the ICORG network. The survey respondents regarded ICORG as well organised and the working relationships with the organisation are considered strong. The following sections will provide a more detailed overview of these outcomes and impacts.

### 5.2.1 Leveraged funding

ICORG is partly funded by the Irish Cancer Society and through the HRB grant awarded by the All Ireland Cancer Consortium. ICORG has received a total of €36.5 million from the HRB since 2002 to build capacity for the conduct of cancer clinical trials in Ireland. Of the €36.5 million, ICORG received €12.5 million over the latest award cycle 1 July 2009 to 30 June 2012. The Irish Cancer Society yearly provides a

<sup>11</sup> ICORG application to HRB, 2012

<sup>12</sup> The industry participants in the survey and interviews were selected by ICORG itself, which might cause a bias in the answers. Only collaborating industry was selected due to limited sources for this study and the expectation that collaborators would be best informed about the impacts of ICORG since they know the organisation.



fund of €300,000. Other funding is leveraged from collaborative groups (for the trials), industry and donations. According to GCO, there is unfortunately no accurate information available about the leveraged funding prior to 2009.

According to the data, the leveraged funding in the past three years was about € 3.8 million on top of the € 12.5 million awarded by HRB.

Figure 30 Leveraged funding 2009-2012 in Euro

	Total	2009 (6 mts)		2010 (12 mts)		2011 (11 mts)	
		GCO	Site	GCO	Site	GCO	Site
<b>Industry</b>	1,211,589	182,374	29,997	5.2.2 44 8,943	120,794	323,393	106,088
<b>Irish Cancer Society</b>	600,000	300,000		300,000		0	
<b>Collaborative Groups</b>	1,743,229	76,619	241,706	233,100	510,229	188,054	493,521
<b>Donations (other)</b>	261,842	49,434		79,549		132,859	

Source: ICORG grant application to HRB, 2012

### 5.2.3 Additional investments made by industry

In the survey, ICORG's PIs also stated that being part of ICORG has helped them to form new collaborations with the industry. ICORG provides a 'quality mark' that benefits the hospitals in the sense that they received free medication or direct contribution to the trial, a form of 'additional investments' made by the industry in ICORG.

The interviews show that different stakeholders have very different views on the value of these drugs. While some external interviewees were sceptical about the actual value of these drugs, most oncologists were positive and they stated that these free drugs do represent a significant sum. One external collaborator noted that ICORG participation in the Herceptin studies allowed patients free access to drugs that cost 50,000 dollars a year.

In the survey, one hospital site described significant savings due to the provision of free drugs through collaboration with industry. They estimated savings of €212,635 in 2009, €278,222 in 2010 and €304,563 in 2011 through the provision of free drugs by industry. One other respondent stated that industry collaboration resulted in a directed financial contribution through a per patient fee which funded approximately one third of their costs – including both personnel-related and non-staff costs.

GCO stated<sup>13</sup> that in 2008, a conservative estimate of the value of medications provided for free to ICORG trial patients receiving them in their licensed settings was €4 million. In that same application document, it was projected for 2009 to grow to a minimum of €6.2 million. Besides this, industry sponsors ICORG by means of funding scans, pharmacy support, and industry resourced research nursing. Unfortunately GCO was not able to provide additional and up to date information about the value of medications provided free-of-charge over the years, or in the past few years.

Only recently ICORG started to actually capture data to analyse the annual investment made by the industry partners. Some information has been received, but GCO expects to complete these data only in the course of 2012. As an example, data recently received from one of the larger partners calculates their YTD investment to be €2.7 million in 2011. This includes resource support (in-house and at sites), the value of comparator drug products (€618k) and the value of tests, scans, investigator fees, EC fees, regulatory fees and volunteer payments. The annual investment for the years

<sup>13</sup> ICORG application to HRB, 2009



2007-2010 ranged from €2.35 million to €2.76 million and the predicted annual investment for 2012 is €3 million.

Based on the information received to date, GCO would estimate the annual value of drug products over the years 2007-2011 to be of the order of €3 million (which is less than the projected value in the 2009 application to HRB), and the value of tests and scans to be an additional €1 million.

#### *5.2.4 Satisfaction of industry and other groups about working with ICORG*

Both industry respondents in the survey and industry interviewees found ICORG very favourable and beneficial for their companies and they consider it a vital resource in planning and executing cancer clinical trials in Ireland. Companies that have collaborated with ICORG consider it a well organised, well resourced and highly professionally body and all respondents plan to collaborate with ICORG again in the future.

All interviewed industry partners applauded the initiative and appreciate the efforts ICORG puts in recruiting patients, funding research nurses and building trust between the partners. ICORG achieves high accrual rates, has dedicated oncologists and provides good access to populations. One company stated they 'only are active in Europe because of ICORG'. They also stated that 'without ICORG funding research nurses, GSK would leave Ireland immediately'. The industry interviewees found that 'ICORG people have good connections and they are very knowledgeable. It is nice working with them because they have a positive can-do attitude'. Most companies who filled in the survey are very positive about the ability of ICORG to manage complex trials. The capacity of ICORG to deliver targets, and their track record, makes the organisation very attractive for industry to work with, they say. Moreover, the affiliated personnel is described as 'professional and dedicated'.

To one of the interviewees ICORG's presence is a 'major selling point' for global R&D headquarters when sourcing studies to Ireland. One respondent in the survey stated to be very positive about 'their consistency of recruitment, quality of data and ability to meet the critical database timelines. We have had three Irish Medicine Board inspections of ICORG sites and we were very happy with the outcome of these inspections'. Another respondent mentioned the positive trend of ICORG being increasingly involved in industry-led studies, and strengthened ties between industry and research in Ireland. One pharmaceutical company representative stated in an interview that a strong feature is that ICORG will not pursue competing studies after a contract has been agreed upon. This exclusivity is very important for industry.

All industry representatives agreed that ICORG facilitated their research enormously by taking the role of a central coordination body. ICORG provides the industry 'one point of contact' that covers the area of cancer clinical trials as opposed to several competing groups. The ICORG model is considered best practice in this respect. If all sites would have to be contacted separately, this would have severely limited the number of studies that would be sourced in Ireland. Indeed, one major pharmaceutical company that actively collaborates with ICORG on a range of studies stated that were it not for ICORG that it would have most likely ceased all cancer clinical research activity in Ireland, as it has ceased research activity in all other disease areas. The company commented that the establishment of ICORG-like structures in other disease areas would have a major positive impact on clinical research activity in Ireland.

Some less positive reactions came from a few interviewed oncologists: they mentioned that not all industry representatives are positive about ICORG, because their fees are considered too high. Other complaints are that the regulatory pressure of the IMB is considered quite high. One oncologist noted that industry is not happy with ICORG acting as a gatekeeper asking for very high fees while competing with CROs with taxpayer's money. Another less positive point raised is that the Irish cancer research is still relatively decentralised.

Virtually all stakeholders mentioned the positive effect they feel ICORG has had on the retention of high-level staff to Ireland. Some professionals have been attracted from other European countries, but mostly Irish scientists now tend to come back from the USA for instance to work with ICORG. According to one policy stakeholder, the effect of ICORG on medical professional's career opportunities and morale is perhaps the most important contribution of ICORG of all. ICORG creates 'an innovative buzz' that is crucial for a good health care system.

#### 5.2.5 Influence on decision-making

The industry-based survey respondents were all very positive about ICORG's influence on decision-making and their attitude towards cooperation. A specific example given was related to ICORG's DSSGs that organise peer reviews for the trial protocols. One respondent in the industry survey stated that her company had changed their protocol design on a number of studies, leading to better outcomes due to these peer reviews and ICORG's influence. Overall, ICORG was a major factor in the business decision to perform clinical trials in Ireland. One company stated:

*"(The company) cut its R&D footprint in one third of all countries across Europe. In Ireland we were also impacted by this decision and we are now not allowed to work in any therapeutic area apart from haematology and oncology. The reason we were allowed to continue in oncology and haematology is because of the ICORG network"*

Another one stated:

*"The decision as to whether or not to place oncology clinical studies in Ireland has been hugely influenced by ICORG's stellar capacity and international reputation. As such, many clinical trials have been placed here."*

Industry representatives mentioned that they prefer ICORG over Clinical Research Organisations because it can provide a higher quality. External collaborators confirm this. They feel that for CROs, with huge turnovers and large studies, research is less important than for ICORG and they feel that they need more time to clean and analyse CRO data compared to ICORG data.

Moreover, according to the GCO, ICORG's collaboration with industry has improved the research infrastructure in Ireland and this could be of use for other disease areas as well. Several pharmaceuticals companies have significantly increased their research infrastructure in Ireland as a result of increasing activity in the cancer clinical trials arena.

### 5.3 Conclusions

ICORG's studies were increasingly sourced by the industry. About 20-30% of the studies was sponsored by the industry, besides sponsoring through the provision of free-of-charge drugs, scans and other in-kind contributions. ICORG also increasingly leverages funding from other sources. The number of companies ICORG collaborates with increased as well over the years, showing the positive stance of ICORG. ICORG closely cooperates with almost all pharmaceutical companies based in Europe, and they have an intense relationship with some of the largest pharmaceutical companies in the world such as GSK and Pfizer. The industry values the collaboration with ICORG as very positive and beneficial. Unfortunately, hardly any data about income generated and value of drugs provided were available prior to 2006, and most of the accurate data only are available from 2009 onwards or are an estimate. This could be improved in the future.

## 6. Opportunities for future collaborations

One of the objectives of the impact assessment was to engage with cancer care policy-makers (e.g. NCCP, Department of Health) and clinical practice leaders in order to identify strategic opportunities by which any future HRB funding of ICORG may have an impact on cancer care policy and practice in Ireland. We have conducted several interviews with different stakeholders within ICORG but also from other organizations, such as from the HSE Cancer Network, the National Cancer Control Programme, the Department of Health, and the Irish Cancer Society. This chapter will provide information on how ICORG supported the implementation of the national cancer control strategy and the shaping of the cancer service delivery according to these stakeholders. Second, this chapter provides an overview of strengths, weaknesses, opportunities and threats as perceived by these stakeholders for ICORG, now and in the near future. It finally touches upon the question how to play a future role in influencing the development of cancer care guidelines, care models, and a cancer strategy in Ireland.

### 6.1 The implementation of the national cancer control strategy and shaping cancer service delivery

In Ireland, all public health programmes are run through the Health Service Executive (HSE). The HSE is responsible for the management and delivery of health and personal social services. It directly manages the funding of the health system and is required under the Health Act 2004 to integrate the delivery of health and personal social services, to have regard to the policies and objectives of the Government and relevant Ministers and to secure the most beneficial, effective and efficient use of resources.

Following a 2006 report ‘A strategy for Cancer Control in Ireland 2006’ the advice was adopted that Ireland needs a comprehensive cancer control policy programme. The NCCP (the National Cancer Control Programme) was set up to achieve this goal and to transform the delivery of cancer care, and ensure that cancer services meet the highest standards.

The 2006 National Cancer Strategy recommended that Cancer Centres should be networked together in Managed Cancer Control Networks. The aim was to equip each of the HSE’s four regions with broad self-sufficiency of services in relation to the more common forms of cancer. Ireland’s 8 Specialist Cancer Centres are now located and networked within each of the four HSE administration regions. Successful Cancer Centre models internationally were examined as part of the process of designating the eight centres in this country. Recommendations were also made to improve the clinical trial entry for patients, to establish a national tissue bio-bank to support research and service delivery and to establish a national cancer research database.

Although there have been meetings between ICORG and NCCP there does not seem to be a direct and structural involvement. Some of the leading members of ICORG are active in NCCP as cancer care professionals. Despite this, interviewees overall felt that ICORG has helped with the implementation of the NCCP, mainly in the breast-cancer area.

In the hospital site survey, PIs were asked to what extent the recommendations related to cancer research in the National Cancer Control Strategy (2006) had been implemented and the level of contribution that ICORG had made to implementation of each of these recommendations. For all three recommendations (improved clinical trial entry for patients; establishment of a national tissue bio-bank to support research and service delivery; and establishment of a national cancer research database) the most common perception among the participant group was that partial

implementation had been achieved, with most progress having been made in improving access to clinical trials for patients.

Most respondents moreover believed that ICORG had contributed highly to improved clinical trial access for patients, while ICORG was mostly rated as having made some contribution to the establishment of a national cancer tissue bio-bank. The lowest contribution for ICORG was given to the recommendation relating to the establishment of a national cancer research database. However, some respondents made the point that the latter two areas were not within ICORG's remit and therefore ICORG's ability to influence implementation of these recommendations was limited.

One interviewed policy stakeholder noted that there are a lot of opportunities for future collaboration with the NCCP. Currently Irish clinicians have much freedom to prescribe what they want. For an affordable high quality healthcare system it is necessary to have more standardised clinical guidelines, ICORG could and should play a role in this. One interviewee also stated that 'ICORG could and should have a much larger impact on clinical practice in care by taking a strategic and holistic view. By working not just with clinicians, but also with support staff there are important benefits to be gained when sharing best practices like planning. An 'ICORG-approved' treatment could be disseminated quickly through other hospitals when found successful in another.' The other way around, it was stated that the NCCP could help ICORG to regulate costs to keep Ireland attractive for industry.

## 6.2 SWOT and future role for ICORG

In the interviews we asked what the stakeholders found strong and weak points of ICORG, and what they saw as opportunities and threats for the future. The statements made by the interviewees are reflected in the following table.

Figure 31 SWOT by interviewees

Strengths	Weaknesses
<ul style="list-style-type: none"> <li>• ICORG provides one access point</li> <li>• ICORG has a proven track record</li> <li>• The collaborative nature of the oncologists working with ICORG (also compared to other disease groups)</li> <li>• Investigators are very open to work with all parties, and deliver on their commitments.</li> <li>• One policy maker stated: <i>'Because of its democratic, peer-driven nature ICORG is very effectively providing oversight en thereby ensuring minimum standards, much more than a top-down policy-driven strategy would be'</i></li> <li>• The cohesion of the medical oncology community has improved vastly through ICORG</li> <li>• The positive contribution to the community spirit, passion and dedication</li> <li>• ICORG creates an atmosphere of intellectual energy and enthusiasm.</li> </ul>	<ul style="list-style-type: none"> <li>• ICORG still operates as a pioneer organisation after 15 years. Everything is done by a handful of people. There is a need for a more professional organisation.</li> <li>• There is a lack of long-term strategy</li> <li>• The number of patients in clinical trials is no longer vastly growing. This could lead to stagnation in developing ICORG.</li> <li>• ICORG's absence from the policy arena limits its visibility</li> <li>• Low frequency of meetings (currently quarterly) implies lost time in agreeing on for instance protocols.</li> <li>• ICORG does not communicate with other disease researchers.</li> <li>• Little transparency on ICORG's funding and funding streams, costing, etcetera</li> <li>• The structural disadvantage of being situated in a small country.</li> </ul>
Opportunities	Threats
<ul style="list-style-type: none"> <li>• Stronger focus on industry-supported research, shifting away from more academic studies (remark made by industry).</li> <li>• Specific opportunities are seen in working with industry in areas such as haematology. Another oncologist stated that because of the infrastructure, which is now in place, it should be easier to get to certain economies of scale,</li> </ul>	<ul style="list-style-type: none"> <li>• Decreasing HRB funding. Industry cannot build up infrastructure such as core staff (research nurses). Most stakeholders identify this threat as the most imminent.</li> <li>• Budget cuts to the general health care system are also a big threat, both the funding for cancer care in general as well as the HRB funding for research.</li> </ul>

<p>resulting in a lower cost per patient.</p> <ul style="list-style-type: none"> <li>Increasing cooperation of ICORG with the NCCP. By continuously pitching the importance of a 'cycle of continuous improvement' which clinical research brings, big budget cuts can be prevented.</li> <li>A clear opportunity is that whereas other European countries are getting a small increase in cancer prevalence, Irish prevalence is projected to increase by over 70% until 2030 due mainly to demographic factors. There will be more need for care and opportunity for research.</li> <li>Cooperation across diseases and aligning with a national clinical research support centre. There is much to gain from sharing expertise, knowledge and infrastructure.</li> <li>Focussing on translational research since this is the new paradigm in oncology research. Using biomarkers and targeted drugs can vastly improve care and save money, since expensive drugs are only given to those who can benefit.</li> </ul>	<ul style="list-style-type: none"> <li>One interviewee also identified an overreliance on HRB funding as dangerous and argued for a diversification into industry, charity and European Framework funding.</li> <li>An increasing level of competition from other countries. The most important measure is the timeline between contract and first patient enrolment. Other countries are improving rapidly.</li> <li>High work pressure, hiring freezes and closure of hospitals is putting the research opportunities under pressure.</li> <li>A lack of communication and explanation of the importance of clinical trial may erode governmental and public support for funding.</li> <li>Competition for resources and researchers is always fierce in oncology research.</li> </ul>
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Based on the interviews with stakeholders

Based on the above-mentioned SWOT by interviewees and the self-assessment by ICORG in the application documents, a number of suggestions for a future role for ICORG to influence the development of cancer care guidelines, care models and cancer strategy in Ireland can be made.

To summarise the SWOT, ICORG is a leading national clinical trials organisation, while the operating environment has become increasingly difficult. ICORG has a proven track record and provides one point for access according to our study results. It has supported the development of a collaborative culture of oncologists in Ireland, and the cohesion of the community has improved significantly. There is a good community spirit, and intellectual energy and enthusiasm.

In a number of different areas the ICORG expects to continue to accrue strongly and contribute to a range of the most interesting research questions. The organisation itself could however further professionalise, and develop a clear long-term strategy in order to sustain the high level of research and accrued number of patients in the trials in different disease areas. External policy stakeholders mention that ICORG could become more important for the cancer clinical care in Ireland by expanding into different disease areas. It could be a more active player in the policy arena and increase its visibility both towards policy organisations as well as charities. Finally, the organisation could increase its financial and organisational transparency and appoint a 'liaison officer' to deal with the communication with other players in the field. The GCO intends to assign a senior management team member responsible for the administration of the Group's funding and grant structure.

Many future opportunities have been identified by the different stakeholders, such as a stronger focus on industry-supported research, and an increasing cooperation with NCCP. GCO is already trying to more regularly speak to policy makers, but also seems to find it hard to deal with the politics. ICORG could however organise a more structural interface with NCCP.

Cancer will remain high on the agenda; therefore ICORG faces many scientific opportunities in the future, with specific attention to translational research. However, the organisation could increase its cooperation with other disease areas and work towards a clinical research support centre.

ICORG will need to deal with the fact that Ireland is a small country and economic developments are not very promising on the short term. HRB funding is decreasing, and general health care budget cuts are a huge threat. ICORG will need to further diversify its sources of income and focus on efficiency to remain strong and on the competitive edge with other countries. An important threat is the high work pressure for the oncology professionals which prevents them to explore possibilities to source

new cutting-edge studies (and phase I studies) and the closure of hospitals is putting the research opportunities under pressure. ICORG envisages for the group and increasing expertise in the area of early phase clinical development. Plans are being put in place to substantially increase the group's activity in phase 1 in the next grant cycle.



## 7. Conclusions and recommendations

In this chapter the main conclusions are summarised and a number of recommendations based on these conclusions and the SWOT are proposed.

### 7.1 Conclusions

For this impact assessment, information was analysed that was captured in progress and interim reports and in the previous two grant applications. Data analysis was furthermore supported by a survey and a bibliometric analysis commissioned by HRB. Furthermore, a number of interviews were carried out and additional data analysed.

It was explicitly not the objective of this study to examine the operational effectiveness of ICORG central office and its coordination and the management of the ICORG network, nor the governance structures of ICORG, processes, or strategic issues relating to ICORG such as scientific prioritisation of clinical studies and the balance of disease sub-groups within the ICORG portfolio.

Based on the logical framework analysis of ICORG and the key evaluation questions posed by HRB, a number of indicators were suggested for measuring ICORG's impacts and effects (chapter 2). For most of the indicators data was (partially) available at least for a number of years (predominantly from 2006 onwards) or based on qualitative assessments made by the stakeholders in the interviews or survey. Overall, it appeared to be rather challenging to collect data for all the indicators. In addition, it was at times difficult to contextualise the existing data (sheets) provided by ICORG through the grant application documents. For that reason we conclude that ICORG could make some improvements in optimising data transparency (what is it you are measuring, since when, and why) and data collection (what do you want to measure in order to be able to steer your organisation in the right direction). The indicators that were not at all populated are:

- The number of presentations in international conferences. ICORG presents visits to conferences, but it has not provided an overview of the speaking events of the ICORG members (or at least PIs) themselves
- Knowledge and understanding amongst patients about clinical research and the newest treatment regimes, and the satisfaction about Irish standards of care
- The exact figures on contact hours with specialists before and during trials for patients
- The exact numbers of income generated by industry sponsored studies, as well as value of drugs provided free-of-charge (these are estimations).
- The number of return requests for studies by industry to ICORG
- Share of patients with survival with or without participation in ICORG clinical trial

Nevertheless, based on our analysis of data available and qualitative assessments, we can conclude that ICORG has had an effect on the quantity and quality of clinical research in Ireland. Over the years, more emphasis was put on improving patient and clinical care, and providing access to newest treatment regimens for patients. Our analysis showed that through the support of clinical trials and new studies, ICORG has been able to deliver treatments to patients that were not available before. It is however not easy to validate that ICORG has had a positive effect on patient care, and it has not put particular emphasis on the development of patient education and outreach programmes, as was suggested in some of the initial documentation and strategic plans of ICORG. Because of the high scientific standards in the trials however, ICORG has been able to attract funding from industry and build strong collaborations with a large number of industry partners.

These effects and impacts are summarised in more detail in the following sections.

#### 7.1.1 Impact on research

In general, ICORG's impact on clinical research in oncology in Ireland has been high, both in terms of quantity and quality. In terms of **quantity**, the HRB funding has allowed ICORG to grow from a small organisation focusing mainly on breast cancer to a large cooperative group that runs trials in several disease areas. The total number of studies open during a year has risen over the years from 11 in 2006 to 41 in 2010, although this trend has reversed recently. There is a consensus that without ICORG the number of studies that are done in Ireland would be a fraction of the current number. ICORG is the **one and only** major cooperative research group in Ireland, not just in oncology. This pattern of **quantitative growth** corresponds with an increase in ICORG funded staff (from 8 FTE in 2002 to 80 FTE in 2011) and the number of members (from 235 in 2005 to 435 in 2011). All relevant hospitals had joined ICORG by 2009.

Through the HRB funding ICORG has been able to create the necessary infrastructure to perform clinical research. This infrastructure appears to be suitable for in-house studies and local studies as well as collaborative and industry studies. While ICORG was mainly focussing on breast cancer at the start, they now perform clinical trials in many (if not all) disease areas. The pattern of distribution of phases is quite pronounced, with a strong focus on phase III studies and increasingly phase II studies, whereas phase I and IV are marginal in number. The low number of phase I studies does suggest that ICORG's main purpose is not purely scientific excellence, although there are a few outstanding examples such as the *Herceptin* study.

ICORG's impact on **quality** of clinical research is high. By providing training for research staff, ICORG ensures that they are qualified to perform clinical research and that they are up to date on current regulations and guidelines. ICORG training activities have enhanced capacities in hospitals through maximising the number of medical and nursing staff able to participate in cancer clinical trials. From 2006-2011 128 **training** sessions have been organised by ICORG. Fifty-five percent of these trainings were on Good Clinical Practice (GCP).

By virtue of its coordinating function, its audit and quality assurance activities, ICORG have contributed strongly in improving and harmonizing clinical trial **guidelines** throughout the participating hospitals. Because of a joint responsibility for the general quality in a study, ICORG support and 'peer-pressure' assure that all **minimum standards** are adhered to.

ICORG's quality is also shown from the **publications** association with its clinical trials. Since 2006, ICORG studies have led to 47 (co)-publications. ICORG papers score strongly above average for citations scores, with a C-index of 3.28. The number of publications and their citations scores also shows a growing trend over the years. ICORG researchers have held **presentations** at major international oncology conferences, but not enough data was consistently captured to put this into perspective. ICORG's contribution to quality can also be assessed by the level of satisfaction of industry and external groups, which are all very positive about ICORG's reliability, dedication and data quality. ICORG has developed **a strong international reputation**, mainly in North America, where it is considered 'one of the best' oncology research groups in certain disease subgroups like breast cancer.

Although part of its original objectives, ICORG has not been able to set up or facilitate the creation of **national key resources** for clinical research, such as **cancer biobanks** and disease-specific cohorts, although ICORG's presence has contributed to raising the profile of this issue among policy makers.

#### 7.1.2 Impact on clinical care

When looking at the effect of ICORG on clinical care, it has definitely increased the **clinical participation rate of Irish patients**. Between 2006 and 2011, ICORG



recruited 4553 patients in their trials, of which more than half breast-cancer patients. Other big disease groups are genito-urinary and gastrointestinal cancer. For breast cancer, the participation rate lays around 16%, which is quite high internationally. The total average accrual percentage, however, is only around 4%. This low rate is an international problem, and not specific to ICORG. Another activity related to patient care is stakeholder **communication**. Although internal communication seems to be adequately arranged, policy makers feel that ICORG is weak on external communication. There is currently no structural communication towards patients around clinical trials, and the extent to which ICORG should play a direct or indirect role is debated.

When considering the impact on **new treatments, diagnostics and prognostics**, it became apparent that ICORG over the past 10 years was able to deliver some very effective new treatments to patients during the trials. ICORG played a leading role in some major international studies which resulted in very successful new treatments. Because of their participation in clinical trials, successful treatments were faster implemented in hospitals that participated. There is also evidence of new diagnostics and prognostics, although these are more limited in scope and number. The ICORG process also ensures the presence and updating of standards of practise and **guidelines**. However, ICORG does not seem to go beyond the minimum standards required for participation in clinical trials, and the function of ICORG as a diffusion network of new treatments and care protocols is limited. On a more indirect level, virtually all stakeholders agree that ICORG has had a large effect in vitalizing the oncology groups in Ireland, resulting in better-qualified staff with more motivation and recent knowledge. Hospitals are proud to participate in international trials, as they yield 'status, honour and glory'. These more subtle and qualitative effects are likely to have improved care for patients as well, although this may be limited by the distance between standard care and clinical trial departments.

The direct effect of providing care for patients while on trial results in **direct benefits for patients**. Especially in breast cancer, a large number of patients directly benefitted from receiving superior treatments through ICORG trials. The benefit accruing to participants in general, regardless of treatment, is more difficult to measure, and at this point there is no conclusive evidence that patients receive consistently better than standard care while being on trial. Looking at **long-term benefits, such as better outcomes and quality of life**, is perhaps even more difficult. It is clear that ICORG has had at least some positive effect on outcomes by providing some successful new treatments in trials and early adaptation of subsequent commercialized drugs, but it is impossible to quantify this effect. There is some qualitative evidence that ICORG's capacity building in breast cancer care and research has helped Ireland to make full use of internationally developing treatments and diagnostics that resulted in a 10% improvement in 5-year survival rate.

### 7.1.3 Economic and financial impacts

Although ICORG does not have a specific **economic** mandate, some impacts on economy have been analysed in this chapter. Data provided by ICORG and HRB shows that over the last six years, about 20-30% of the ICORG studies were **sponsored by industry**, and an increasing share of the total number of ICORG studies was sourced by the industry. € 1.2 million was invested by industry in ICORG in the last three years up to 2011. On top of this, the industry has provided **free-of-charge drugs**, scans and other in-kind contributions to ICORG, with a stable annual estimated value is of € 3 to 4 million over the last six years. From other sources ICORG says to have **leveraged** about € 2 million (of which about € 1.7 from collaborative studies and the rest from charities and other sources) and this amount is increasing every year.

It seems that the number of companies with which ICORG collaborates increased significantly over the years, showing the positive stance of ICORG. ICORG closely cooperates with almost all pharmaceutical companies based in Europe, and they have an intense relationship with some of the largest pharmaceutical companies in the

world such as GSK and Pfizer. The **industry values the collaboration** with ICORG as very positive and beneficial. They consider ICORG as professional and well organised with the ability to manage complex trials with high accrual rates and good quality data. For many of them, ICORG is the **reason to be active in Ireland** in oncology research and they strongly recommend the development of ICORG-like organisations in other clinical fields as well.

## 7.2 Recommendations

- Cancer will remain high on the agenda; therefore ICORG faces many scientific opportunities in the future, with specific attention to translational research. However, the organisation could increase its cooperation with other disease areas and work with any national clinical research support centre. It could make more efficient use of resources by for instance working with the Irish Cancer Society and develop a stronger interface with the NCCP.
- Our analysis shows that ICORG has had significant impact on the quantity and quality of clinical research in Ireland. This has had some effects already on clinical practice and patient care. However, ICORG currently has no explicit strategy to improve patient care and contribute to the development of clinical standards in oncology across the board. Policy makers however seem eager to use the unique opportunity that the ICORG network offers to also work more explicitly on jointly raising the quality of cancer care in general. We recommend to ICORG therefore developing an explicit strategy by, for instance, strengthening the cooperation with the NCCP and other care stakeholders.
- Moreover, ICORG could better monitor and map its added value for patient care and the healthcare system in order to convince decision-makers to continuously support collaborative oncology research in Ireland.
- ICORG will need to deal with the fact that Ireland is a small country and economic developments are not very promising on the short term. HRB funding is decreasing, and general health care budget cuts are a huge threat. ICORG will need to further diversify its sources of income and focus on efficiency to remain strong and on the competitive edge with other countries.
- An important threat is the high work pressure for the oncology professionals which prevents them to explore possibilities to source new cutting-edge studies (and phase I studies) and general budget cuts in the healthcare system are putting research opportunities under pressure. In the past, ICORG has built its (international) reputation by managing a broad base of high-quality studies while also pursuing a select number of exceptionally innovative studies. Given the limited time and resources for the clinical researchers to pursue many of these innovative studies, ICORG should proactively foster those studies where international (scientific) impact is highest and disseminate the results broadly.
- ICORG could improve its organisational data management and monitoring systems in order to increase transparency to its funders and its internal management.

## Appendix A List of key evaluation questions

### Impact on cancer clinical research

- What impact has ICORG had on the quantity and quality of clinical cancer research in Ireland? Has ICORG-related research been published in high impact journals, in cancer research reviews and research syntheses?
- Have the results of ICORG clinical trials been disseminated through invited presentations and keynote speeches at major oncology conferences?
- Are there other successful cancer clinical research networks and collaborations in Ireland operating outside of ICORG?
- What training and education in clinical research has been carried out by ICORG?
- What impact has ICORG had on quality and standard setting for cancer clinical trials in Ireland?
- Has ICORG funding led to the creation of key resources for high-quality cancer clinical research, such as cancer biobanks, new disease-specific cohorts and datasets?
- What national and international linkages (partnerships and collaborations) have ICORG forged to facilitate it in delivering its core objectives?

### Impact on cancer care and clinical practice

- What impacts has ICORG as a coordinated network had to date on cancer clinical practice with regard to clinical guidelines, new/improved treatments and treatment regimens, and new/improved diagnostic / prognostic tests?
- What benefits accrue to patients whilst participating in ICORG clinical trials, such as improved quality of care?
- What longer-term benefits to cancer patients generally can be attributed to ICORG clinical trials, such as improved survival or improved quality of life?
- What impact has ICORG had on the clinical trials participation rate of Irish cancer patients in relation to international norms?

### Indicators of economic impact

- How many industry-sponsored studies has ICORG participated in? How were these studies costed and much income was generated from them?
- What was the value of drugs provided by industry free-of-charge for investigator-led studies, which replaced drugs that would have been otherwise funded through the health service?
- What collaborations with industry have developed over the last decade, and how does industry value those collaborations?
- What if any industry decisions have been based or influenced on the collaboration with ICORG?
- How much non-exchequer funding has ICORG leveraged from charitable or international sources?

### Opportunities for future collaborations

- What role has ICORG played to date in facilitating the implementation of the national cancer control strategy and in turn shaping cancer service delivery?

- What opportunities exist for ICORG to play a future role in influencing the development of cancer care guidelines, care models, and cancer strategy in Ireland?

## Appendix B List of interviewees

Figure 32 List of interviewees

<b>Name</b>	<b>Position and affiliation</b>
<b>Dr Ray McDermott</b>	ICORG Chair 2012-
<b>Prof Paul Browne</b>	ICORG Chair 2009-2011
<b>Prof John Kennedy</b>	ICORG Chair 2006-2009
<b>Dr Brian Moulton</b>	ICORG GCO CEO
<b>Dr Maccon Keane</b>	Principal Investigator ICORG hospital site Galway
<b>Prof Frank Giles</b>	Director HRB Clinical Research Facility Galway
<b>Dr Peter Doran</b>	Director HRB Clinical Research Facility UCD
<b>Prof Charles Coombes</b>	Head Dep. Cancer Medicine, Imperial College London of Sciences
<b>Prof Patrick Burns</b>	Prof Internal Medicine at University of Iowa
<b>Mr Kilian McGrane</b>	HSE Cancer Network Manager East
<b>Dr Mary Hines</b>	HSE Cancer Network Manager West
<b>Dr Susan O'Reilly</b>	Director National Cancer Control Programme
<b>Ms Mary Jackson</b>	Head of Cancer Policy Unit, Dept. of Health
<b>Mr John McCormack</b>	CEO Irish Cancer Society
<b>Ms Orlaith Gavan</b>	Medical Advisor, Pfizer
<b>Dr Karine Egan</b>	Medical Director, Abbott
<b>Ms Grainne Power</b>	Clinical Research Manager, Glaxo-Smith Kline
<b>Ms Mary-Ann Lindsay</b>	CEO Translational Research in Oncology (TRIO)

Technopolis Group, 2012.

## Appendix C Interview guide example

Three separate interview guides have been designed: one for ‘ICORG stakeholders (GCO, PIs, etc)’ one for ‘external stakeholders active in the research domain’, and one for ‘policy stakeholders’. The following is an example of the ‘ICORG stakeholders’ guide.

Interviewer:

Interviewee:

Date:

### **Background**

The Health Research Board (HRB) has asked Technopolis Group to perform an impact assessment of the All-Ireland Oncology Research Group (ICORG). ICORG has been funded by the HRB since 2002 and is currently defining the terms of reference for continuation of its funding for after June 2012. In order to make a fully informed decision, the HRB would like to gain insight into ICORG’s impact in three areas:

- impact on cancer clinical research;
- impact on cancer care and clinical practice; and
- economic impact.

Additionally, the HRB is interested to identify strategic opportunities to result in a higher impact in the future.

We would hope to discuss these aspects of ICORG’s performance with you and identify the impact ICORG has made based on your valuable experience.

### **C.1 Introduction**

- What is your function?
- What do you know about ICORG? What is your relation to or with ICORG?
- Why was ICORG established? (to solve what problems?)
- What are the most important objectives of the organisation? (Probe: to increase the number of trials? To increase the number of participation patients? To increase quality of care? To attract international funding?)
- What is your general impression about the organisation, its objectives, activities and impacts?

### **C.2 Impact on cancer clinical research**

#### **Quantity of clinical research:**

4. In what way has ICORG contributed to the increase in clinical research (trials) in Ireland?

5. Why was and is ICORG so important? (attribution) (could this have been done by other, existing organisations?)

#### **Quality of clinical research**

6. What impact has ICORG had on the quality of clinical cancer research in Ireland? (probe as suggested below)
  - [ ] More 'state-of-the-art', highly innovative research
  - [ ] Better compliance with (EU) regulations
  - [ ] Better data analysis
  - [ ] Better dissemination of results
  - [ ] Other, namely ....
7. What did ICORG do to influence standard setting for cancer clinical trials in Ireland? Why was this successful or not? (why?)
8. Are you aware of any standard operating procedures that changed because of ICORG trials? Was this to your satisfaction?
9. Are you aware of any (clinical) research policy changes because of ICORG actions? Was this to your satisfaction?
10. What role has ICORG played to date in facilitating the implementation of the national cancer control strategy and in turn shaping cancer service delivery?

#### **Impact on Infrastructure**

11. What is your opinion about the current infrastructure for clinical trials in Ireland? Has this changed over the years? If so, what was the role of ICORG (if known).
12. Has ICORG funding led to the creation of key resources for high-quality cancer clinical research, such as cancer biobanks, new disease-specific cohorts and datasets?

#### **Training and education**

13. Have you been involved in training activities in whatever way? If so, are you satisfied with the way the training supported the improvement of quality?

#### **GCO specific questions for data collection**

14. **(GCO)** Is there an overview of the number of yearly started clinical studies ? (in excel?) and per clinical trial list of participant organisations and the number of accrued patients?
15. **(GCO)** Why do Belfast City Hospital and two others not receive HRB funding for participation in ICORG?
16. **(GCO)** Where to find information about total number of clinical trials in Ireland (ICORG and non-ICORG)

### **C.3 Impact on cancer care and clinical practice**

17. Are patients generally aware of the possibilities of clinical research and the newest treatment regimes? Where do they get this knowledge?

18. What has ICORG done to educate patients and develop outreach programmes? Was this successful in your opinion? Why (not)?
19. What benefits accrue to patients whilst participating in ICORG clinical trials, such as improved quality of care, access to new promising treatments, increase in contact hours with clinician etc.
20. What longer-term benefits to cancer patients generally can be attributed to ICORG clinical trials, such as improved survival or improved quality of life?
21. Are you aware of treatment regimens or other clinical practices that changed because of ICORG trials? How were these influenced by ICORG?
22. What opportunities exist for ICORG to play a future role in influencing the development of cancer care guidelines, care models, and cancer strategy in Ireland?

GCO specific questions for data collection

23. **(GCO)** How often was ICORG's website visited? How many times the App was downloaded?
24. **(SDMO/GCO, clinical practice)** What impact had the outcomes of the clinical studies on treatment/guidelines/test development? How to measure?

#### C.4 Economic impact

##### Collaboration

25. How does ICORG foster collaborations between industry and international cancer research groups?
26. Is Ireland attractive to international cancer groups and industry? Why (not)? If not, what are the main barriers for these groups to start studies in Ireland?
27. How does industry (in your opinion) value the collaboration with ICORG that has been built over the past decade?
  - Which aspects are seen as specifically positive?
  - Which aspects could have been better?
28. Why would you, (as researcher or industry) cooperate with ICORG clinical trials?

##### Funding and investment

29. How did ICORG attempted to attract funding (non-exchequer)? Was this successful?
30. Has ICORG activities led to increased investment in R&D activities based in Ireland? If yes, how much?

##### (inter)national reputation

31. Has ICORG succeeded in attracting and retaining world-class physicians?
32. What is, in your opinion, the (inter)national reputation of ICORG? Did this change over the years? Why?
33. Are there other successful cancer clinical research networks and collaborations in Ireland operating outside of ICORG? What can be learned from them?

GCO specific questions for data collection



- |   |
|---|
| <p>34. <b>What was the value of drugs provided by industry free-of-charge for investigator-led studies, which replaced drugs that would have been otherwise funded through the health service?</b></p> <p>35. <b>How much non-exchequer funding has ICORG leveraged from charitable or international sources?</b></p> |
|---|

**C.5 Other:**

36. What are the strengths and weaknesses of ICORG (internal) in your opinion?
37. What are opportunities and threats (external) for ICORG, in your opinion?
38. Do you have any relevant information regarding ICORG's impact over the past decade which has not yet been discussed?
39. What would (not) have happened without ICORG?

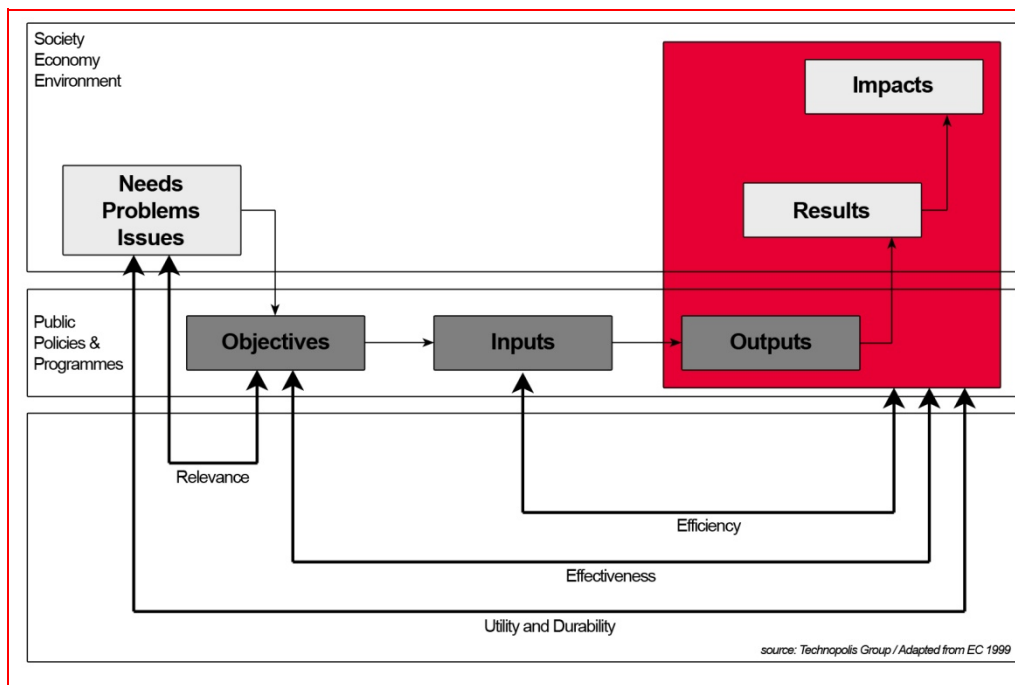
## Appendix D Sources

- ICORG website;
- Interim progress reports and activity reports from the years 2005 to 2011;
- Call document for proposals for funding to strengthen clinical trial capacity in Ireland, 2001;
- Background document for the establishment of the co-operative group to coordinate All-Island Cancer Clinical Trials;
- Application form for establishment of a co-operative group to coordinate All-Island Cancer Clinical Trials (2002);
- Application form for HRB (2009);
- Press Release Cancer Clinical Trials (2003);

## Appendix E Background to the logical framework analysis and indicator development

A logical framework analysis (LFA) is often used for (programme) planning purposes, but as said before, can be also very useful for evaluation. In this study we mainly focus on the effectiveness of ICORG. The issue of effectiveness is especially pertinent in the context of a midterm and ex post evaluation. It consists of asking whether results and impacts generated by the activities that are supported correspond with the objectives. An evaluation can also be concerned with issues of relevance, efficiency, utility (expected and unexpected effects that relate to the original needs) and sustainability (continuation of positive impacts into the future). These elements are visualised in the following figure.

Figure 33 Evaluation elements



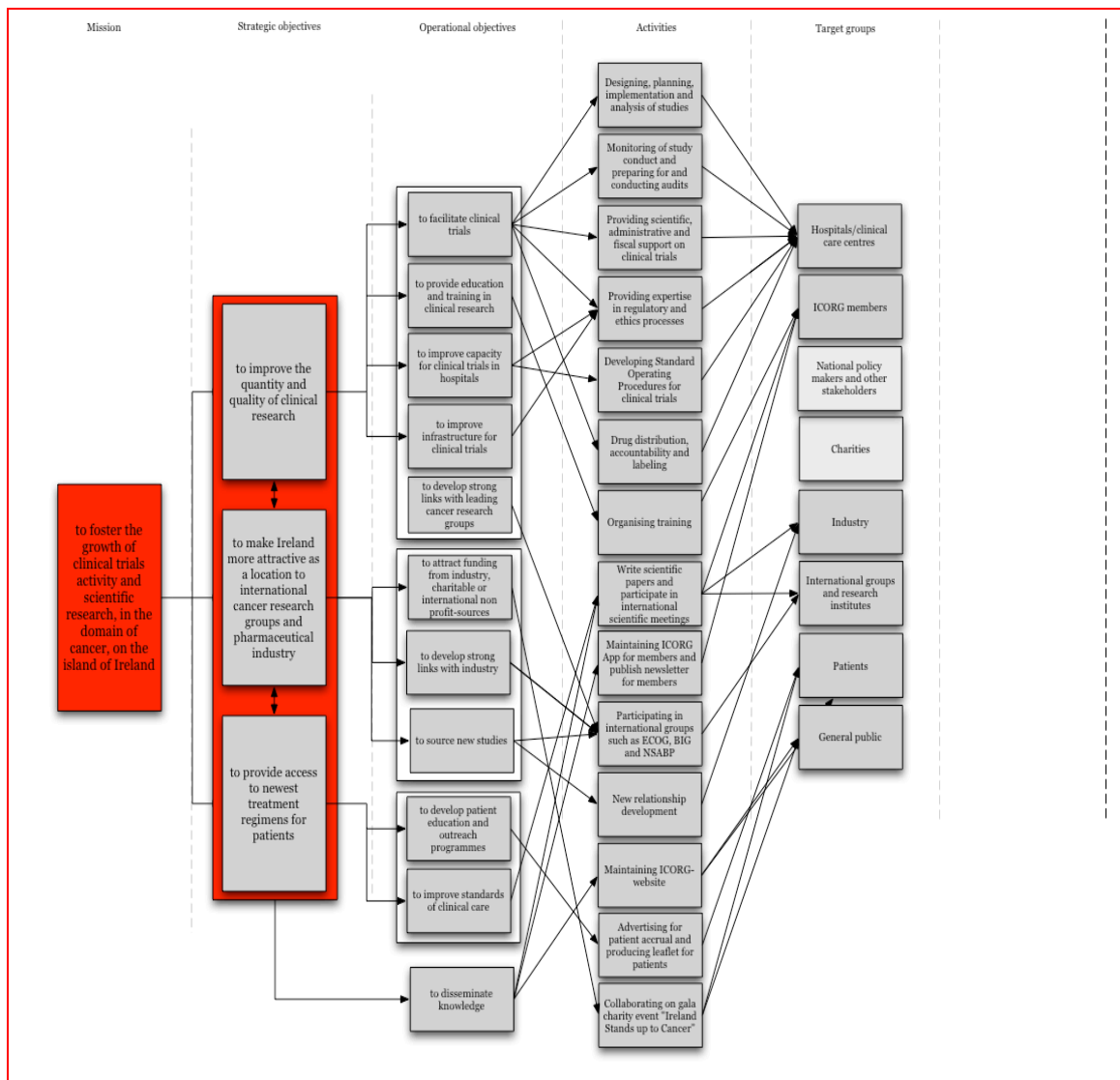
Source: Technopolis Group.

This document sketches a framework for evaluating the effects and impacts of ICORG based on the questions and indicators already provided in the terms of reference for the project as well as the LFA. It addresses different indicators but not all of them will be measured during this impact assessment. However, HRB might find the framework useful as reference for future monitoring and evaluation as well.

### E.1 ICORG's mission, objectives, activities

The following sections describe the mission, objectives, and activities of ICORG. These are visualised below. As sources of information, we used documentation provided by HRB (such as the 3-yearly applications and ICORG progress reports), interview outcomes, and the results of the surveys, and bibliometric analysis. It is important to mention that the framework is based on the initial objectives of ICORG since it is only fair to measure impacts related to the initial objectives. However, ICORG is facing a new period of funding and new challenges in Ireland, which might lead to a revised set of funding objectives.

Figure 34 Logical framework of ICORG



Technopolis Group 2012

### E.1.1 Mission

HRB funds ICORG as part of its strategic aim to build and support a skilled workforce capable of advancing high quality research to maintain and improve health within a knowledge-based health service. ICORG is a clinical research organisation whose mission it is *"to foster the growth of clinical trials activity and scientific research, in the domain of cancer, on the island of Ireland"*.<sup>14</sup>

This mission can also be found on the ICORG website, where different words are used to describe ICORG's purpose<sup>15</sup> This tells us more about the reasons for ICORG's existence, which apparently are:

<sup>14</sup> Progress Report, Group Central Office and Statistics & Data Management Office, 1 July 2010 – 30 June 2011

<sup>15</sup> <http://www.icorg.ie/about-us/about-us>

- to create more research opportunities for patients
- to make Ireland more attractive as a location to international cancer research groups and the pharmaceutical industry.

ICORG was established in 1996. It was initiated by a group of PIs and cancer consultants who had worked or studied in the US and who were experienced with executing clinical trials.

ICORG received funding from the HRB from 2002. The decision by the HRB to fund ICORG was mainly influenced by two national policy documents: (1) the 1996 National Cancer Strategy, (2) a Memorandum of Understanding establishing the Cancer Consortium, signed in 1999 by senior health officials in the Republic of Ireland, Northern Ireland and the USA. The National Cancer Strategy called for the establishment of a more formal and coordinated approach to cancer clinical research, including clinical trials. The strategy recognised the importance of clinical research to the steady advance in the understanding and treatment of cancer. In the words of the Strategy, ‘systemic application of clinical research is the pathway to clinical excellence’.<sup>16</sup> Through the Cancer Consortium the HRB aimed to establish a clinical trials infrastructure and to provide training facilities. HRB’s funding aimed to create an all-island capacity to participate in local and international clinical trials under a reorganised and strengthened ICORG, which would provide the organisational, statistical and scientific support to affiliated hospitals. The preferred model for the development of clinical trials infrastructure was based on the model of cancer cooperative groups funded by the National Cancer Institute (NCI) in the USA.<sup>17</sup> Currently, the USA has no active involvement in ICORG.

#### E.1.2 Objectives

ICORG’s mission is translated into several objectives. We have divided those into strategic objectives and operational objectives. These objectives are all found in the documentation provided to us.

##### *Strategic objective:*

- To improve the quantity and quality of clinical research. This objective was one of the important objectives at the start of ICORG, but the balance has shifted in the last few years towards improving patient and clinical care.
- To provide access to newest treatment regimens for patients;
- To make Ireland more attractive as a location to international cancer research groups and the pharmaceutical industry.

The operational objectives are categorised in research, care and economic objectives. Operational objectives are those that found in the documentation describing what ICORG planned to do to reach its strategic objectives.

##### *Research objectives*

- to facilitate clinical trials;
- to provide education and training in clinical research (e.g. GCP training);
- to improve capacity for clinical trials in the hospitals (e.g. through recruitment of clinical research nurses)
- to improve infrastructure for clinical trials

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<sup>16</sup> Call document for proposals for funding to strengthen clinical trial capacity in Ireland, 2001

<sup>17</sup> Group Central Office and Statistics & Data Management Office Interim Report, 1 July 08 – 30 June 09

- to develop strong links with leading cancer research groups and other international research collaborative groups.

*Economic objectives*

- to attract funding from industry, charitable or international non profit-sources;
- to develop strong links with industry;
- to source new studies (scientifically excellent industry studies).

*Care objectives*

- to develop patient education and outreach programmes;
- to improve standards of clinical care.

In addition to these objectives there is a more general objective, which is the dissemination of knowledge.

E.1.3 Activities

The GCO and the SDMO are responsible for many of the tasks involved in order to pursue the organisation's mission and objectives. The GCO has a role in project management, pharmacovigilance (PhV), on-site monitoring, Group meetings and international collaborations. The GCO has also employed experienced Data Management and Statistics professionals. The GCO also coordinates the activities of the Disease Specific Sub-Groups (DSSGs) through which the scientific development of ICORG is directed and monitored. It provides local expertise in regulatory and ethics processes in Ireland, the UK and Europe. The GCO is also responsible for drug distribution, accountability and labelling. The SDMO, which has been funded in full by the HRB since April 2010, is tasked with responsibility for all quantitative aspects of cooperative group activity, and with contributing to the overall management of the Group. In this impact assessment no distinction is made between GCO and SDMO, they are both called 'ICORG' here.

In the documentation we have found a range of activities mentioned as being carried out by ICORG:

- Designing, planning, implementation and analysis of studies;
- Providing scientific, administrative and fiscal support on clinical trials;
- Monitoring of study conduct, including compliance with protocol, source data verification and drug accountability;
- Preparing for and conducting audits;
- Providing expertise in regulatory and ethics processes;
- Developing Standard Operating Procedures for clinical trials;
- Drug distribution, accountability and labelling;
- Organising training on GCP;
- Writing scientific publications for international scientific community;
- Maintaining ICORG App for members;
- Publishing newsletter for members;
- Maintaining ICORG-website;
- Advertising for patient accrual;
- Producing leaflet for patients;

- New relationship development;
- Participating in international groups such as ECOG, BIG and NSABP;
- Participating in international meetings;
- Collaborating on gala charity event "Ireland Stands up to Cancer"

#### E.1.4 Target groups

Several target groups can be distinguished for ICORG:

- Hospitals/clinical care centres;
- ICORG members;
- National policy makers and other stakeholders;
- Charities;
- Industry;
- International groups and research institutes;
- Patients;
- General public.

## E.2 Outputs, outcomes, impacts

The above mentioned objectives and activities should ideally lead to a number of outputs, outcomes and impacts, and it is our task in this study to identify which of those have been achieved. It is important to mention that the following list is, again, derived from documentation provided to us and is the result of our own analysis of what, in the light of the objectives, could be expected outcomes and impacts. However, it will be obvious that if objectives have been formulated, but ICORG has not initiated targeted activities in this area, one cannot expect much outcomes and impacts, unless triggered by other activities or external factors.

#### E.2.1 Outputs

Expected outputs of ICORG's activities are:

- Increased quantity of clinical cancer studies in Ireland
  - Increased number of *collaborative* clinical cancer studies in Ireland
  - Increased *participation of industry* in clinical cancer studies in Ireland
- Increase in number of (high-quality) professionals working in hospitals on clinical cancer research
- Increased training opportunities for cancer clinical studies in Ireland
- Increased number of (high-impact) publications and (international) presentations based on cancer clinical studies in Ireland
- Increased number of (and rate) patients participating in clinical studies in Ireland (improved trial entry)
- Improved information delivery to stakeholders (patients, researchers, industry) about cancer clinical research (including regulation, ethics)

#### E.2.2 Outcomes

Expected outcomes of ICORG's efforts are:

- Increased number of new/improved treatments and/or diagnostics introduced into the clinical practice in Ireland

- Improved infrastructure for clinical trials such as cancer biobanks, disease-specific cohorts and datasets
- Increased contact hours with patients before and during trials
- Increased knowledge and understanding amongst patients about clinical research and the newest treatment regimes
- Increased income generated by industry-sponsored studies
- Increased leveraged funding for cancer clinical trials in Ireland over the years from public and private sources (non-exchequer)
- Increased savings for the Irish government from drugs provided free-of-charge by industry
- Developed guidelines and standards for clinical cancer research in Ireland
- Reduction of barriers to involve in clinical research in Ireland for professionals and industry

#### E.2.3 Impacts

Expected, longer-term impacts of ICORG's efforts are:

- Increased quality of the clinical cancer research in Ireland
- Improved standards of clinical care in Ireland
- Improved benefits for cancer patients in Ireland
- Increased attractiveness of Ireland for cancer clinical research (for industry and world-class physicians)
- Increased awareness in Ireland about (the importance of) cancer clinical studies

### E.3 Deriving performance indicators

When a public policy initiative is designed, it is important to set the indicators or measures that will be used to guide it, ensure the necessary corrective actions are taken if things do not go according to plan and assumptions, and identify the effects it has produced. One useful way of thinking about indicators is 'what signs or changes will tell us that we have achieved our objectives?'

Indicators are often quantitative – you can count or measure them. They can be based on facts (e.g. number of articles published) or opinions (e.g. % of patients satisfied with ICORG achievements). When a good intervention logic is developed, indicators should be easy to construct, as each box in the intervention logic holds a potential measure. Indicators are used to measure or demonstrate change or progress: it is therefore important to not only know where you are heading for (the target/objective) and where you are compared to that, but also where you started (the baseline). In the case of ICORG no baseline study has been performed, but it is clear that not much clinical cancer research activity was being carried out in Ireland at the start of ICORG. More importantly though, ICORG (or HRB) has not set clear targets for its activities, so these are reconstructed for the sake of this study based on an initial logic chart with objectives provided by HRB.

Indicators can be categorised according to the information they provide to the evaluation:

- **Input indicators** are used to describe the resources used for the implementation of ICORG (e.g. the funding, human resources needed for the initiative).
- **Output indicators** relate to goods, services, technology and knowledge directly produced due to ICORG activities (e.g. the number of clinical trials facilitated).



- **Outcome indicators** show the initial results of the intervention providing the reason for the programme and are less tangible than outputs (e.g. the new treatments, diagnostic tests, and care standards developed because of trials)
- **Impact indicators** measure the long-term socio-economic changes the intervention brings about (e.g. the increase in quality care for people suffering from cancer).

A useful tool for designing the indicators is the table shown in Figure 35. Ideally, this model ensures that the defined indicators measure those aspects that they are intended to, that external factors are identified so the strength or weakness of the indicator can be assessed, and the source and method of collection of the data is recorded. Using this framework, a judgement can be made on the indicators that can be collected and how they will be used. In the case of ICORG, success criteria or targets have not been clearly set to our knowledge.

We will therefore analyse the effects and impacts of ICORG in relation to its objectives, but it will not be possible within the scope of the project to judge these effects and impacts in relation to success criteria, since these have not been sufficiently transparent.

Figure 35 Indicator analysis framework

<b>Intended activity/output/output/ outcome/impact</b>	<b>Success criteria</b>	<b>Indicator</b>	<b>Source of data</b>
What is the stated objective	How will you know when it has been achieved	What measure will you use?	Where will you get the data from and how will you or somebody else collect it?
↑	↑	↑	↑
<i>From the LFA</i>	<i>What (realistic) targets have you set?</i>	<i>Have you a clearly defined indicator (RACER)?</i>	<i>What will be the resources and cost of collecting the indicator</i>

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