

# A PICTURE OF HEALTH 2008

A selection of outcomes from HRB funded research



Improving people's health through research and information



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**Published by:**

Health Research Board  
73 Lower Baggot Street  
Dublin 2  
Ireland

**t** +353 1 234 5000  
**f** +353 1 613 0337  
**e** [pictureofhealth@hrb.ie](mailto:pictureofhealth@hrb.ie)  
**w** [www.hrb.ie](http://www.hrb.ie)

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# Acknowledgements

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The images for this publication were sourced primarily from Getty Images and iStock photo.





**BETTER HEALTH  
RESEARCH  
MEANS BETTER  
HEALTH CARE**



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# Foreword



Better health research means better health care – *A Picture of Health* illustrates this concept well. This book showcases some of the latest advances in Irish health research funded by the Health Research Board and demonstrates how these investments deliver real benefits to improve people’s health as well as the care they receive.

We are all aware that research and development transforms our lives. However, people don’t always make the link between research and the health care they receive, so it remains an ‘unseen force’. The HRB currently has €180 million worth of investments in the Irish research system. Through our funding, we want to boost and drive innovation in Irish health care. We do this by focusing on building people’s research skills, underpinning innovative programmes of research and developing strong infrastructure networks which provide the environment in which the researchers can conduct their work.

Research can take time, but it brings great rewards. In health care we see these rewards in the form of more effective treatments, preventative medicines, new approaches to health care and decisions made on solid evidence.

We discovered in the past year that a quarter of Irish people did not know that health research even took place in Ireland. Many people also said there was not sufficient promotion of the research done in Ireland. We hope that *A Picture of Health* will help spread the message that we carry out a lot of top class health research in Ireland and that it is delivering real results.



**Enda Connolly**  
Chief Executive – Health Research Board

# Introduction

## About the HRB

The Health Research Board (HRB) is the lead agency in Ireland supporting and funding health research in Ireland. Our aim is to improve people’s health through research and information. We want to deliver more effective treatments and medicines, provide efficient services, drive innovative new technologies and develop new approaches to health care based on strong evidence.

We can achieve this by providing funding to develop people’s research skills and capability, to support innovative projects and programmes and to build a strong infrastructure network that will underpin a robust health research environment. This, in turn, will help to attract and retain the best health professionals, deliver efficiencies in the health system and contribute to our knowledge economy.

With an annual budget of approximately €50 million and a total research investment portfolio of over €180 million throughout the Irish research system, the HRB is leading the step change in health research. We are strongly committed to communicating the outcomes and impact of our funded research to a wide audience. One of the ways we do this is through our annual *A Picture of Health* publication.

## About *A Picture of Health*

*A Picture of Health* is a snapshot of just some of the latest outcomes from research funded by the HRB. It is written for non-technical audiences with an interest in health research. In 2007 a total of 68 projects reported the results and outcomes of their HRB funded research. *A Picture of Health* features just 17 of these projects, but it still reflects the research of 50 researchers from 13 hospitals and academic institutions throughout Ireland.

To find out more about the HRB and the research funding opportunities we have available, or to view previous editions of *A Picture of Health*, please visit our website at [www.hrb.ie/researchstrategyandfunding](http://www.hrb.ie/researchstrategyandfunding)



## Antioxidants for snoring disease?

**S**NORING CAN BE INFURIATING FOR THOSE who have to listen to it. But did you know it can also be a major health problem? Many cases of snoring are actually a disorder called obstructive sleep apnoea (OSA) which is marked by interrupted breathing (apnoea) during sleep. A weakness of the upper airway muscles means they fail to oppose the sucking pressure when someone breathes in,

leading to a temporary collapse of the airway. This failure causes intermittent reductions in blood oxygen levels (hypoxia) which can damage the heart and brain. Although people with OSA often snore, some do not (and not all snorers have OSA).

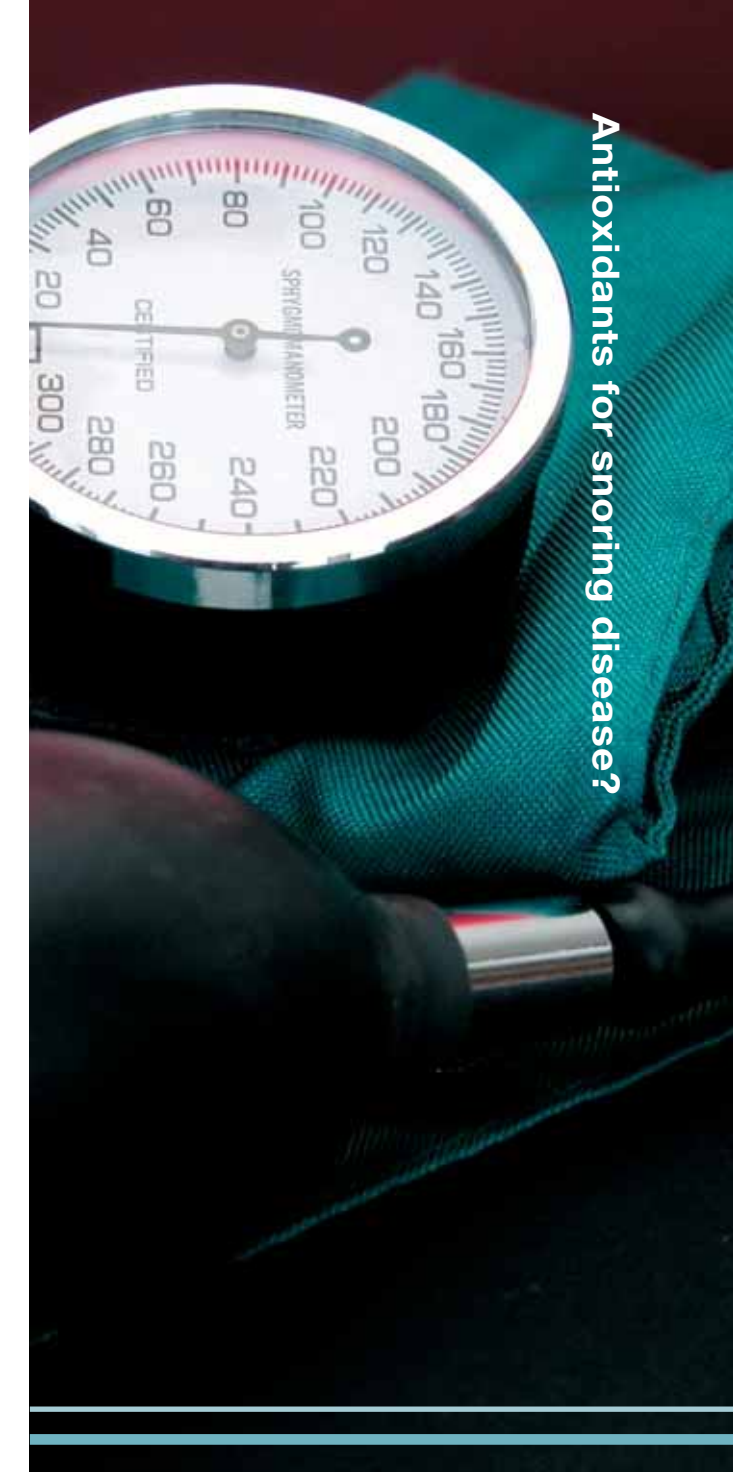
‘We are very interested in the function of the upper airway muscles in obstructive sleep

apnoea and why they are failing to keep the airway open,’ says Professor Aidan Bradford, Department of Physiology and Medical Physics, Royal College of Surgeons in Ireland.

His team, in collaboration with Dr Ken O’Halloran in University College Dublin, has already created a lab model which mimics many features of human OSA, such as having high blood pressure, high haemoglobin and, importantly, intermittent hypoxia. ‘We developed a technique for changing the level of oxygen very quickly – twice a minute – because we specifically wanted to model sleep apnoea,’ explains Bradford. They have already found that intermittent hypoxia reduces upper airway muscle endurance and impairs the upper airway reflex responses coming from the brain. In other words, hypoxia may actually make OSA worse, trapping the patient in a downward spiral which is likely to impair their long-term health. The researchers focused on the possibility that oxidative stress was playing a part in the upper airway damage in OSA. Oxygen is essential to life - but its biochemical reactions in cells can lead to

toxic by-products and a state called oxidative stress which damages tissues and plays a role in many chronic diseases – including, perhaps, OSA.

To test the oxidative stress idea, Bradford used prooxidants and antioxidants in experiments with the OSA model. Prooxidants increased the damage done by intermittent hypoxia, while antioxidants decreased it. ‘We would suggest that antioxidant therapy might be beneficial in patients with obstructive sleep apnoea by, among other things, helping to keep the airways open during sleep,’ says Bradford. Of course, this has not been tested in humans yet. But antioxidants, such as vitamins C and E, are readily available in fresh fruit and vegetables (or in supplement form). Beating OSA – and maybe even snoring – could be another benefit of a healthy diet.



Antioxidants for snoring disease?





## Healing with honey

**T**HERE MAY BE A NATURAL WAY OF HEALING painful ulcers on the leg. Up to 2% of the population is affected by leg ulcers and healing fails in around half of these cases. Georgina Gethin, a specialist wound care nurse at the Royal College of Surgeons in Ireland runs a clinic for patients with complex chronic wounds. ‘This is a challenging group to nurse because they are running out of

treatment options,’ she explains. In 2003, some patients heard that manuka honey could heal chronic ulcers and asked Gethin to give it a try.

‘We wanted to set ourselves an extra challenge, so we selected a sub-group whose wounds had at least 50% dead tissue,’ she says. The aim of the study was to find out

not just if honey could heal the ulcers, but also how – thereby shedding new light on the pathology of these wounds.

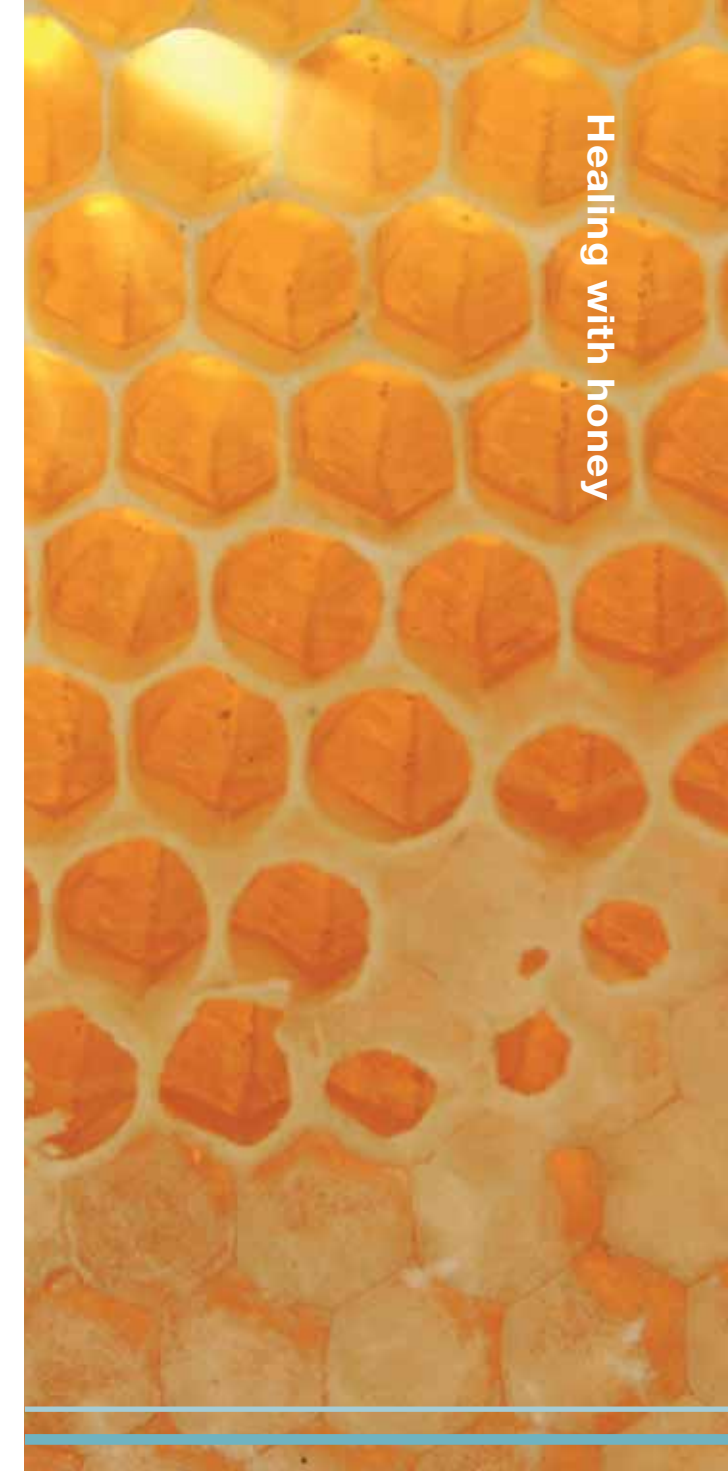
In the first clinical trial of its kind, 108 patients received either manuka honey or standard hydrogel treatment. At four weeks, those in the honey group had more dead tissue removed than those in the hydrogel group. Removal of dead tissue, which can harbour infection, was linked to decreased wound size. At 12 weeks, the wounds of those treated with honey were more likely to be healed than those treated with hydrogel. Where more than half of the dead tissue had gone, healing was over three times more likely, compared to where less had gone. Moreover, 16 of the wounds were infected with the much-feared and hard-to-treat methicillin resistant *Staphylococcus aureus* (MRSA) infection. Honey eradicated it in 70% of cases, compared to only 16% with hydrogel.

The researchers also found that honey, which is acidic, made the wound measurably less alkaline and reduced the level of tissue-

destroying proteins in wound fluid. This, in turn, led to a measurable reduction in wound size. ‘No-one has ever measured this before,’ says Gethin.

Manuka honey is now available as a medical therapy for wound treatment. It increases the options available to patients with chronic ulcers and Gethin’s work provides a new level of evidence for its use. But don’t go out and buy your own – it must be medical grade honey which is sterile and safe to use.

“The aim of the study was to find out not just if honey could heal the ulcers, but also how – thereby shedding new light on the pathology of these wounds”







## Exercise keeps the brain young

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### S THE BRAIN AGES, CHANGES HAPPEN

which can result in memory loss and maybe even dementia. Current research focuses upon the hippocampus, a brain region which is particularly vulnerable to ageing. 'We know the hippocampus is involved in learning and memory. Damage to the hippocampus can impact on the ability to form new memories, and lead to memory loss,' says Dr Áine Kelly,

Senior Lecturer in Physiology at Trinity College Dublin. She has been looking at whether exercise can improve hippocampal function and so protect the brain from degenerative change.

'There is already evidence that older people who have been active through their lives – or take up exercise in their later years – do

better in cognitive tests and have a reduced risk of developing Alzheimer's disease and other forms of dementia,' she says. 'It looks as if exercise is protective in some way – but we do not yet know the cellular mechanisms involved.'

The experiments measured brain activity in rats using both electrical measurements of the hippocampus and also the animals' ability to find a hidden platform in a water maze (the latter being a well-known technique for memory researchers). Young animals tended to do better than older ones in these tests, suggesting superior hippocampal workings. The researchers also looked at a group of proteins called neurotrophins, which act as growth factors, in the animals' brains, to see if these could be linked to the observed age-related differences in hippocampal function.

Then some of the animals were exercised on a treadmill – for an hour a day for a week (similar to mild to moderate exercise in humans). 'We found that learning improved in both younger and older animals after exercise,' says Kelly. They also found an

increase in activity of a neurotrophin called brain-derived neurotrophic factor (BDNF).

Similar experiments involving long-term exercise also demonstrated the benefits of exercise to the hippocampus. 'The take home message is that exercise protects our ability to think, remember and plan,' she concludes. Although the research reveals the importance of BDNF, it is not yet clear how exercise triggers its increased activity. The findings complement recent evidence that exercise can improve neurogenesis – the birth of new cells – in the brain, a relatively recently-discovered phenomenon. Kelly's team now aims to look at neurogenesis through the entire life span and to explore further the role of BDNF in this process. Their work should encourage us all to keep exercising – to keep the brain young.

“Their work should encourage us all to keep exercising – to keep the brain young”



Exercise keeps the brain young





## Cells could help with diabetic blood vessel repair

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IABETES REMAINS THE MOST COMMON cause of blood vessel disease, leading to serious complications like leg ulcers that could require amputation. ‘The aim of our research is to examine why diabetes has such an adverse effect upon blood vessel formation and to find ways to reverse this,’ explains Dr Aaron Yie Loong Liew, of the Regenerative

Medicine Institute (REMEDI), National University of Ireland, Galway. His work involves endothelial progenitor cells (EPCs) which are produced from the bone marrow in response to oxygen deprivation, as often happens in diabetes. These cells aid new blood vessel formation.

‘We have shown that patients with diabetes produce fewer EPCs than healthy people. Furthermore, their EPCs are dysfunctional, which may be why blood vessel repair is delayed,’ Liew says. ‘We have also found that these cells can be genetically modified to carry specific genes without causing an adverse effect on the cells themselves or to the patient.’

Diabetic patients with blood vessel disease are at high risk of needing amputation of the lower limb. The resulting severe disability is a personal tragedy and a huge loss to the economy. Liew’s work suggests that transplantation of the patient’s own EPC’s, genetically-modified, may be a promising new approach to the problem of diabetic blood vessel disease.

**What is diabetes?**  
Diabetes occurs when the sugar (glucose) level in the blood is too high. This happens when the body is not burning up carbohydrates properly due to a defect in the pancreas, the gland that produces insulin. Insulin is the hormone which keeps blood sugar levels within the normal healthy range. Diabetes may be present either when no insulin is made or when insulin is made but not working properly. In Ireland, it is estimated that there are 200,000 people with diabetes and many people in this group don’t know they have it. For more information visit [www.diabetesireland.ie](http://www.diabetesireland.ie)

“Diabetic patients with blood vessel disease are at high risk of needing amputation of the lower limb. The resulting severe disability is a personal tragedy and a huge loss to the economy”



Cells could help with diabetic blood vessel repair





# Getting a hold on Dublin yeast

**Y**EAST, SUCH AS *CANDIDA* SPECIES, ARE actually present in most people's bodies. However, they don't cause any problems in a healthy person, because the immune system keeps them in check. But if cancer, organ transplantation, or AIDS undermine immunity, then a potentially fatal *Candida* infection may take hold. *Candida albicans* is the species most likely to cause one of these so-called

opportunistic infections. However, in 1995, Dr Derek Sullivan and Prof. David Coleman, at the Dublin Dental School and Hospital, Trinity College, found a closely related species as part of a Health Research Board funded project. They named it *Candida dubliniensis* after the city where it was discovered and it is proving a useful tool in understanding yeast infections.

'Yeasts are good at sticking to the host's body tissue and this increases their ability to cause disease,' says Sullivan. The research team is using DNA technologies to find out whether *C. albicans* and *C. dubliniensis* differ in their ability to stick to the host's cells, such as the tissue lining the mouth.

They have already learned that there are four types – known as genotypes – of *C. dubliniensis*. One of these proves to be far more 'sticky' than *C. albicans* – even though the latter is known to be the more likely of the two to cause disease.

'This tells us that the ability to stick may not be the whole story when it comes to understanding why a yeast species is harmful,' says Sullivan. However, the most sticky genotype of *C. dubliniensis* is often associated with mouth and throat infections in people with HIV, although modern antiviral therapy has made this problem less common.

Using high-tech molecular methods, the researchers have identified the proteins responsible for the way *Candida* species stick

to tissue, which opens up the possibility of maybe blocking them to prevent infection.

**What is *Candida* infection?**  
*Candida* infection, also known as candidiasis, candidosis or thrush, is a yeast infection caused by *Candida* species usually *Candida albicans*. *Candida* infections occur in a wide range of human tissues and organs including the skin, mouth, oesophagus, digestive tract, vagina and the blood system. Certain conditions, such as antibiotic use, can disturb the natural balance of microbes in the body and allow an overgrowth of *Candida* to cause thrush.

“Yeasts are good at sticking to the host's body tissue and this increases their ability to cause disease”



Getting a hold on Dublin yeast





# Health inequalities in the spotlight

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RE SOME PEOPLE IN IRELAND MISSING OUT on health care because of the system? There's been a lot of research on health inequalities elsewhere, so Professor Brian Nolan (formerly of the Economic and Social Research Institute, now of University College Dublin) carried out a study Programme to see what is happening here. 'There is a very big gap in our knowledge about how Irish people use

the health service and how it relates to their socio-economic status and other factors,' he explains. 'We wanted to find out if there are structural inequalities in Ireland compared to other countries.'

The ESRI researchers used the latest statistical and analytical tools to 'number crunch' large datasets from household surveys,

working with the University of Ulster to get a comparison between North and South. A key finding was the impact of the medical card on GP visiting. In the South, those in the bottom fifth of the population, according to income, get a medical card and so do not have to pay to visit their GP, while those in the next fifth up must pay. Those in the North, being part of the UK, are covered by the National Health Service where no-one pays. 'People in the bottom fifth income bracket visit the GP more in the South than the North,' says Nolan. 'In the next fifth up, they visit less in the South than in the North. These substantial differences in the pattern of visiting the GP are linked to the peculiarities of the Irish health care system.'

This study could not prove that lack of a medical card deters people from going to the GP (it is hard to get people to admit this). But the ESRI researchers were able to infer this is so by taking the health status of the various groups into account.

The study also revealed significant variation in the efficiency of hospitals across the

Republic. 'Efficiency, put simply, is how good a hospital is at turning its beds and its doctors into the number of patients treated,' explains Nolan. It's not clear why these variations exist, because of the way hospital information systems are currently designed. The discovery suggests these systems must change – so that the reasons why some hospitals are less efficient can be uncovered.

The Programme's findings are not only informing the policy makers – they are also sure to make a major contribution to the ongoing discussion on the future of Ireland's health care system. 'There is a lot of concern at the moment over equality of access to health care,' says Nolan. 'These results will help frame the debate on the direction the health system should go in.'

The full account is given in Nolan B (ed.) (2007) *The Provision and Use of Health Services, Health Inequalities and Health and Social Gain*. Dublin: The Economic and Social Research Institute.







## Improving the lives of Irish children

**K**IDS LOVE TEXTING AND EMAIL, BUT WHEN it comes to their health and wellbeing, nothing beats face-to-face communication and ‘real’ relationships with family, friends and teachers. That’s a key finding from a major new study on Irish children which also reveals how smoking is on the decrease but that many children, especially girls, are dieting even though they are not overweight.

And some children are coming to school, or going to bed hungry because there is no food at home.

The Health Behaviour in School-aged Children (HBSC) study, an international survey into children’s health, which is endorsed by the World Health Organisation, has been running in Ireland since 1994. The Irish HBSC

study investigates health-related issues such as smoking, dieting, watching TV, oral health and injuries among children aged 10-17 years. A unique aspect of this survey is the inclusion of data on social issues around friends, family and school life among children. ‘This kind of national lifestyle study in Ireland can help in taking an evidence-based approach to youth health,’ explains principal investigator Dr Saoirse Nic Gabhainn of the National University of Ireland, Galway. ‘These data can be used in health policy planning and evaluation.’

Nic Gabhainn has made considerable progress in exploiting the HBSC data for policy makers and in distributing it as widely as possible among health professionals, teachers and parents. As well as ensuring the quality of the data, her team looked at some novel issues in children’s health behaviours, such as electronic communications and how they perceive their local community. The role of children in this research is key – not only do they answer the questions, they also help devise them, and they look at the data generated.

Getting the information to those who can use it to make decisions and design interventions is key. A major outcome has been the launch of a dedicated website (<http://www.nuigalway.ie/hbsc>) which includes a set of factsheets about school children in Ireland derived from the HSBC dataset and downloadable by anyone in the country who needs them. This, says Nic Gabhainn, is an important resource. ‘We have to create a sense of ownership of this data,’ she explains. ‘Children gave us this information and we have an ethical imperative to use it to help improve their lives.’

“The role of children in this research is key – not only do they answer the questions, they also help devise them, and they look at the data generated”



Improving the lives of Irish children





## Tackling the antibiotic resistance problem

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NTIBIOTIC RESISTANCE IS AN INCREASINGLY worrying problem. The weapons that scientists have developed, since penicillin, for fighting infection are losing their power. One of the main culprits, when it comes to resistance, is a bug called *Pseudomonas aeruginosa*. It's responsible for many severe hospital-acquired infections among patients with weakened immune systems, and is the

main cause of lung disease in people with cystic fibrosis. The development of multi-drug resistance (MDR) is responsible, in part, for the high mortality associated with these tricky infections. Moreover, *P. aeruginosa* tends to develop into a complex structure called a biofilm which encourages its resistance to antibiotics. The emergence of MDR strains has led doctors to fall back on some of the

older antibiotics, including colistin, a natural defence molecule. Should *P. aeruginosa* now develop resistance to colistin, there will be one fewer weapon in the armoury against this dangerous infection.

‘Antibiotic resistance continues to increase and a clinical priority is to come up with new strategies against it,’ says Fergal O’Gara, Professor of Microbiology and Director of the BIOMERIT Research Centre of UCC. He has been looking at how resistance emerges in the *P. aeruginosa*/colistin combo. Bacteria can accumulate changes called mutations which help them either actively block an antibiotic or develop ways to survive while exposed to it. O’Gara fast-forwarded the process by random mutation of *P. aeruginosa*, looking at variants that showed increased resistance. This identified five types of genes which allowed the microbe to survive better when exposed to colistin. They also looked at how the bacteria responded to very low levels of colistin, which is an emerging interest area, as both hospital and community environments tend to have a ‘background’ level of antibiotics from overprescribing

and people not finishing their courses. The researchers found that low levels of colistin led to activation of a communication system between the microbes, followed by switching on of genes involved in biofilm formation. ‘This data is significant and exciting,’ says O’Gara. ‘The bacteria sense the presence of a stressor in their environment and begin to mount their defence.’

These findings provide possible new targets for combination drug therapies against stubborn infections. They may also influence clinical practice in the way antimicrobial therapies are managed and monitored.

“This data is significant and exciting,’ says O’Gara. ‘The bacteria sense the presence of a stressor in their environment and begin to mount their defence”



## Mapping schizophrenia genes

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CHIZOPHRENIA IS A MAJOR MENTAL ILLNESS, and one which often runs in families. If the genes involved in schizophrenia could only be identified, the prospects for new treatments might become a whole lot brighter. Dr Derek Morris, a Lecturer in the Department of Psychiatry, Trinity College Dublin, is part of the International Schizophrenia Consortium which is working to pinpoint these elusive genes.

We do not know how many schizophrenia genes there are – there could be ten, twenty or even a hundred or more. Each one likely contributes only a small proportion to the total risk of developing schizophrenia and the only way of tracking them down is to work with other international research groups, on samples of thousands of patients. Morris says it’s also essential to take a ‘whole genome’

approach – that is, to search across the entire amount of genetic material (around 30,000 genes) contained in the cell.

The researchers now have high-tech tools like DNA chips, which allow them to put together specialised genetic maps, which record tiny variations between people across the entire genome. They then compare these maps between people with schizophrenia and healthy controls, to determine which genes might be important in the disease.

One of the most interesting genes to come out of this study so far is called Dysbindin which is known to be involved in a major brain chemistry circuit.

People with schizophrenia show a defect in how they process visual signals in the brain – a finding which might be a sign of the disordered thinking that is the hallmark of the disease. ‘We discovered a link between the variation at Dysbindin and this functional effect,’ Morris says, for the dysbindin variant affected performance on tests of visual processing. ‘Our long term goal is to

improve the understanding of the biology of schizophrenia, which will lead to new and more effective treatments for the disease,’ Morris concludes.

### What is schizophrenia?

Schizophrenia is a serious mental illness characterised by disturbances in a person’s thoughts, perceptions, emotions and behaviour. It affects approximately one in every hundred people worldwide and the first onset commonly occurs in adolescence or early adulthood. For more information see the Schizophrenia Ireland website ([www.sirl.ie](http://www.sirl.ie))

“Our long term goal is to improve the understanding of the biology of schizophrenia, which will lead to new and more effective treatments for the disease”





## Modelling a drug user's 'career'

**T**HE MISUSE OF OPIATES, ESPECIALLY HEROIN, in Ireland and around the world creates many problems for the user, their family, and society as a whole. Drug-users report higher levels of mental disease, early school leaving and reduced educational opportunity, homelessness, incarceration and poorer health than non drug-users, says Dr Emma White, of the Economic and Social Research

Institute (ESRI), Dublin. She and Dr Catherine Comiskey of National University of Ireland, Maynooth have adopted a 'brand new' approach to understanding the drug user's 'career'. They see this as the journey from starting drug-use, progress to dependence, the treatment-relapse cycle and, eventually, removal from the drug-using population - that is, giving up drugs for good, or death.

'There is a large and well-acknowledged gap in our knowledge of the drug-user, because we are dealing with a hidden population,' she says. 'However, we believe that drug use in society shares characteristics with epidemic behaviour.'

Epidemiology is the study of the origins and spread of disease. It is a branch of medicine often applied to prevention and treatment of infectious diseases like TB and typhoid (and, more recently, HIV and SARS). But the application of epidemiology to problem drug-use is novel. Mathematical modelling and computer simulation are tools that can be used to ask 'what if?' questions where direct experiments are unethical or impractical. White has used these techniques to apply epidemiology to problem drug-use, looking at populations that were either HIV-positive or HIV-negative.

She found that the new model works for drug-use and, as in any infectious disease, prevention is better than cure. Therefore, relapse to problematic use tends to occur when drug-users in treatment are in contact

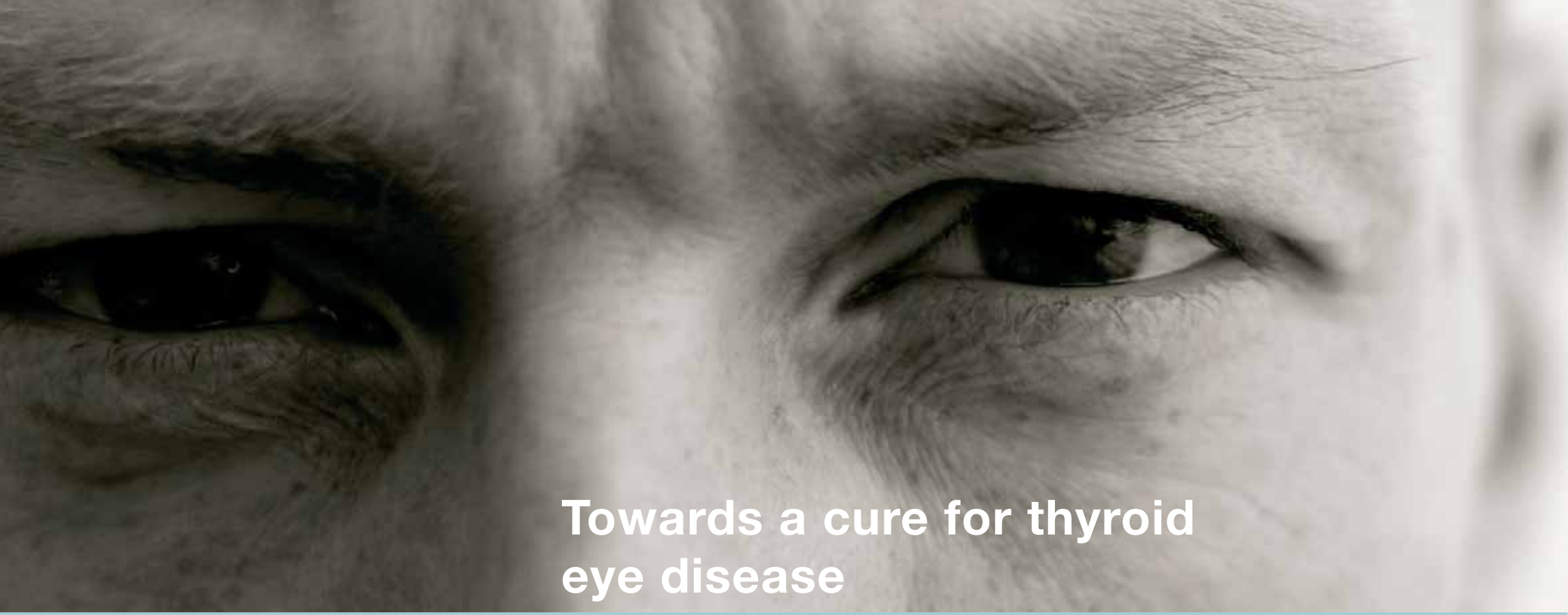
with those who are not. But relapse does not increase the incidence of HIV infection. HIV testing, in or out of a treatment environment, tends to decrease the incidence of HIV infection. These findings suggest that at the start of a drug-use epidemic, efforts are better devoted to preventing its spread, but once an epidemic is established getting people into treatment is very important.

“At the start of a drug-use epidemic, efforts are better devoted to preventing its spread, but once an epidemic is established getting people into treatment is very important”



Modelling a drug user's 'career'





# Towards a cure for thyroid eye disease

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LMOST ONE IN EVERY 50 PEOPLE SUFFERS from a thyroid condition called Graves disease. And half of these will develop thyroid associated ophthalmopathy (TAO), also known as thyroid eye disease, which can cause a painful swelling behind the eyes, protrusion of the eyeball, pain and double vision.

TAO can make people look upset and angry, by causing deep furrows in the brow because of prolonged squinting due to the pain caused by ambient light.

An HRB-funded study has now led to a potential treatment which may provide

relief to patients with TAO. Dr Tom Cawood, formerly of University College Dublin, says: ‘I found it very difficult to be faced with patients with TAO in the endocrine clinic, to get some idea of their distress, yet have very little to offer.’ He teamed up with endocrinologist Dr Donal O’Shea who had some ideas for new treatments for TAO. ‘Whilst we were interested in the pathology of TAO, our main aim was the practical one of trying to bring new treatments a step closer.’ Local consultant surgeon, Mr Paul Moriarty, provided tissue from TAO patients for the research. All three were interested in how smoking makes TAO worse and used that as a starting point for their explorations.

They used a lab model of TAO consisting of fibroblast cells cultured from eye-socket tissue. ‘We also rigged-up a smoking machine so that we could expose our previously happy fibroblasts to the equivalent of a good night out in a Dublin pub, before the smoking ban,’ he says. They found that both cigarette smoke and one of the inflammatory molecules,

interleukin 1, promoted some of the key pathological processes, and the two together had synergistic effects.

Therefore, blocking interleukin 1 might dampen down the disease both directly and by helping prevent cigarette smoke from inflaming the whole process. ‘In a nutshell, we identified a potential new treatment that might help treat thyroid eye disease,’ says Cawood. He adds that the work has led to them setting up a combined ophthalmology/endocrinology clinic, where a co-ordinated approach to TAO can be offered, including the best current treatments but also new treatments, as part of multi-centre clinical trials.

“In a nutshell, we identified a potential new treatment that might help treat thyroid eye disease”







# Heart disease – understanding one of the risk factors

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ATING YOUR GREENS HELPS ENSURE A GOOD intake of folic acid, a B vitamin. One role folic acid plays is lowering levels of a harmful substance called homocysteine in the blood. Elevated homocysteine is a known risk factor for heart disease, deep vein thrombosis and thromboembolism – all conditions involving the formation of unwanted blood clots. ‘Researchers have been interested for a long

time in cardiovascular risk factors,’ says Patrick Collins, Professor of Biochemistry at the Royal College of Surgeons in Ireland. ‘I came across homocysteine and it began to intrigue me because a lot of reports say it increases the tendency of blood to clot, although there is no explanation for this.’ Platelets, a type of red blood cell, start off

the clotting process by sticking together, a process which is linked to a change in shape of molecules on the cell surface called integrins. Once this happens, the integrins bind to a clotting molecule called fibrinogen and this increases platelet stickiness.

Collins focused upon one of the integrin molecules, to see how it interacts with homocysteine at a molecular, cellular and clinical level. He also looked at other aspects of platelet functioning, in the hope of discovering just why homocysteine promotes formation of dangerous blood clots. Collins did a study of platelet function in three groups of individuals with different levels of homocysteine in their blood: (i) a healthy control group (less than 12 homocysteine units), (ii) a group with increased levels (12-50 units) and (iii) a group born with the congenital disease, homocystinuria, (homcysteine up to 300) which is accompanied by a very high risk of heart disease.

Collins found that exposure to homocysteine causes the integrin to change its shape and its molecules started to clump together. Both groups with raised blood levels showed

increased degrees of integrin activation but other aspects of platelet function did not change. ‘It is as if homocysteine can ‘prime’ the integrins so they will more readily bind to fibrinogen given some kind of stimulus,’ he says.

In the short term, it is hoped these findings can offer new hope to patients with homocystinuria in the Children’s Hospital. At the moment, they have no options other than trying to manage the disease with preventive folic acid and aspirin. In the longer term, the goal of this work would be to help the whole population deal better with this potent risk factor for heart disease.

“Elevated homocysteine is a known risk factor for heart disease, deep vein thrombosis and thromboembolism – all conditions involving the formation of unwanted blood clots”



Heart disease – understanding one of the risk factors





## Medics’ attitude to prostate testing impacts cancer figures

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EW CASES OF PROSTATE CANCER ROSE dramatically in the Republic of Ireland between 1994-2000, but did not do so in Northern Ireland. These differences between South and North cannot be explained by our knowledge of the disease. The underlying reason may have more to do with the increased frequency of PSA testing in the South. Men concerned about the risk

of prostate cancer often ask for a PSA test. PSA (prostate specific antigen) is a protein produced by the prostate gland, whose levels may be higher when a man has cancer. However, the role of the PSA test in prostate cancer remains controversial, for it hasn’t yet been shown to reduce mortality from the disease. In Northern Ireland, the UK National Screening Committee recommended that

PSA testing not be used in a routine way for prostate cancer screening. In the Republic, there are no such official guidelines, although the Irish National Cancer Forum also came out against routine PSA testing in 2006.

Dr Frances Drummond, Project Manager at the Irish National Cancer Registry, has been exploring how far attitudes to PSA testing can explain the differences in prostate cancer incidence in the two regions. A positive PSA test may be followed by a biopsy and then diagnosis. ‘In Northern Ireland, there is a registry of all PSA tests and access to data on biopsies. In the Republic, we don’t have this, so we had to find out who was doing testing and which men were having biopsies,’ she explains.

In total, they collected data from over 1.1 million PSA tests and more than 25,000 biopsies, surveyed GPs, urologists and radiologists, and analysed trends from the two national cancer registries. They found a massive increase in PSA testing in the Republic since 1999. GPs, urologists and radiologists here are enthusiastic about

testing – if a man asks for a PSA test, he’ll likely get one and, indeed, the doctor may suggest it. This is far less likely to happen in the North.

Based on this work, new information on PSA testing will now be issued so men can be better informed before opting to have one. ‘The message is that while PSA testing has its place in prostate cancer diagnosis, there is still no evidence that it decreases the rate of prostate cancer mortality,’ says Dr Drummond.

“The message is that while PSA testing has its place in prostate cancer diagnosis, there is still no evidence that it decreases the rate of prostate cancer mortality”



Medics’ attitude to prostate testing impacts cancer figures





# The challenge of community involvement in primary care

**I**NVOLVING THE COMMUNITY IN THE decision-making and delivery side of health care is a popular notion. It seems to sit well with Irish health strategy and policy, which puts the patient at centre stage of the system. And the Primary Care strategy also has a strong focus upon the community angle. ‘There is a lot of interest in community involvement

in health care,’ agrees Fiona O’Reilly of the Royal College of Surgeons in Ireland. But what is the reality? O’Reilly has worked as a researcher in a GP practice in North Inner City Dublin, acting as an observer in both community and marginalised groups in order to see how – and, indeed, if – community involvement works in practice. She found that, despite Dublin’s strong community

infrastructure, patients themselves appear to have little power in the decision-making process. In fact, the conventional authoritarian medical model still rules. ‘There is no shortage of community health activity and some groups are actually funded by the Health Service Executive. But the activity is rather fragmented,’ she says.

O’Reilly worked as an intermediary between a focus group of drug users and health service providers. Doing this, she was able to bring about some important changes for this vulnerable group, including the provision of an outpatient detox instead of lifelong methadone maintenance and the speedy provision of medical cards. O’Reilly’s work has led her to more questions about what community involvement in health care is and how it can really work.

‘The idea of getting people’s voices heard may sound lovely but I would be cautious about taking it at face value,’ she concludes. ‘There needs to be a lot more analysis of the power involved in health care provision and who holds it.’

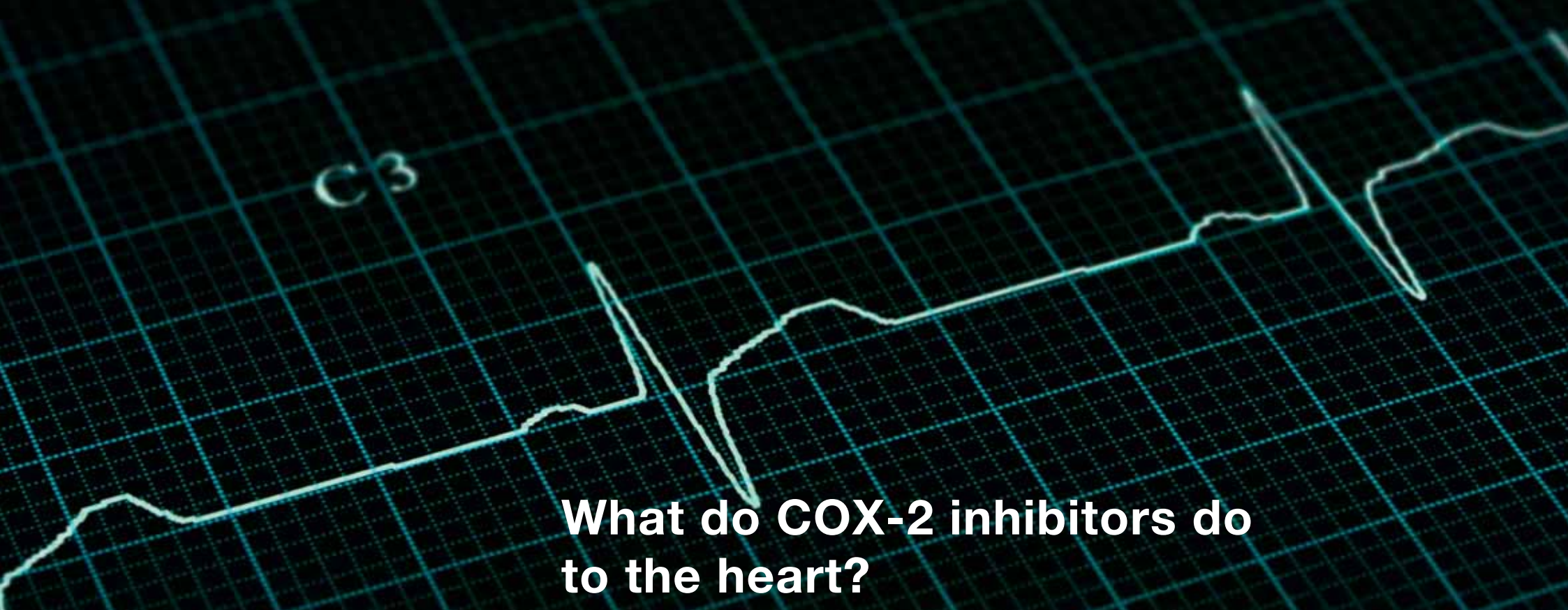
**What is primary care?**  
Primary care is the term for the health services that play a central role in the local community; GPs, pharmacists, dentists and midwives. The services provide first-level contact that is fully accessible by self-referral and have a strong emphasis on working with communities and individuals to improve their health and well-being. Primary care is the first point of contact that people have with the health services and should be available to all people regardless of who they are, where they live, what their income is or what health problems they may have. For more information see the website of The Department of Health and Children ([www.dohc.ie](http://www.dohc.ie))

“There needs to be a lot more analysis of the power involved in health care provision and who holds it”



The challenge of community involvement in primary care





## What do COX-2 inhibitors do to the heart?

**I**N 2004, THE DRUG VIOXX WAS WITHDRAWN from sale after reports that it increases the risk of heart attack and stroke. Vioxx, or rofecoxib, is a type of drug called a COX-2 inhibitor, which is used to relieve pain and inflammation in conditions like arthritis. COX-2 stands for cyclooxygenase-2, the name of the enzyme that Vioxx and similar drugs block. These drugs are sometimes also known

as ‘superaspirins’ because they combine the advantages of aspirin without the drawbacks of stomach upsets and bleeding.

‘The COX-2 inhibitors are controversial,’ says Dr Orina Belton, a researcher at University College Dublin with a longstanding interest in how such drugs work. ‘Clinical trials have shown they do increase the risk of

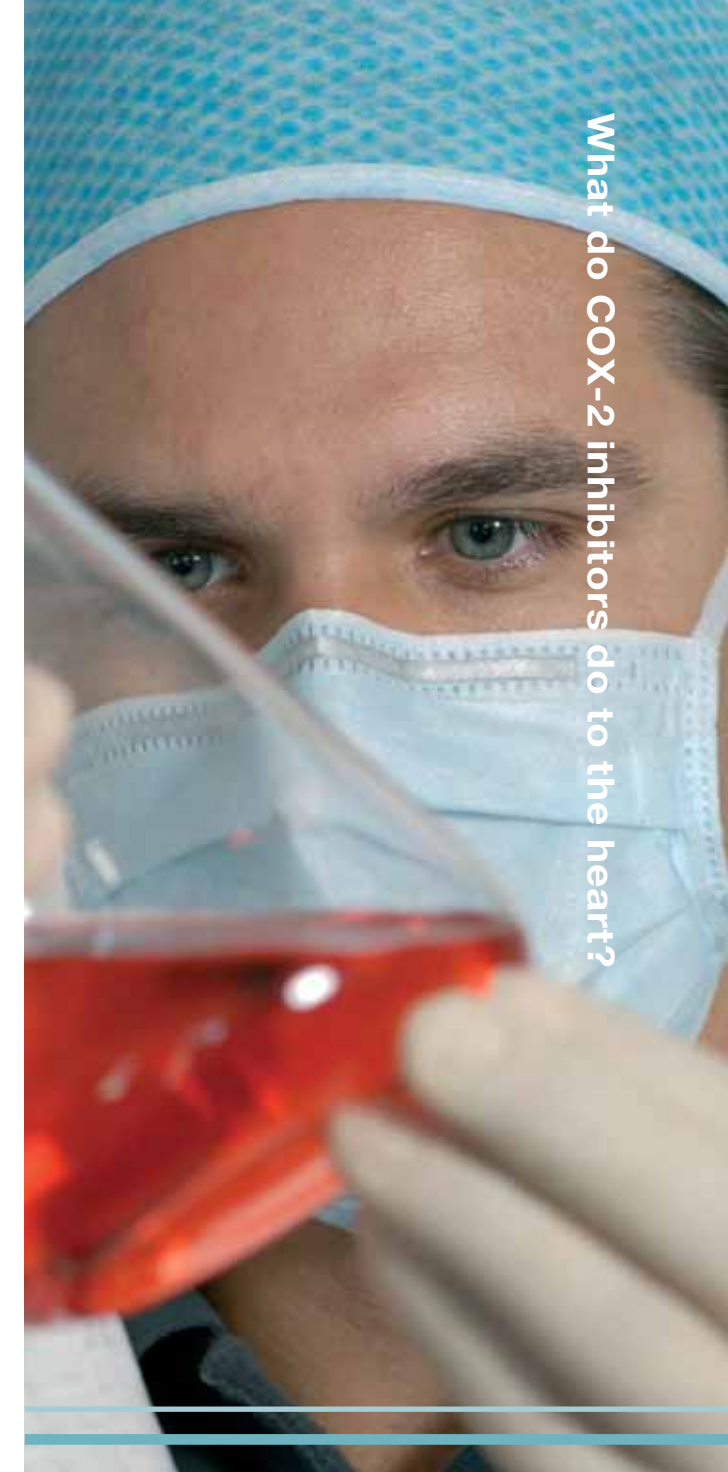
cardiovascular events. But how this occurs has not fully been defined.’ She has been trying to work out the role of the enzyme in vascular disease, and the effects of its inhibitors on the development of vascular disease – that is, the thickening of the blood vessel lining which so often leads to heart attack and stroke. The research focuses on the differences between COX-2 and a related enzyme called COX-1. Aspirin, perhaps the most popular drug of all time, works by preferentially blocking both of them. The COX-1 action of aspirin has an adverse effect on the stomach lining, which can lead to bleeding. Get rid of this, but keep the COX-2 action and you should have a safer, more selective drug. That was the idea, but Belton knows the issue is not this simple. It has proved difficult to separate out the role of these two enzymes in vascular disease using selective inhibitors, but Belton’s team has made an important breakthrough in this respect.

‘We were the first to create animal models of vascular disease in which either one gene or the other is ‘knocked out’ or ‘deleted’,’ she says. Thanks to advances in gene technology, such ‘knock out’ models have become

important tools in the study of disease. Belton’s experiments show that deleting COX-2 has no effect in the early stages of vascular disease. But once vascular disease has progressed, COX-2 deletion makes the problem worse – shedding new light on why those clinical trials showed Vioxx increased heart attack and stroke. ‘We now have very strong evidence that people with heart disease, or at risk of it, should not take COX-2 inhibitors, particularly not long term,’ she says. Short-term use, however, in healthy people – for problems like back or dental pain – may be safe, however, trials to address this must be continued.

“But once vascular disease has progressed, COX-2 deletion makes the problem worse – shedding new light on why those clinical trials showed Vioxx increased heart attack and stroke”

What do COX-2 inhibitors do to the heart?







## Monitoring baby brainwaves

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RESEARCH BASED AT CORK UNIVERSITY  
Maternity Hospital (CUMH) aims to give the most vulnerable members of society – sick newborn babies in intensive care units – a better start in life. Around 10% of all babies delivered require admission to the special care baby unit. Some of these babies are at increased risk of developing seizures or ‘fits’ which, if untreated, may lead to brain

damage or even death. Clinical scientist, Dr Geraldine Boylan, an expert in neonatal neurophysiology, says ‘Babies have immature nervous systems. So they do not have seizures like older children and adults – they do not necessarily jerk or shake.’  
  
She maintains that many seizures in newborns are undetected, putting the baby

at risk of medical difficulties later on in life. The only reliable method of detecting most seizures in this vulnerable group is to record the electrical waveforms from the babies’ brains continually for hours or even days using an EEG (electroencephalogram). But neonatal EEGs require specialist interpreters and these are in very short supply worldwide. The research team in CUMH, which includes neonatologists, nurses and scientists, would like to see neonatal EEGs eventually performed as routinely as the heartbeat and other vital physiological data collection. Dr Sean Connolly at St Vincent’s University Hospital Dublin, an expert in EEG analysis and principal investigator on the HRB-funded project, is working with the team to analyse the EEG data and develop an automated seizure detection system that can be used readily at the cot side.

The initial HRB-funded work has, they say, put CUMH on the international map for its neonatal EEG monitoring expertise. The team has studied a group of 70 high-risk babies admitted to the neonatal intensive care unit over a two-year period to gather

EEG and other data such as heart rate, that could be used to devise an automated seizure detection system. This is now being explored with engineers at University College Cork. The research team has also gathered clinical data from these infants from the outset and has recently received an important new HRB grant to follow these babies up clinically to the age of five years to see if seizures around the time of birth lead to learning difficulties or other problems later in childhood. It is a project that has parents’ wholehearted approval. ‘Parents greatly appreciate the fact that we’re monitoring their babies so closely after a difficult start in life,’ Boylan says.

“Parents greatly appreciate the fact that we’re monitoring their babies so closely after a difficult start in life”



Monitoring baby brainwaves





## Life with lower vision

**D**ID YOU REALISE THAT SOMEONE CARRYING a white stick may still be able to read a newspaper? Most people with a visual impairment have low vision – rather than no vision – but this is not generally recognised. According to Bláithín Gallagher of Queen's University, Belfast, such lack of public understanding can be a big issue for people with visual impairment. 'There has previously

been very little research in Ireland on people with vision impairment as a group,' she says. 'Most work has been on specific diseases, like cataract or age-related macular degeneration. But with an aging population, there will be an increase in the number of people with a visual impairment.'

Gallagher studied how visual impairment

affects a person's quality of life (QOL) and which issues most concern them. A total of 222 people over 60, including both urban and rural residents throughout Ireland, North and South, took part, completing two QOL questionnaires (one vision-specific). One hundred and twenty one others participated in 14 focus groups to further explore issues that were uncovered during the interviews.

QOL was better in the South than in the North, with Dublin residents scoring highest and Belfast residents lowest. A major issue is fear of falling, which affects 73% (with almost one in five being so afraid they will not venture out alone). The study found that more than three of every five participants had experienced a fall related to their visual difficulty and half had been injured in such a fall. Gallagher also notes many small daily problems for this group – such as bus drivers forgetting to tell them when to get off and hazards like street boards and uneven pavements. Many would love to get out more, but are very dependent upon their families for help with this. Staying at home can lead to social isolation, loneliness and depression.

As one participant put it 'The loneliness can be overpowering.'

Only 26% of all interviewed had received mobility training of any kind and only 12% had the full, formal mobility training. Gallagher would like to see this figure a lot higher with more people taking up the offer of training to make the most of residual vision.

People with vision impairment feel there is acceptance and understanding of their condition within their own community, but not in the wider world. And when asked what they'd like to do to change their lives, almost all of them responded that they would like to get their eyesight back.

“A major issue is fear of falling, which affects 73% with almost one in five being so afraid they will not venture out alone”













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