PICTURE OF HEALTH 2013

A snapshot of HRB-funded research

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Health Research Board

Improving people's health through research and information

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Enda Connolly,
Chief Executive, HRB

Foreword

Better health research: better health care

Research is of most benefit when it is applied in policy or practice. Through our strategic business plan 2010 - 2014, the Health Research Board has focused on developing clinical research and building capacity in population health and health services research. This edition of *A Picture of Health* clearly illustrates the impact our funding approach is starting to have in terms of delivering improvements in people's health, patient care and health service delivery.

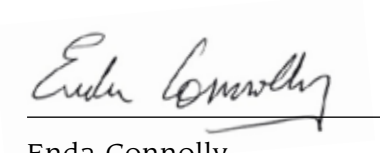
A *Picture of Health* captures just some of the broad range of outcomes from our funded research, but it clearly demonstrates the calibre, innovative thinking and the expertise of the health professionals and academics involved in health research here in Ireland. They must be encouraged in their pursuit of better treatments, innovative approaches to care and provision of strong evidence to support changes in policy and practice.

During 2012, the outcomes from all 117 HRB grants completed include:

- 19 new products and interventions in development
- 104 influences on policy and practice
- 3830 patients able to participate in 255 clinical studies
- 304 international collaborations
- 248 research-related jobs supported across the health services and academia
- €32.4 million leveraged in additional research funding for Ireland

International experience tells us that if we want health care interventions that are grounded in the latest evidence, we need health professionals that are involved in both research and practice. Our investments in clinical research infrastructure and capacity building are starting to yield strong results, with almost one third of the researchers supported in 2012 coming from a health professional background. This is a major step in relation to integrating research at the heart of health care.

It is clear from this report that the investments we are making through our strategic business plan are delivering better treatments, new approaches to care as well as supporting the economic agenda. It is essential that the innovative ideas and new evidence generated are now implemented through policy and practice.



Enda Connolly
Chief Executive

Contents

IMPROVING PATIENT CARE THROUGH RESEARCH

Delivering a better environment for diabetic wound healing

If a cut, sore or ulcer doesn't heal up, that can lead to bigger problems such as infection, or even amputation in severe cases. But in diabetes, the important process of wound healing can be compromised.

"Diabetic wound healing is an unresolved problem," says Prof Abhay Pandit, Director of the Network of Excellence for Functional Biomaterials, who has been leading HRB-funded research to develop materials that can create a better environment for wounds to heal.

"People who have diabetes have poor blood supply and the level of inflammation is very high, and this creates a difficult environment for wounds to repair," he explains. "So we took a pathology-driven approach to examining the problem."

In the lab, his group activated the immune cells involved in healing, called macrophages, to simulate the kind of stress they would experience in diabetes. Then they looked at what happened to biochemical pathways in the cells involved in inflammation and in creating new blood vessels.

"We decoupled those processes in the cells and identified important genes that were up regulated and down regulated," explains Prof Pandit. "Then we developed a biomaterial system which can deliver multiple molecules to target these processes."

The resulting biomaterial has shown its mettle in the lab and is now the subject of a patent application. "We hope to take it forward and carry out a clinical study for non-healing wounds where there is no treatment option," says Prof Pandit. "We want to see if applying this biomaterial, which is tailored to the biology of the wound, makes a difference to wound healing."

OUTCOMES

- Identified genes involved in diabetic wound healing.
- Developed a tailored biomaterial delivery system to promote healing.

CERVIVA research helps to fight cervical cancer

Cervical cancer is a silent killer, particularly of young women. Yet if the cancer is detected early in the neck of the womb, it can often be treated effectively. HRB-funded research is transforming screening and clinical management of cervical pre-cancer and cancer, both in Ireland and internationally, through the CERVIVA programme.

In its first round alone, CERVIVA has assessed and developed digital technology to improve screening of samples, it has identified numerous biomarkers of more aggressive disease and it has identified several areas where education could help women overcome potential barriers to going for screening.

Its innovations are now being used internationally to make primary screening more effective and to stratify women who present with abnormal cervical smears into high and low risk for cancer, according to Prof John O'Leary, Principal Investigator with CERVIVA, Consultant Histopathologist at St James's Hospital and Director of Pathology at the Coombe Hospital. "We set out to develop a research programme that would contribute to a quality cervical screening programme in Ireland and internationally, and we have achieved that."

Pathology goes digital

When the CERVIVA programme was established with HRB funding back in 2005, cervical smear tests were scanned manually by cytologists, which was a labour-intensive process. So CERVIVA sought to find out whether initially scanning the slides digitally using 'automated cytology' could offer a more useful approach.

During the study CervicalCheck, the national cervical screening programme, rolled out in Ireland and CERVIVA analysed a total of more than 35,000 cervical smear samples to compare manual and automated cytology.

The overall results favoured the use of automated platforms to screen samples initially and mark potentially abnormal cells in individual samples that could then be followed up by the human eye.

"We found that automated cytoscreening is as good as manual cytoscreening, and that at about 50-60 per cent of the cost, the automated approach is also more cost-effective," says Prof O'Leary.

"We set out to develop a research programme that would contribute to a quality cervical screening programme in Ireland and internationally, and we have achieved that."

CERVIVA research in conjunction with Irish company SlidePath (now part of the Leica group) also fed into the development of a virtual, slide-based, external quality assurance tool that lets people share digital versions of samples for external validation and quality control. This initial research contributed to an app being developed by SlidePath.

"That app is now widely used internationally, and it means you don't have to move physical slides between labs, which takes longer and slides can become damaged," says Prof O'Leary.

New biomarkers point the way in the clinic

If a woman's cervical smear sample shows some abnormal cells, what then? CERVIVA research has brought forward numerous biomarkers to help clinicians decide how to manage an individual patient.

"Several biomarkers have now been taken forward and are used routinely in the clinic," says Prof Cara Martin, Assistant Professor of molecular pathology at TCD and the Coombe and Programme Manager with CERVIVA.

"The biomarkers can help identify which women are at low risk of cancer and can be branched off the intensive monitoring or treatment path earlier, thus sparing the women themselves and more generally the Irish healthcare system from lengthy monitoring or unneeded interventions. Prof Charles Normand, a health economist at Trinity College Dublin, is leading the cost-effectiveness analysis of such interventions and tests in the context of cervical screening and management of cervical pre-cancer," says Prof Martin.

A CERVIVA study with The Coombe Women's Hospital has also found that testing women for Human Papilloma Virus (HPV), which causes cervical cancer, after they have had cancerous cells removed from the cervix can quickly identify whether the woman has a high risk of recurrence. "We are now seeing that being used in the clinic in Ireland for women who have had treatment," says Prof Martin. "And through these tests, we can see the follow-up period for a woman who has had treatment go, in some cases from 10 years down to 24 months."

"The biomarkers can help identify which women are at low risk of cancer and can be branched off the intensive monitoring or treatment path earlier, thus sparing the women themselves and more generally the Irish healthcare system from lengthy monitoring or unneeded interventions."

Addressing barriers to cervical screening

If regular cervical screening offers a relatively simple way of identifying early changes in the cervix, what stops women stepping forward for the test? CERVIVA research has identified several areas where education could be – and has been – improved, particularly around the link with HPV, which can be passed between sexual partners.

The research, led by epidemiologist Dr Linda Sharp from the National Cancer Registry, found that early on in the programme many women did not understand the link between HPV and cervical cancer, but that knowledge has grown as CervicalCheck and the HPV vaccination programme have been rolled out in Ireland.

Based on the findings, CERVIVA is now carrying out further research and interventions relating to HPV and other psychosocial barriers to cervical screening and follow up.

Collaboration increases value

"The original €1.25 million in HRB funding for CERVIVA has been multiplied by 10 through national and international collaboration, including EU-funded projects and partnerships with agencies such as Harvard School of Public Health and the International Agency for Research on Cancer," notes Prof O'Leary. "The effective value of the project became €12.5 million, and these new partnerships and programmes grew on the basis that CERVIVA was a research consortium with a wide range of expertise that had access to biomaterials and good data," he says. "It's a real Irish success story."

CERVIVA2, also funded by the HRB, will now run as a continuation of the original programme.

"The original €1.25 million in HRB funding for CERVIVA has been multiplied by 10 through national and international collaboration."

OUTCOMES

- Evidence that automated cytology of cervical smears is as good as, and more cost-effective than, manual screening.
- Web-based system to share and externally validate cervical smear samples.
- Development of numerous biomarkers to better inform clinical management of patients with cervical abnormalities.
- Proof that HPV testing after treatment for cervical cancer can identify patients at low risk of recurrence and reduce their follow up time.
- Tracked awareness of risk factors and barriers to cervical screening, developed interventions designed to improve knowledge and uptake of smear tests.

Giving nerve signals a leg-up in diabetes

In the long term, diabetes can lead to nerve damage in the extremities, particularly the toes and feet. This 'peripheral neuropathy' can increase the likelihood of falls, and it can also mean a person may not notice small cuts or potential irritants like a pebble in their shoe, leading to injury, infection and possibly even amputation.

HRB-funded researchers at NUI Galway have been developing technology to boost the nerve signals coming back to the brain from the foot. The aim is to help overcome some of the problems related to peripheral neuropathy and improve quality of life, according to researcher, Dr Leo Quinlan, a Lecturer in Physiology at NUI Galway's School of Medicine.

"Management of neuropathy in diabetes at the moment is through vigilance – watching for wounds and keeping the extremities clear of infection," he explains. "We are trying to manage it better to lead to better outcomes."

The technology developed during the project places electrodes above the ankle to apply subsensory noise of a particular frequency or 'stochastic noise' to nerve paths from the foot back to the spinal cord to boost sensory signals as they travel from the foot.

"Placing the stimulus on the nerve path rather than the foot itself is an innovative approach, and it would make the technology potentially easier for patients to use," explains Dr Quinlan.

The study found that applying the noise could enhance sensation by approximately 16 per cent in a group of younger, healthy adults and in older adults, some with diabetes, who had clinically significant levels of neuropathy – and this 16 per cent made a difference: applying the signal also increased awareness of ankle position, balance and walking stability.

Prof Gearóid Ó Laighin from NUI Galway, who was principal investigator on the project, explains that the next step will be to assess the efficacy and safety of applying the noise to the nerve paths for longer periods.

OUTCOMES

- Developed and assessed technology to improve sensation in nerves from feet.
- Applying specific electrical frequencies to nerve paths can improve sensation by 16 per cent.
- Paves the way for commercial device to improve quality of life in patients with nerve damage.

A tablet a day keeps breast cancer at bay

Women who do not take oral hormone therapy as prescribed following breast cancer have up to a three-fold greater risk of cancer recurring than women who persist with the hormone therapy, according to a HRB-funded study.

"The aim of hormone therapy is to help prevent the recurrence of certain types of breast cancer," explains principal investigator Prof Kathleen Bennett, Associate Professor of pharmacoepidemiology at Trinity College Dublin.

However, hormone therapy is typically prescribed for five years, and many women experience side effects when they take the hormones, such as joint pain and hot flushes. Previous work at Trinity College indicated that as many as one-third of women stop taking the medication as prescribed, and the current study looked at the potential impact of non-persistence.

By linking anonymised information from cancer registry and prescription databases, researcher Dr Ian Barron was able to match disease outcome with persistence to therapy. His analysis showed that where a woman did not persist with the oral hormone therapy as prescribed; there was 2.88-fold increase in risk of cancer recurrence.

"The benefits of taking the drugs clearly outweigh the risk of not taking them, in spite of the unpleasant side effects," says Prof Bennett. "The women who were non-persistent increased their risk of recurrence three fold, while taking the hormone therapy for the five years reduced the risk of death by a quarter."

The researchers are now building on the findings to explore in more depth why women do not take the medication as prescribed, and they hope to develop interventions that can help women to adhere to oral hormone therapy after breast cancer.

OUTCOMES

- Discovery that non-persistence with prescribed hormone therapy after breast cancer increases the risk of cancer recurrence almost three-fold.
- Basis to investigate why women do not adhere or persist with these prescriptions in order to develop interventions to reduce recurrence of cancer in this group.

When there's more than one disease – tackling cardiovascular multimorbidity improves care

Cardiovascular disease, chronic kidney disease or diabetes. Having any one of those conditions carries its own health burden, but what about when a person has more than one at the same time?

"Cardiovascular multimorbidity (CM) – where a patient has two or more of these diseases simultaneously – can complicate treatment, yet we haven't known much about how prevalent it is," says Dr Liam Glynn, a Senior Lecturer in General Practice at NUI Galway and a GP in Co. Clare.

But now a HRB-funded study led by Dr Glynn has shed light on CM in Irish primary care. The research analysed the health records of almost 10,000 primary care patients through the Western General Practice Research and Education Network (WestREN).

Out of that cohort eight per cent, or 778 patients, had CM – and of those 180 patients had all three conditions. "It was surprising, we didn't think the numbers would be so high," says Dr Glynn. "And Cardiovascular multimorbidity tended to mean higher rates of healthcare utilisation and poorer psychosocial scores."

The better news was that recognising CM seemed to benefit patients. "The results suggest that when you focus on cardiovascular multimorbidity, the efforts to reduce cardiovascular risk are successful," explains Dr Glynn.

The researchers also identified how CM could be tackled – including the need for education, psychological support, improved self-management and an enhanced role for practice nurses and community pharmacists.

The HRB-funded study has led to Dr Glynn and his team partnering in a large European study funded by the EU Northern Periphery Programme, which seeks to implement connected health solutions in identified patient groups, including those with multimorbidity.

OUTCOMES

- Measured the prevalence, risk factors and healthcare utilisation associated with CM in primary care in Ireland.
- Revealed that identification and management of CM is linked to better patient outcomes.
- Identified factors to improve management of CM in primary care.
- Leveraged additional funding through the EU for multimorbidity study.

Mild lack of oxygen at birth can have a long-term impact

Even a relatively mild lack of oxygen around birth can be linked to long-term effects on a child's development. That's according to HRB-funded research at University College Cork, which has identified the need to monitor at-risk children for learning and behavioural difficulties.

The study looked at newborns who had experienced hypoxic-ischaemic encephalopathy, or HIE, in which the baby's brain lacks oxygen around the time of birth. HIE affects about three in every 1,000 babies born in Ireland, it is a leading cause of neonatal death and survivors are at risk of disability including cerebral palsy, epilepsy and intellectual disability, according to Prof Geraldine Boylan, who carried out the research with HRB Clinician Scientist, Dr Deirdre Murray.

They recorded EEG or 'brain waves' of 60 babies with HIE and found that even where the HIE was relatively mild, in some cases it was linked with developmental delays as long as five years later.

"Most previous research has indicated that only infants with moderate or severe HIE experienced long term difficulties," says Prof Boylan. "But by using EEG measurements to assess HIE within hours of birth and then following up with those children over five years, we found that subtle learning deficits are common following both moderate and mild HIE."

In the Cork study, 18-20 per cent of infants who had mild HIE at birth had learning or behavioural difficulties at five years, including speech delay, autism, attention deficit and dyspraxia. And both moderate and mild cases of HIE were linked with overall blunted IQ scores, decreased processing speeds and poor working memory.

"Infants with moderate HIE are currently offered therapeutic hypothermia to help address the condition, but infants with mild HIE are not," says Prof Boylan. "This is due to the previously held perception that mild HIE has no long-term consequences, but our work is showing that some children who experience mild HIE could benefit from repeated follow up and assessment during early childhood."

OUTCOMES

- Established link between mild lack of oxygen around birth and with learning or behavioural difficulties at age five.
- Identified need to monitor and follow up babies who experience a mild or moderate lack of oxygen around birth.

A test for muscle tone that's easier for patients to swallow

If you can't swallow effectively, perhaps due to stroke, Parkinson's disease, cancer, dementia or a genetic condition, it can soon lead to problems. In the short term there's a risk of choking, dehydration and lung infection if food and drink drips down into airways. And over the longer term swallowing problems can lead to malnutrition, weight loss and tube feeding.

Measuring a person's swallow often involves taking X-ray and video images as they swallow a contrast liquid, which is time consuming and inconvenient. But speech therapist and HRB Fellow, Julie Regan, is exploring a more convenient and three-dimensional approach using a device developed by Crospon called EndoFLIP.

It works by placing a probe into the lumen of the upper oesophageal sphincter, a ring of muscle that is involved in swallowing. As the balloon fills with a saline solution, the device can measure how the sphincter responds.

"If the sphincter is happy to get wider and wider as the balloon gets bigger it indicates that the sphincter does not have very good tone," explains Regan. "But if the sphincter stays very tight despite the balloon getting bigger, then you know there is very good tone."

For her PhD at the Department of Clinical Medicine in Trinity College Dublin, Regan has used the EndoFLIP technology to test sphincter responses in healthy adults and in patients following laryngectomy, a surgical operation that removes part or all of the larynx. "It was clear that the patients who underwent the laryngectomy had very little sphincter tone compared to the healthy adults, so EndoFLIP could work as a diagnostic tool in this part of the body," she says. "The tool is also much more convenient for patients, who were keen to use it because it can be done in a few minutes in outpatients or at the bedside – there's no need to go to radiology and have an X-ray as you swallow liquids."

Regan is now going to extend the clinical studies and develop useful ways to visually represent the data during the exam.

OUTCOMES

- Assessment of new technology to examine muscles involved in swallowing.
- Could offer faster, more informative tests for patients with impaired swallowing.

A friendly approach to socialising for people with mental illness

Could something as simple as having a dedicated friend to go out with and a few Euros to spend help people with serious mental illness to overcome their reluctance to socialise in the community? A HRB-funded trial found that a small investment and a little moral support helped mental health service users to build their confidence in regular social settings, and reduce their loneliness and isolation.

"For many mental health service users it can be difficult to socialise outside of service-organised activities," explains Dr Ann Sheridan, a lecturer at University College Dublin's School of Nursing, Midwifery & Health Systems.

She led a randomised controlled trial that matched 52 mental health services users with volunteers and signed up 55 'controls'. All the study participants got €20 per month to socialise, and the volunteers met their assigned friends each week for nine months.

"There weren't too many rules," says Dr Sheridan. "We wanted people to establish an ordinary friendship, and we were there in the background if people needed us."

Participants went to the cinema, swimming, opera, art exhibitions and gigs and visited gardens, and volunteers would invite them to parties.

Data collected before, during and after the nine-month study period showed that in both groups social functioning had increased significantly and family loneliness and social loneliness had decreased, and those who had been assigned volunteers found their social confidence had increased.

"Investing a small amount of money may pay bigger dividends," says Dr Sheridan, who is now linking with community groups to encourage similar 'friend' schemes for people recovering from mental illness. "Giving people 20 Euro and letting them go out and socialise and be part of their community could offer big dividends in terms of them being socialised."

OUTCOMES

- Having a volunteer friend to socialise with helps people with serious mental illness to go out in the community.
- For people with mental illness, community socialising with a volunteer friend improved social functioning and reduced loneliness.

Cancer survivors: more exercise needed

When a person gets diagnosed with and treated for cancer, exercise might not be a priority. But physical fitness can be an asset during and after cancer treatment, and a lack of physical activity has been linked with the recurrence of some cancers later on.

Through HRB-funded research, Dr Julie Broderick objectively measured physical activity and fitness levels in a group of 100 cancer patients in Ireland, and found they were low at time of diagnosis. "The levels were much lower than predicted fitness by a scale used by oncologists," says Dr Broderick, a Research Fellow at the Department of Physiotherapy in Trinity College Dublin.

Did things improve after chemotherapy? Not so, according to Dr Broderick's findings when she followed up with 29 patients for a year after treatment for breast or colon cancer. "Physical activity stayed low and didn't improve over that year – even though these survivors were finished their chemo they hadn't picked up, they remained very inactive," she says.

To help address the issue, Dr Broderick ran an eight-week exercise programme, where 23 cancer survivors who had finished chemo came to the hospital for exercise classes. Compared to control patients who did not do the classes, the participants did not show increases in physical fitness, but they did find improvements in quality of life and general fatigue.

The findings should help to increase awareness of the importance of physical activity during the cancer journey, according to Dr Broderick.

OUTCOMES

- Identified low levels of physical activity in cancer survivors.
- Evidence that exercise after chemotherapy can improve quality of life and reduce fatigue.

Sleep for your heart's sake

Not getting enough sleep is bad for your heart, but why? It could have to do with the way your body controls blood pressure, according to HRB-funded research.

The study helps to explain a long-standing puzzle in health, according to researcher Prof Jack James from NUI Galway.

"On one hand, population surveys show that chronic sleep deprivation contributes to the development of hypertension, or high blood pressure, and cardiovascular disease," he says. "On the other hand, experimental studies indicate that sleep loss has little or no acute effect on blood pressure level. This appears contradictory, because blood pressure level is a major predictor of cardiovascular health."

"But the effects – at least in the shorter term – could be happening at the level of a person's 'haemodynamic profile' or the physiological mechanisms that control how the heart pumps blood around the body," he explains.

The experiments measured the haemodynamic profile of healthy volunteers who got shortened and normal amounts of sleep. The results suggest that acute sleep deprivation has negative effects on the underlying haemodynamic profile without affecting blood pressure in the short term, according to Prof James.

"However, we believe that the short-term effects of sleep deprivation on haemodynamic profile may activate atherosclerotic processes or 'hardening of the arteries' that, if continued over time, contribute to the development of hypertension, or increased blood pressure, and other cardiovascular pathology," he says. "The findings can now help to inform health promotion and clinical management strategies that focus on the relationship between sleep and cardiovascular disease."

OUTCOME

» Identified potential mechanism for how a lack of sleep affects the cardiovascular system.

Giving children a say in decisions about their healthcare

Children with acute and chronic illnesses want to be involved in decisions about their healthcare, but they are not being given enough of a voice. That's the finding of a HRB-funded study led by Prof Imelda Coyne, Professor of Children's Nursing at Trinity College Dublin's School of Nursing and Midwifery, which analysed interactions at a hospital in Ireland.

The research observed 10 children aged eight to 15 with long-term or acute conditions, and also interviewed their parents and healthcare providers. The exercise gathered information about interactions between the children, their parents and health professionals relating to their care.

Separately, the study ran focus groups with a different group of 12 children aged eight to 16 to discuss the findings and to get a deeper understanding of their experiences.

"The results showed that children and adolescents had a limited role in decision-making and that the attitudes of the adult had more of an influence than the child's competence," explains Prof Coyne.

"Adults saw including the child as a way of gaining their co-operation for procedures rather than an actual right of the child," she says. "And adults tended to only start involving adolescents aged 14 years upwards in decisions for chronic illnesses, even though we found that children aged eight were highly knowledgeable about their own condition."

"Children valued being included, but often became resigned to their lack of voice if it wasn't being sought," she adds.

"The adults separated decisions into the big decisions like surgery, and the small decisions such as everyday decisions like timing of care – but children do want to be involved in those 'small' decisions, and they want to be involved in discussions around major decisions," says Prof Coyne.

The study results have underpinned an information leaflet and have been discussed with health professionals working with children.

OUTCOMES

- Identified that children want more of a say in healthcare decisions.
- Information resources to encourage greater involvement of children in healthcare.

It's all relative – new insights into sentence processing in Specific Language Impairment

'The boy rode the horse that Ann put in the field.' It sounds like a simple statement, and if you grew up speaking English, you could probably use a sentence like that with relative ease. Yet if you take it apart, its syntax is quite complex.

The estimated seven per cent of children with specific language impairment (SLI) find it difficult to process relative clauses in such sentence constructions, but to date the area has been understudied.

Now HRB-funded research has analysed how children with SLI approach relative clauses, and it has identified how they lag behind their typically developing peers.

Dr Pauline Frizelle at the Department of Speech and Hearing Sciences in University College Cork made the findings when she asked 32 six-seven-year-old children with SLI and 32 age-matched typically developing children to repeat 52 sentences with complex structures. She also carried out the test with a group of younger, typically developing children aged four and a half.

"Sentence recall is a very good psycholinguistic marker of children with SLI and the sentences in this study represented the full range of syntactic roles," she explains. "What it showed was that those children with SLI have a significantly greater difficulty with these complex structures than their age-matched peers, and also than children who are an average two years younger."

Dr Frizelle's research identified how, in the case of SLI, sentence structures and word choices affected the children's ability to recall the sentences. "The new insights into relative clauses as a 'marker' can help therapists identify SLI in children and also point to the appropriate intervention for that individual child," she says. "By using this approach we could better identify the problem a child with SLI is having, and tailor the next step in therapy accordingly."

OUTCOMES

- Measured delays in understanding and using relative clauses in specific language impairment.
- Offers an approach for speech and language therapists to identify the most appropriate next step within complex syntax for children with SLI.

SEARCHING FOR BETTER TREATMENTS

Tilting the immune balance against tuberculosis

Tuberculosis (TB) infects one in three people around the world and kills one and a half million people annually. And the emergence of multi-drug-resistant TB strains in recent years is a new cause for concern.

"TB is a disease that is neglected by science, and it's a priority public health issue in Ireland, where we have numerous outbreaks," says HRB Clinician Scientist, Dr Joe Keane, Professor of Medicine at Trinity College Dublin and a Consultant Respiratory Physician, St James's Hospital.

He has been involved in HRB funded research to understand how Mycobacterium tuberculosis, the bacterium that causes TB, interacts with the human immune system. "This work will inform new therapies and vaccines," says Dr Keane.

Using non-infected lung cells from patients undergoing lung procedures and human samples from the National Tuberculosis Reference Laboratory, he and colleagues at Trinity and University College Dublin have been looking at the interplay between the bacterium and specific cells of the human immune system, including lung macrophage.

Macrophage can 'eat' and kill the bacterium, but the bug has its own cunning strategies for thwarting the body's defences, as Dr Keane and colleagues discovered.

"We have figured out that the bug interferes with microRNA, which is a molecule that programmes the macrophage for success or failure against this awesome pathogen," explains Keane. "The research has also pointed to vitamin A and immune-boosting medications as potential agents to help tilt the immune odds in favour of the human cells against TB," he adds.

"We are now seeking to translate observations from the lab and the clinic to patients who are not responding to treatment or who have multiple drug-resistant TB, so they can benefit from adjustments to their immunity," says Dr Keane.

OUTCOMES

- Discovered how TB bacteria interfere with a specific human immune response.
- Evidence that vitamin A could boost immune response to TB.

Who will respond to treatment for Hepatitis C?

Hepatitis C is a major health burden – it's estimated that one per cent of all humans have been infected with the Hepatitis C virus (HCV). Why is this important? Chronic infection with the virus can lead to liver damage and the need for a transplant.

There are some drugs to treat the infection, but not everyone will respond to them by clearing the virus – and those who don't respond may just get the side-effects of the drug rather than the benefit.

A HRB-funded study has now found a potential way to identify in advance which patients infected with HCV are likely to respond to a commonly used treatment called interferon.

"The study used blood cells generously donated by Irish women who had been infected with HCV through contaminated anti-D product," explains researcher Prof Cliona O'Farrelly, who is Professor of comparative immunology at Trinity College Dublin. "We can learn from the biology of the patients themselves about why some people respond to treatment and some don't," she says.

The study exposed cells from infected, but as yet untreated patients, to interferon in the lab and measured the cellular responses. Then the researchers tracked how the patients themselves responded when they started treatment with interferon.

"We found that, in the lab, the patients' cells were able to predict in advance whether the patients themselves would respond well to the interferon," says Prof O'Farrelly. "And by looking at how the cells responded we also identified an important signalling protein called STAT3 that is involved in the successful response to the interferon."

The Trinity group is now building on the discovery to develop specific tests that could help identify which patients will respond to treatment and those who will not, she explains: "Predicting patient responses will reduce ineffective treatments and thereby minimise the costs for Irish healthcare services and stop patients suffering unnecessary side-effects."

OUTCOMES

- Identified measurable differences in HCV patients that could predict whether they will respond to standard therapy.
- Basis to develop a blood test to predict patient responses to treatment.

A look inside the living brain in motor neuron disease

When a person has ALS, a type of motor neuron disease, it can take up to a year to get a definite diagnosis, and even then it is often unclear how the person's brain will be affected over time by the neurodegenerative condition.

MRI, which scans the brain of a living person, is currently only used in ALS to rule out possible alternative diagnoses. But could MRI scans also be used to speed up diagnosis and identify better ways to treat the patient? In a HRB study, specialist registrar in neurology at Beaumont Hospital and Trinity College Dublin, Dr Peter Bede, looked to find out.

"With 'very touching generosity' 60 patients underwent one or more MRI scans, gave DNA samples and underwent neurological and psychological tests," explains Dr Bede, who also carried out MRI scans on the brains of around 60 healthy volunteer 'controls'.

The study found that the degree to which an area of brain called the motor cortex is damaged in ALS correlates sensitively with the patient's level of disability. "This could potentially be very helpful, not only to speed up diagnosis of patients, but also to objectively assess the effects of new drugs in clinical trials," he says.

"The Beaumont-Trinity research also showed that patients with a mutation in a gene called C9orf72 undergo more extensive structural damage in the brain, which is likely to explain the distinctive psychological symptoms these patients experience in ALS," explains Dr Bede. "MRI could be a tool to confirm the diagnosis at an earlier stage, so we can plan and commence management earlier," he says. "Along with genetic information it could also give us more insight into the natural disease trajectory that the patient might have, so we can tailor their clinical management in a more informed way."

OUTCOMES

- Mapped structural changes in the brain in ALS.
- Demonstration of the anatomical signatures of genetic factors.
- Evidence that MRI could speed up diagnosis and help predict disease course in patients.

An immune link between belly fat and cancer

The fat inside a 'beer gut' is special – and not in a good way. That visceral fat is far from inert: it can become inflamed in obesity and it has been linked with an increased risk of several cancers, including one called oesophageal adenocarcinoma.

The incidence of this particular cancer has doubled in Ireland in the last two decades and with more than 300 new diagnoses per year the numbers keep rising, according to Dr Joanne Lysaght, who is an Assistant Professor at the Department of Surgery in Trinity College Dublin.

With HRB funding she has been looking at why obesity is so closely linked with this cancer, and she has found some clues in the immune cells that turned up in deep in obese belly fat.

When Dr Lysaght analysed visceral fat samples from 40 patients undergoing surgery for oesophageal adenocarcinoma, she discovered that the fat from obese patients contained high levels of active immune cells called T cells.

"We found that about 40 per cent of T cells were activated and inflammatory, and these are the types of T cells that you want to kill a tumour."

The discovery has opened up many questions about why so many activated T cells are sitting in the fat and Dr Lysaght is now looking for more clues.

"These T cells could be contributing to inflammation, which is generally linked to cancer, or the visceral fat could be acting as a 'sink' for these cells, meaning they can't go and fight the tumour," she says. "There's a lot still to find out, but the findings should help to shed light on how we could intervene to ensure the T cells are doing their job of fighting cancer."

OUTCOMES

- Discovered high levels of inflammatory immune T cells in belly fat which could potentially kill cancer cells.
- Points to potential link between obesity, immune system and oesophageal adenocarcinoma.

Another brick in the wall for artery disease?

Your heart pumps blood around your body through a network of arteries. If the walls of these arteries 'harden' in a condition called atherosclerosis, it can put pressure on the heart and damage the cardiovascular system over time.

But why do artery walls harden and develop plaques that can block the blood supply? A HRB-funded study has found a link between 'progenitor' cells in the blood and damage to the artery wall.

Previous work had shown that these primitive progenitor cells came out into the blood after arteries were injured in animal models, and the HRB study sought to examine the situation in patients.

"We wanted to see in patients if there was a relationship between this cell and atherosclerosis," says consultant cardiologist Prof Noel Caplice, who directs the Centre for Research in Vascular Biology at University College Cork.

The circulating cells themselves are low in number, so the researchers looked instead for a molecule that the cell produces called ISL1.

The study took blood samples from around 250 participating patients who came into Cork University Hospital for interventional cardiology procedures. The researchers were able to see how damaged the artery walls were and how much ISL1 was in the blood. "Very few of the patients with healthy arteries had any evidence of ISL1," says Prof Caplice. "Whereas a significant number of patients with atherosclerosis had elevated levels of this molecule in their blood. And we showed there was an associative relationship – the more of this factor was present, the higher the extent of coronary artery disease burden in the patient."

"The finding could pave the way for a new blood test to predict which patients are likely to have a heart attack," he explains, "and the next step would be multi-centre clinical studies. Meanwhile understanding the biology of this cell may be very important in terms of what regulates disease and what happens in the artery wall."

OUTCOME

» Identified an association between a molecule in the blood and artery damage in patients.

Why do some patients develop sepsis?

For some patients, a bout of pneumonia or an infection through a perforated bowel can mean serious illness, but with the help of antibiotics they get better relatively quickly. For other patients though, it's a different story; they develop a condition called sepsis, which can lead to organ failure and in some cases death.

"The clinical question is why do some people recover from infection without complication but others develop sepsis – is there a difference at the cellular level within the patients that has a clinical impact?" says Dr Robert Grealy, who investigated this question as a HRB Clinical Research Fellow based at the intensive care unit in St James's Hospital.

Previous studies have shown that in sepsis, the body's own immune system appears to 'over-react' to the infection and cause damage in its own right, but so far new treatments directed towards the immune system have shown little clinical benefit in sepsis, according to Dr Grealy. That's why he wanted to get a better understanding of the immune response to infection in patients who develop the condition.

With HRB funding, he homed in on a type of immune cell in the blood called a monocyte. He analysed monocytes in blood samples from patients in intensive care who had developed sepsis and compared them with monocytes from the blood of healthy controls. Using a technique called next-generation sequencing, Dr Grealy identified over 1000 genes that appear to be turned on or off in these cells in sepsis, and the findings now provide an important resource for further research into the cellular response. "This gives us insights into potential further targets for treatments for sepsis," he says.

OUTCOMES

- Identified changes in hundreds of genes activated during sepsis in a type of human immune cell in the blood.
- Offers a resource for looking for new therapeutic targets for sepsis.

A potential route to dampen the fire in multiple sclerosis

What if there was a slow-burning 'fire' in your body and it damaged the nerves that allow you to move, remember and see? The nervous system is normally protected from chronic inflammation, but in conditions such as multiple sclerosis, chronic inflammation seems to run riot and damage important tissues in the nervous system and brain.

"A short burst of inflammation can be protective, to help clear an infection, but when inflammation doesn't resolve and becomes chronic it can damage tissues instead," explains Prof Paul Moynagh, who directs the Institute of Immunology at NUI Maynooth.

Through HRB-funded research, his group has discovered that a protein in brain cells called NFkB appears to be a driver of prolonged inflammation in brain cells, because this protein doesn't get inactivated as it normally would.

The study looked at brain cells called astrocytes in the lab – using a cell line from humans and cells taken from a mouse model of multiple sclerosis – and found that NFkB was hanging around for far longer than usual.

"We know that NFkB inside cells drives inflammation, but it normally doesn't stay active for long because it also turns on another molecule that inhibits it," explains Prof Moynagh. "But we saw that the 'off-switch' for NFkB wasn't being activated, and we think this is an important step."

He is now looking to develop routes to turn the 'off-switch' back on, which could help to extinguish the inappropriate inflammation and thus reduce the damage. "That could offer a way of limiting the length of time that NFkB is active, and the hope is that it could cut down on inflammation and damage to the nerves in multiple sclerosis," he says.

OUTCOMES

- Identified a mechanism underlying brain inflammation.
- Potential route to dampen inflammation in conditions such as multiple sclerosis.

We need to talk about RON – for asbestos-related cancers

Exposure to asbestos can cause a particularly aggressive form of cancer called mesothelioma. Patients with this cancer in the lungs have limited treatment options and the majority die within two years of diagnosis, according to Dr Steven Gray, who has carried out HRB-funded research into potential new drug targets for the condition.

"There's an urgent need to identify new targets and potential therapies," says Dr Gray, a Senior Clinical Scientist with the Thoracic Oncology Research Group at the Trinity Centre for Health Sciences.

Together with researcher Dr Anne-Marie Baird, they identified a particular protein called a receptor tyrosine kinase on the surface of cells that is present on mesothelioma cells. "We ran a specialised assay to screen for activated receptors in a panel of cell lines and primary tumours, and identified this receptor as 'RON'."

Further work confirmed that this RON molecule is overexpressed in human tumour samples, and Drs Gray and Baird tested various methods to block it. They found that a small molecule inhibitor, which was specifically developed by a Canadian company to target the receptor's action, could induce mesothelioma cells in the lab to die. "It caused significant cell death and put the brakes on proliferation in mesothelioma cells," says Dr Gray.

The researchers are now collaborating with three pharmaceutical companies to test RON-blockers with the ultimate aim of moving to clinical trials and new treatments.

The group at St James's Hospital is a member of ETOP, a European network of oncologists that promotes clinical studies in lung cancer. ETOP is preparing a subgroup, MESOSCAPE, to improve collaboration on mesothelioma trials. "This grant has opened up a lot of opportunities for us internationally," says Dr Gray.

OUTCOMES

- Discovered a molecule overexpressed on cancer cells in mesothelioma.
- Identified potential mechanisms to block the molecule and develop potential new treatment.

Sleep and brain inflammation – uneasy bedfellows

How might be the body clock be affected following critical illness? A preclinical study funded by the HRB has found that brain inflammation associated with severe infection may disrupt the 'circadian clock' of mice.

The study, led by Dr Andrew Coogan at NUI Maynooth, used a mouse model of brain inflammation which developed and persisted following on from a strong challenge to the immune system. "The severity of the neuroinflammation that you get long term in this model looks similar to the low-grade inflammation you tend to see in the normal healthy aged brain," explains Dr Coogan.

On the face of it, the animals with brain inflammation showed no obvious disruption of their 24-hour clock, but the researchers were able to tease out more subtle effects by altering light/dark timings to mimic jetlag.

The responses they saw in the 'neuroinflamed' mice were similar to the kinds of changes expected in older mice, and the genes that control the body clock changed their expression pattern. And if the researchers blocked the severity of the inflammation, the circadian clock was less altered.

The next step is to look at circadian patterns in humans who have long-term brain inflammation, possibly following sepsis or as a result of chronic inflammatory conditions or ageing, according to Dr Coogan. "But so far the findings suggest that managing the body clock could offer a route to improve quality of life," he adds.

"One of the nice things about circadian rhythms is that you can use some fairly simple interventions such as light treatment, melatonin and even simple behavioural steps like setting scheduled mealtimes and having good sleep hygiene. And managing circadian rhythms may, in turn, feed into long-term quality of life."

OUTCOMES

- Identified links between infection, brain inflammation and body clock disruption.
- Suggests that managing the body clock could support patients and improve quality of life following infection.

Pointing to the needle in the haystack during drug discovery

How do you find a needle in a haystack? It helps if a computer program can reduce the size of the haystack. So with HRB-funding, Dr Noel O'Boyle has developed software to aid the search for potential new drug compounds by computing the chemical behaviours of a compound and filtering out the ones that won't work.

"The key issue for structure-based design is the lock and key, where you are trying to fit the molecule into the protein to find drugs that could work," explains Dr O'Boyle, who carried out his research as a Post-Doctoral Researcher at the School of Pharmacy in University College Cork. "But every potential drug can adopt a large number of shapes, and some will fit in to the 'lock' and some won't. So the key is to generate all the possible shapes you can have and see what shape fits in."

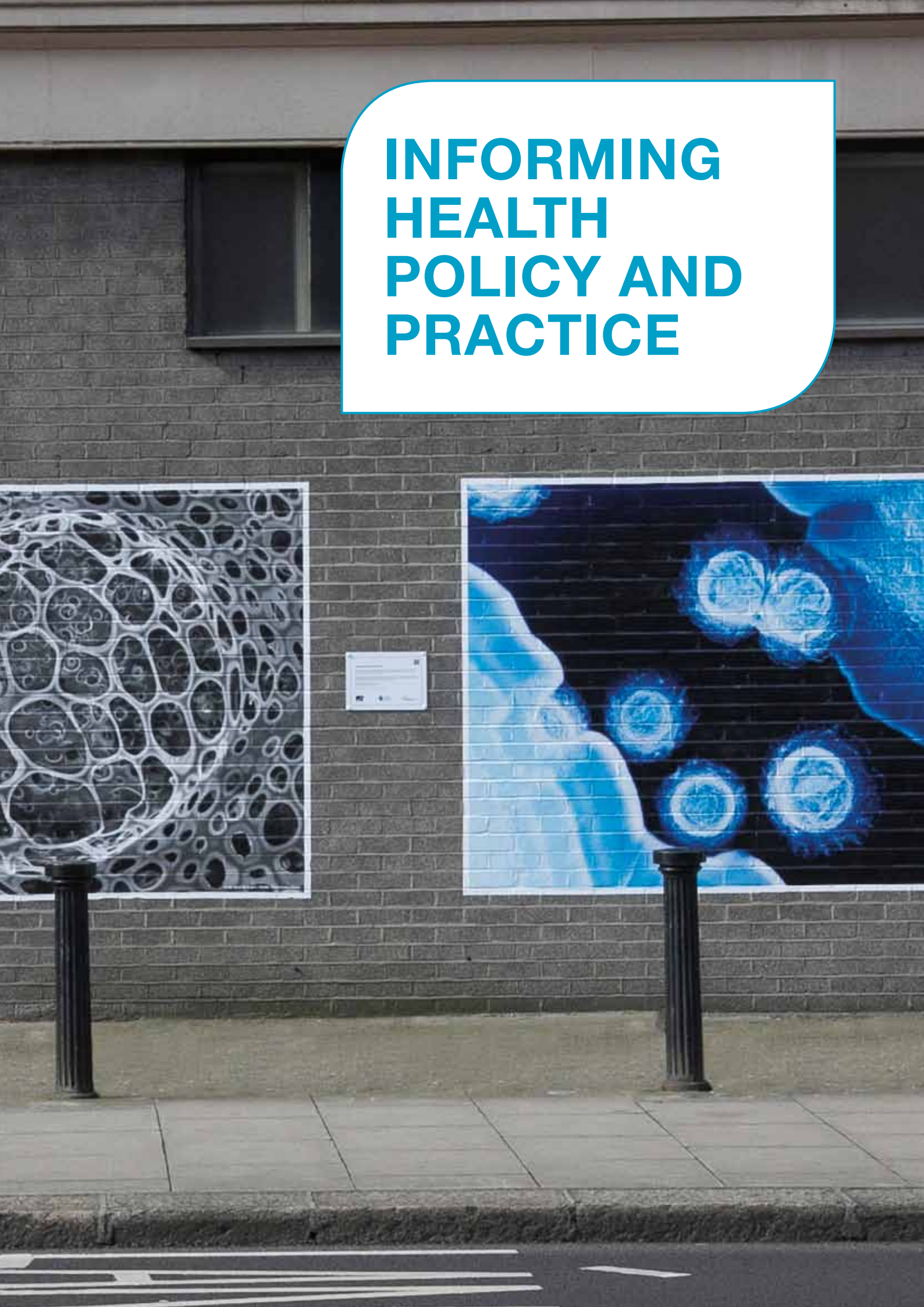
The software that Dr O'Boyle developed can analyse a potentially interesting compound and generate up to one million different shapes it can take, to check whether it will be a good 'fit' for the target of interest.

"You would filter beforehand to find molecules which are drug-like, which means having certain characteristics of a molecule, then this software would find the shapes of those particular molecules that are a good fit," says Dr O'Boyle. "At that point you would go and do the experiments in the lab with these compounds, but using the software beforehand increases the chance of finding the needle in a haystack."

"The software developed at UCC will soon be integrated into other programs that are widely used in drug discovery," explains Dr O'Boyle. "It should give researchers a better insight into how molecules are going to behave or interact," he says.

OUTCOME

» Software developed to inform early-stage drug discovery.



INFORMING HEALTH POLICY AND PRACTICE

A new look at ageing with intellectual disability

What is it like to age with an intellectual disability? For the first time, we are getting some robust insight into that question thanks to the Intellectual Disability Supplement of The Irish Longitudinal Study on Ageing (TILDA).

The unprecedented initiative, which is funded through the HRB and the Department of Health, is capturing information about physical and mental health and social engagement among people in Ireland who are living with intellectual disability, or ID.

"The need for such data has been internationally recognised, but until now no country has managed to systematically study ageing over time in individuals," explains Prof Mary McCarron, who leads IDS-TILDA.

"This is the first time in history that we have had an older population with ID, and there's a huge gap in knowledge about how this population ages," explains Prof McCarron, who is also Dean of the Faculty of Health Sciences at Trinity College Dublin. "Cross-sectional studies have given us some clues that this group has a greater variety of health concerns that are often unmet and unrecognised, but people with ID have not been included in previous longitudinal studies of ageing internationally."

Until now, that is.

Set up to complement TILDA, a longitudinal study of more than 9,000 people aged over 50 in Ireland; IDS-TILDA involves more than 750 participants living with ID. Traditionally one of the barriers to studying ageing with ID has been recruitment, but the HRB-run National Intellectual Disability Database made it possible for IDS-TILDA to select a nationally representative cohort of people with ID to take part.

"We were able to recruit participants that represented all living circumstances, including people living on their own or with family, as well as people living in community and residential settings," says Prof McCarron.

"Traditionally one of the barriers to studying ageing with ID has been recruitment, but the HRB-run National Intellectual Disability Database made it possible for IDS-TILDA to select a nationally representative cohort of people with ID to take part."

IDS-TILDA looked at key determinants of health and wellbeing of people with ID and compared them to the outcomes in the main TILDA study, and added some specific measures for the ID cohort too – including looking at the slightly younger age group 40 to 49 as well as older participants. So what did they find?

"Ireland has been the first country to mount and successfully run a supplement to a generic ageing study that systematically includes people with ID," says Prof McCarron. "It is a real case of Ireland leading the way."

"People generally reported good health, but for physical health we saw that, compared to the general population, people with ID appear to exhibit different patterns and combinations of diseases and chronic conditions, and those conditions can progress in different ways," says Prof McCarron.

Multiple morbidity, where an individual has more than one chronic condition, was higher among people with ID than in the general population – and higher rates of risk factors linked with cardiovascular disease stood out, according to Prof McCarron.

"Overweight and obesity, high levels of physical inactivity and high levels of cholesterol were a concern across the board, even in the younger cohort," she says. "Though interestingly there were low levels of hypertension (chronically high blood pressure) even where risk factors were present, which is something we are looking at now."

People with ID can also be at higher risk of bone problems such as osteoporosis, yet hardly any had undergone a bone density test before taking part in IDS-TILDA. Meanwhile, falls were more prevalent, as was depression and other mental health issues.

Many participants reported engaging in social activities, but few used electronic media to keep in touch, as Prof McCarron describes: "There's a huge gulf between people with ID and the general population with respect to the use of technology. We are in the digital age yet more than 75 per cent had never used social media or texts or emails, and fewer than 50 per cent had used a telephone to make contact."

The study also identified other issues, such as long-standing literacy and numeracy problems and limited education, and the difficulties people with ID have in getting around their communities without assistance. In cases where people with ID were living with family carers, carers often reported providing many hours of caring assistance and felt that they needed more supports.

Several of these factors are now being explored in the second wave of IDS-TILDA, which is building on the findings of the initial phase, and Prof McCarron is working with stakeholders to help inform policy in the area.

"There are similarities, but there are also a lot of differences in how people with ID are ageing, and this study has helped to shine a light on the reality of the health disparities for people with ID," she says. "And I think the evidence we have found will promote their inclusive, rather than separate, consideration in policies affecting older adults – there's much to be gained if people with ID are included in mainstream policies."

"The initiative has also put Ireland on the map by raising the standard of research in this area and attracting international interest in replicating the study elsewhere," she notes.

"Ireland has been the first country to mount and successfully run a supplement to a generic ageing study that systematically includes people with ID," says Prof McCarron. "It is a real case of Ireland leading the way."

OUTCOMES

- First major study of ageing with intellectual disability in Ireland.
- Identification that people ageing with ID show specific patterns of disease – they are particularly susceptible to epilepsy, osteoporosis, falls and mental health problems and have high risk factors for heart disease.
- Discovery that older people with ID are not engaging with technology to keep in touch with family and friends.
- Evidence to include people with ID in mainstream health policies around ageing.

Psychosis: Early treatment is key for discovery

A series of HRB-funded research studies show that shorter delays to treatment for people with psychosis are associated with long-term benefits at many levels. The research is also paving the way for more effective treatment in the early phase of recovery.

Getting treatment early in psychosis is linked to long-term benefit

If you catch and treat heart disease or cancer early, there tends to be a better outcome. So it seems intuitive that the longer a psychosis goes untreated the worse the outcome and that starting treatment quickly would be of benefit. Now a HRB-funded study has shown that the impact of delays to treatment in psychosis can be seen as long as 12 years later.

The findings have their roots in a study in Dublin in the 1990s, which involved 171 people with a first episode of psychosis and individuals were followed up at intervals of six months, four years and eight years after treatment. Those who had a shorter delay to treatment generally had fewer symptoms and better general functioning, according to Consultant Psychiatrist, Dr Mary Clarke, who works with the DETECT early intervention for psychosis service, a HSE service managed by the Cluain Mhuire Community Mental Health Service of the St John of God Community Mental Health Services Ltd.

The new study shows that even 12 years on from initial treatment, people who had experienced shorter delays to treatment had fewer symptoms and better quality of life. "It makes a strong argument for early treatment in psychosis," she says.

And delay to treatment is something we can address, notes Niall Turner, project manager and the Head of Occupational Therapy at DETECT. "A lot of the predictors of outcome for people with schizophrenia and psychosis are fixed – like gender or family history – but treatment delays are malleable. And through DETECT, with the co-operation of primary care and community mental health services, we have reduced delays by more than 50 per cent in our area."

"The findings of the 12-year follow up study should inform a move towards early detection and treatment of psychosis in line with the public health messages used for heart disease and cancer," he adds.

What helps to improve quality of life in early recovery from psychosis?

When someone starts on treatment for psychosis, hopefully their journey of recovery will see psychotic symptoms such as delusions and hallucinations abate. But what about other factors,

such as quality of life? Clinical Nurse Specialist Dr Laoise Renwick carried out a HRB-funded PhD to examine quality of life in the early phase of treatment for psychosis, and the findings should help inform more effective interventions and supports for recovery.

In the first study of its kind in Ireland, Dr Renwick gathered information about quality of life from more than 220 people during their first year of treatment for psychosis.

Those who had long periods of untreated psychosis generally had a poorer quality of life. "People who spent a longer time being unwell before coming to treatment had more negative feelings at one year," says Dr Renwick, who carried out the study through the DETECT service.

More generally, people in this early phase of recovery expressed a desire to be integrated into the community, and most of the participants who were not in paid employment wanted to be working. The findings should help inform future studies and assessment of people undergoing the initial stages of treatment for psychosis, according to Dr Renwick, who is now a post-doctoral researcher at King's College London.

"The results highlight the importance of early intervention in preventing the loss in quality of life that can be associated with psychosis," she says. "And it points to psychosocial areas that could potentially be targeted during recovery to help improve the 'bigger picture' of quality of life as the psychotic symptoms abate."

Cannabis and psychosis – interventions in a challenging area

It's known from previous studies that people who use cannabis in the early course of psychosis are likely to have poorer outcomes in the longer term. So HRB-funded research looked at the effects of treatments aimed at reducing cannabis use in patients with psychosis.

In particular, it sought to find out whether a group-based psychological intervention using cognitive behavioural therapy and motivational interviewing could be more effective than the standard treatment, where individuals attend as outpatients.

The study found that the group-based treatment did not affect cannabis use, but it did improve how the participants perceived their quality of life for up to a year after the eight-week intervention.

"We found there was a mild but sustainable improvement in subjective quality of life, which was a positive outcome," says Kevin Madigan, a Senior Nurse Manager at Cluain Mhuire. "And this highlights the potential benefits of group interventions in addressing the losses in quality of life that can be associated with psychosis."

"The research also highlighted the challenge of recruiting cannabis users for the psychological treatments," adds Mr Madigan, who worked on the study with a team that also included the National Drug Treatment Centre, Cavan-Monaghan Community Mental Health Services and the Royal College of Surgeons in Ireland.

"We initially had 230 referrals, but ultimately 88 participants took part in the randomised controlled trial," he says. "And that would be in line with international experience."

Mr Madigan was awarded a bursary named after the late Prof Eadbhard O'Callaghan, who was initially Principal Investigator on this project. This bursary supported a conference on future directions in the research and treatment of cannabis dependence in early psychosis which was co-funded by the HRB. "We have now set up a network with colleagues in Denmark and the UK to look at how we can develop interventions specifically for people with psychosis and co-morbid cannabis misuse," he says.

OUTCOMES

- The impacts of delays to treatment for psychosis are evident even 12 years after the start of treatment.
- Shorter delays to treatment for psychosis generally lead to fewer symptoms and better quality of life.
- People in the recovery phase want to be integrated into the community and be in paid employment.
- Group psychological intervention can improve perceived quality of life in people who use cannabis early in psychosis.
- International network to develop interventions specifically for people with psychosis and co-morbid cannabis misuse.

Professor Eadbhard O'Callaghan

TRIBUTE:

Professor Eadbhard O'Callaghan was a consultant psychiatrist at the Cluain Mhuire Community Mental Health Service and the Newman Professor of Psychiatry at University College of Dublin. As both a clinician and researcher Eadbhard was driven by a need to find the best solutions to improve the outcomes of people with psychosis and assist families to play an active role in their relatives' recovery. An early study led by Eadbhard found that persons who used substances at the time of a first episode psychosis experienced a higher number of readmissions to hospital, were less likely to be in employment and experienced more suicidal thoughts than non-substance users. This compelled him to lead a large scale multicentre randomised controlled trial of psychological interventions to help assist this patient group achieve better outcomes. Findings from other research he undertook led to the establishment of the DETECT Early Intervention in Psychosis Service in South Dublin and North Wicklow. His practical approach as well as a humble, compassionate nature endeared him to his patients, their families and the many colleagues he inspired. Eadbhard passed away on the 2nd of May 2011. May he rest in peace.

National cancer screening – fine-tuning could improve existing systems

How cost-effective are screening programmes for cancer? For an individual whose cancer is diagnosed early and successfully treated, the value is immeasurable. But for a national programme, what's the right approach to take to make sure resources are used wisely?

"When done right, cancer screening can be very cost effective, but when done wrongly the opposite is the case," says Dr James O'Mahony, whose HRB-funded research has looked at fine-tuning existing cancer screening to improve prevention. "So it pays to get it right."

Now a Post-Doctoral Researcher in Cost-Effectiveness Analysis at Trinity College Dublin's Department of Health Policy & Management, Dr O'Mahony's PhD looked at the cost-effectiveness of refining cancer screening regimes that are already in place.

With colleagues at the Erasmus University Medical Centre in Rotterdam, he worked with a Dutch model to address specific questions, such as how should we assess the optimal screening intensity in the era of Human Papilloma Virus (HPV) vaccination. The work showed that it is more cost-effective to tailor screening strategies separately for vaccinated and unvaccinated women, because vaccinated women are anticipated to be at lower risk of disease and less intense screening may be more appropriate for them.

Dr O'Mahony is now looking to apply the findings from his modelling studies to an Irish context. "There can be a gulf between the models producing the policy recommendations and the policy questions they are trying to answer, and it's important that we try and close that gap as much as possible," he says. "Otherwise as we embrace new technology in our current screening programmes we could have poor clinical outcomes and waste money."

OUTCOMES

- Analysis of potential cost-effectiveness of 'fine-tuning' cancer screening in large populations.
- Evidence that taking cancer risk factors into account could improve cost effectiveness.

Folic acid: older people in Ireland are not running low

Adding a nutrient to staple foods is one way of increasing intake in a large population. Countries including the USA, Canada and Chile have mandatory fortification of flours with folic acid, with the aim of reducing the risk of neural tube defects developing in early pregnancy. In Ireland, many food companies voluntarily add folic acid to products and mandatory fortification has been debated in recent years.

In September 2013 the Food Safety Authority of Ireland advised that there would be no additional benefits for mandatory folic acid fortification of bread in Ireland, but they are continuing to monitor the situation.

To increase our understanding of folic acid in Ireland, Dr Mary Rose Sweeney led a HRB-funded study to examine folic acid levels in the older Irish population, who could be vulnerable to potential safety concerns linked to excess folic acid intake – including the masking of pernicious anaemia.

"We are already exposed to a food supply in Ireland which is extensively fortified with folic acid on a voluntary basis, so we wanted to measure the levels of unmetabolised folic acid in older people here," explains Dr Sweeney, who is a Lecturer at Dublin City University's School of Nursing and Human Science.

The research analysed blood samples and dietary information from 137 participants aged 60 to 86 in the Lifeways Cross-Generation Cohort Study and found that more than 90 per cent of the elderly group had low levels of unmetabolised folic acid in their blood samples, even though they had been fasting overnight.

"These findings suggest a persistent presence of the synthetic vitamin in blood that has not been converted to folate," says Dr Sweeney of the findings, which were published in *The American Journal of Clinical Nutrition*. "It adds weight to the argument against additional mandatory fortification at present, and this is the kind of information that can help to inform policy in the area."

OUTCOMES

- Evidence that folic acid intakes are most likely sufficient in the elderly population in Ireland.
- Findings that can help to inform policy on fortification.

Adolescent boys view depression in peers negatively

How do children perceive their peers with mental health problems? It depends on how you ask, according to a HRB-funded study, which found that teenage boys tend to have a negative perception of other adolescent boys with depression. Meanwhile, children with mental health problems report being on the receiving end of stigma from their peers.

The study used vignettes and questionnaires to gauge how boys and girls aged between 10 and 16 perceive other children around the same age who have been diagnosed with conditions such as depression or ADHD.

"Based on the questionnaires, the children did not hold very negative attitudes about peers with mental health problems," says Dr Eilis Hennessy from University College Dublin's School of Psychology, who carried out the study with Dr Caroline Heary at NUI Galway. But going beyond the questionnaires revealed an important nuance.

"It's possible that the children knew what is socially acceptable to say on the questionnaire, so we also used a reaction time test to see how quickly they associated positive and negative words with mental health problems," explains Dr Hennessy.

This 'implicit associations test' showed that, unlike adolescent girls, adolescent boys have negative attitudes towards other adolescent boys who are depressed. "If we were to think about intervention, the group that we need to target are adolescent boys and depression," she says.

Meanwhile, children aged 10 to 16 who had been diagnosed with mental health problems perceived stigma not only from their peers but also from adults, the study found. "A lot of them spoke about not telling anyone they had a diagnosis – they would prefer to be seen as badly behaved than that they had ADHD," says Dr Hennessy. "We also have evidence that they may be internalising those negative views of themselves – feeling badly about themselves in line with how they felt other people thought."

OUTCOMES

- Identified that adolescent boys tend to have negative perceptions of male peers with depression – which highlights an area for intervention.
- Found high levels of perceived stigma among adolescents diagnosed with mental health problems.

Chemistry in the air – towards an early-warning system for pollution and health effects

Air quality can have a profound impact on health – and particularly for conditions that affect the lungs such as asthma and allergies. Monitoring air quality means we can deliver early warnings for people likely to be affected, but could there be an easier and cheaper way?

With funding from the HRB, Principal Investigator, Dr Stig Hellebust, and his colleagues, Dr David Healy and Dr Daniel O'Sullivan, explored the possibility of whether monitoring the chemistry of air pollution in real time could more effectively predict when air pollution could cause health problems.

"Currently it's a very slow and expensive process to determine how toxic the particulate matter is," explains Dr Hellebust, who carried out the study at University College Cork. "But it is possible to monitor chemical information more or less in real time – so we wanted to see if it could offer a more rapid approach."

The research reviewed and consolidated results from previous, EPA-funded research carried out at UCC on atmospheric particulate matter in Cork Harbour and its toxicological effects in the lab. And in this dataset he was able to link chemical quality with toxicological response in the cells.

"There was a relationship between the chemical information and the pathological information," says Dr Hellebust. "In our samples there were links between iron and copper and the production of reactive oxygen species in the cells, which indicates the cells are under stress."

"The findings pave the way for developing a real-time chemical pollution monitoring system that could automatically send out early warnings, but that would require more research and collaboration," he explains.

"The next steps would be to target some chemical species that would be suitable for monitoring on a real-time basis, which you can use to create early warning systems."

OUTCOMES

- Proof of concept that the measurable chemical quality of air pollution is linked to toxicological effects.
- Paves the way for a real-time chemical monitoring and alarm system for air quality linked to potential health conditions.

Smoking by numbers – vulnerable communities in Ireland

In March 2004, Ireland blazed its way into the tobacco control history books by implementing a 'smoking ban' in the workplace. Yet despite the cleaner air, around 5,750 people die in Ireland each year from smoking-related diseases.

To help inform further education and tobacco control in Ireland, Dr Zubair Kabir collected and analysed data on smoking rates among vulnerable groups in Ireland, and he also looked at the impact of the smoking ban on growth restriction in pregnancy.

"As we develop more comprehensive smoke-free policies, it's more likely that the gap which already exists between the general population and more vulnerable communities will widen," explains Dr Kabir, who is a Senior Lecturer at the Department of Epidemiology & Public Health in University College Cork.

His HRB-funded research, conducted in the Tobacco Free Research Institute Ireland, found that Polish, gay and lesbian communities in Ireland have around double the rates of smoking compared to the general population and Muslims in Ireland, and that around half of schoolchildren in Ireland are exposed to second-hand smoke in the home.

However there's good news too: Dr Kabir found that within just a month of the smoking ban being implemented, the number of small-for-gestational-age babies born in Ireland fell by around five per cent.

The data will help to inform more nuanced and culturally aware education and tobacco-control policies in Ireland, according to Dr Kabir.

"Smoke-free homes, smoke-free vehicles and culturally-sensitive targeted anti-smoking interventions must help narrowing the gap in smoking rates within vulnerable populations in Ireland," he says.

OUTCOMES

- The smoking ban had a rapid and positive impact on pregnancy complications in Ireland.
- Identified vulnerable communities in Ireland with high rates of smoking and exposure to tobacco smoke.

A model to address more efficient provision of wheelchair services in Ireland

Wheelchairs are essential for those who use them – if a wheelchair is not available or working properly, it can have a major impact on the person's health and wellbeing.

A HRB-funded study – in partnership with SeatTech, Enable Ireland (as the host organisation) and the University of Limerick – has worked with key stakeholders to identify system improvements and to develop a strategy for more efficient provision of wheelchair services.

"Everyone wants to provide or receive the best wheelchair services possible, as a wheelchair cannot be replaced by the assistance of another human being, it is essential," says Dr Rosemary Joan Gowran, a Lecturer in Occupational Therapy at the University of Limerick, who carried out the study. "The use of a wheelchair is not just about mobility from A to B, it can impact a person's ability to sit up, breathe, swallow and communicate, and getting the best service affects every aspect of a person's life, this is a human rights issue."

The study brought together 35 stakeholders, including service users, service providers, healthcare professionals, clinical engineers, administrators, suppliers, manufacturers, regulators and policy makers. "Working together and sharing a real understanding of the issues in order to take effective action was a key aspect of this study," says Dr Gowran.

Their discussions highlighted bottlenecks across the wheelchair provision process, such as access to services, waiting times, funding streams, device regulation and emergency services.

A series of workshops involving stakeholders also explored the feasibility for change to meet people's needs throughout their lifetime, an example being to implement regulated out-of-hours wheelchair repair and emergency services.

"The study resulted in a strategy document for more sustainable wheelchair and seating provision, as well as a model to review and, in turn, inform policy for wheelchair and seating provision in Ireland and internationally as part of larger studies in the future," explains Dr Gowran.

OUTCOMES

- Brought together stakeholders in wheelchair and seating provision in Ireland.
- A strategy document for sustainable wheelchair and seating provision and a model to address sustainable healthcare provision in context.

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