

RESEARCH HORIZONS



In this issue
PUBLIC HEALTH
plus frugal innovation,
egg-sharing and
the future of speech
technology



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Contents Issue 18, May 2012

Research news 3–5

Spotlight: Public health 6–17

Rooted in evidence: a public health response to dementia 6–7

Meliodosis: exposing the 'Great Mimicker' 8–9

The human cost of economic policy 10–11

Unhealthy diet and physical inactivity: understanding these silent killers 12–13

Winds of change for pollution sensing 14

Old enough to know 15

With the people, for the people: applying mental health research 16–17

Intoxicating history 18–19

Preview 20–21

Frugal innovation

Features 22–31

A new dimension to DNA and personalised medicine of the future 22–23

Life is for sharing 24–25

Call of the wired 26–27

Death and the image: an introduction to palliative filmmaking 28–29

Into eternity: the nuclear waste challenge 30

Egg Cetera: Nature's paradoxical packaging 31

The back page 32

Artwork by Anna Betts, Illustrator (www.annabetts.com/), taking inspiration from articles in this issue's Spotlight on public health research related to diet and physical activity, mental health and dementia, clean water, education, pollution, intoxicant addiction, and economic policies.

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Public health



Public health has been described as the organised efforts of society to improve the health and well-being of whole populations. Putting it into practice – such as through cancer screening or vaccination programmes, controlling tobacco consumption or encouraging healthy behaviour – has had major impacts worldwide, resulting in longer, healthier lives.

Its success is clearly related to the availability and progress of medical interventions. But it's also related to innovations in agriculture, architecture and engineering, and a deeper understanding of the social science of behaviour and many other areas. Public health is a truly multidisciplinary undertaking, which is why in Cambridge we have recently created PublicHealth@Cambridge, a Strategic Network that draws together 300 researchers from the arts, humanities, social sciences, technology and biomedicine who have an interest in public health (and some of whom feature in this issue of *Research Horizons*).

The need for public health research is as great as it ever was. Longer life means a rise in dementia and other diseases associated with ageing. The emergence of epidemics of non-communicable disorders such as cardiovascular disease, cancer, chronic lung diseases and diabetes, which kill three in five people worldwide, pose challenges in the developed and developing world alike. And, re-emerging communicable diseases, resistance and the role of infection in chronic diseases are also public health concerns.

The cost of making poor decisions about public health will have profound consequences and necessitates some tough questions to be asked: can we alter health outcomes by influencing whole societal structural change? How should investment in prevention be balanced with investment in treatment? How, and based on what evidence, do we implement new technologies? Will health systems provide affordable care for everyone everywhere?

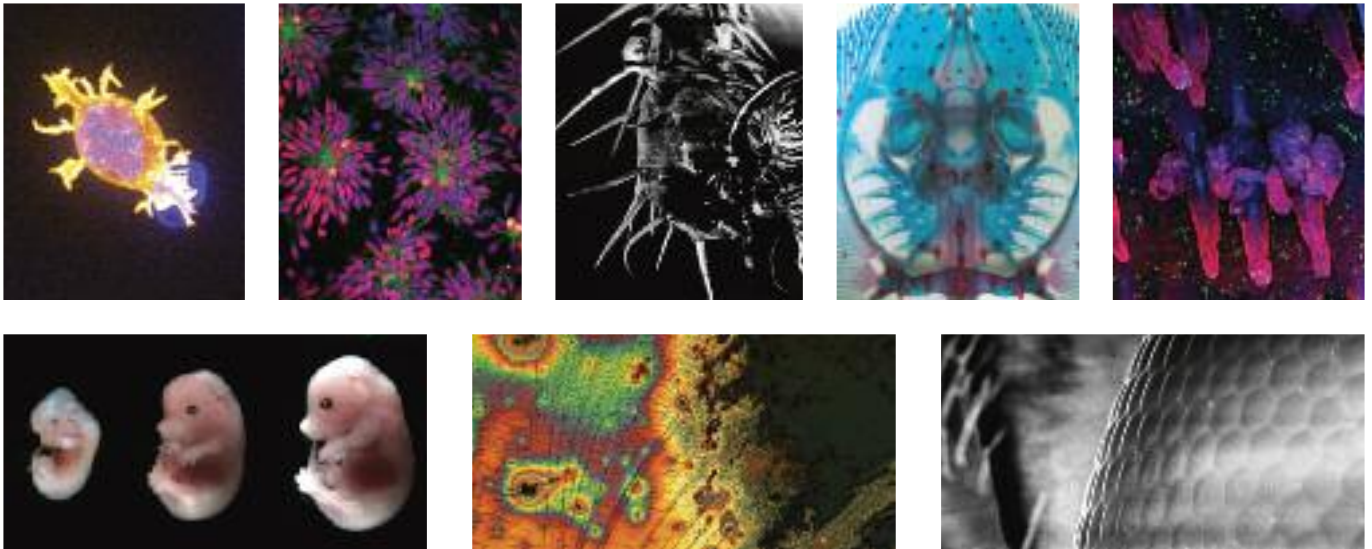
Add to this the manifold changes taking place in English public health services and research, as the government sets out its vision for improving well-being across the whole population, it's as critical to ensure that we draw on a rich mix of disciplines to inform public health as it is to align research to health, social care and commissioning provision.

Our vision for PublicHealth@Cambridge is to develop synergy across Cambridge in areas of public health importance such as international health, social and behavioural science and methodological advances. By co-ordinating research and activities, kick-starting new approaches and new programmes – from molecule to policy making, regional to global, campus to community – we aim to generate fresh insight into the health and well-being of populations.

Professor Carol Brayne, Director of the Cambridge Institute of Public Health and Chair of the PublicHealth@Cambridge Strategic Network

A million views under the microscope

A series of bite-sized videos that show glimpses of the natural and man-made world in stunning close-up has been watched over a million times.



Videos and images created by University of Cambridge researchers across the fields of science and technology are featured in a series called 'Under the Microscope'. Available on the University's YouTube site, the series of 16 films highlights the amazing world that can be found at microscopic level – from fruit fly guts to nanowires, liquid crystals to daisies – and have collectively garnered over 1 million views online since release began in January.

Produced by award-winning filmmaker Patrick Chadwick at the University's Office of

External Affairs and Communications, the engaging one-minute films are each accompanied by a 30-second explanation by the researchers, telling the story behind the imagery.

'Under the Microscope', which has been run in collaboration with Io9, one of the most popular science and technology blogs, includes the most-watched film to date on the University's YouTube channel. The film, featuring the research of Professor Gillian Griffiths and PhD student Alex Ritter at the Cambridge Institute for Medical Research,

shows a killer T-cell of the immune system attacking a cancer cell.

"Online channels like YouTube and Vimeo provide a great way of presenting these beautiful microscopic images to wide and diverse audiences," explained Chadwick. "The project has also given some of the early career researchers here at the University a chance to show off their fascinating work."

To view the whole series, visit www.youtube.com/user/cambridgeuniversity

Strengthening the bond between policy and science

Policy makers and scientists have come together to create a new science-policy research agenda.

One only has to be reminded of the BSE crisis and the MMR vaccine scare to recognise the importance of having policy informed by the best available science. Now, a collaboration of over 50 academics and policy makers from around the world have come together to agree a new research agenda on the role of science in public policy.

The importance of using science for public policy has long been recognised, but recent years have seen a growing debate over how this is best achieved. 'Evidence-based policy' has become the desired norm, and this has led to a greater embedding of scientists alongside other specialists in public policy. Nevertheless, relations between science and policy periodically erupt into controversy.

The aim of this project was to identify key questions which, if addressed through focused research, could both answer important theoretical challenges and also improve the mutual understanding and

effectiveness of those who work at the interface of science and policy.

Professor William Sutherland, from the Department of Zoology, working with the University's Centre for Science and Policy (CSaP), convened a unique workshop that brought together 52 leading scientists and policy makers to agree a new research agenda. They came from a wide range of academic disciplines (including the physical, biological, environmental, medical and social sciences) as well as government, NGOs and industry.

Explaining the significance of the research, Sutherland said: "When public policy is supported by scientifically sound evidence, it is to the benefit of all of society. In order to strengthen the relationship between science and policy, we have, for the first time, compiled a clear set of research questions on scientific advice to governments."

The final questions include an examination of how the design of scientific advisory systems affects policy outcomes,

whether making science advice more transparent has improved its quality, and how to ensure early identification of policy issues that require scientific advice.

Dr Miles Parker, Director of Science at Defra, said: "As a science adviser to government, I want to know 'what works' when it comes to ensuring that sound evidence informs public policy. This collaborative, multidisciplinary approach to devising a research agenda was very worthwhile."

Dr Robert Doubleday, Head of Research at CSaP, added: "This is a critically important step as too often in the past there has been a serious disconnect between the theory and practice of science policy. This paper will help overcome this gap. At CSaP we are committed to assessing progress made towards addressing these questions."

For more information, please see the findings published in *PLoS ONE*, March 2012, Vol.7, e31824.

Mission to map the Milky Way

A three-dimensional map of over a billion stars in the Milky Way is to be created by a pan-European consortium in which the University of Cambridge is a leading partner.

The next major European Space Agency (ESA) satellite, Gaia, which will orbit the Sun at a distance 1.5 million km from Earth, is due for launch in August 2013. It's been hailed as a transformative mission: the premier astronomy space mission of the decade, and the first to deliver an extraordinarily precise census of the Milky Way, in three dimensions.

A team based at the University's Institute of Astronomy (IoA) will play a key role in the Europe-wide effort by taking responsibility for processing and releasing all the imaging data sent back to Earth by the satellite. Gaia is one of the most important current space projects for the UK, which has won approximately €80 million of contracts from ESA to build the spacecraft.

"As Gaia slowly spins, it will create a billion-pixel video of the Milky Way, watching

everything move, and deducing what is there, and where it is," explained Professor Gerry Gilmore, from the IoA and the UK Principal Investigator for all UK involvement in the mission. "On its five-year mission, Gaia will produce a vast amount of information – almost inconceivable in its scope."

Gaia is expected to discover a multitude of new objects both within our solar system – including brown dwarfs and white dwarfs, supernovae and extra-solar planets – as well as probe the distribution of dark matter and map over 500,000 quasars in the Universe.

Remarkably, its two optical telescopes are capable of measuring the positions of celestial objects to an accuracy of up to 10 microarcseconds, comparable to the diameter of a human hair at a distance of 1000 km. To determine the properties of stars, Gaia will also split their emitted light into a spectrum before communicating the data back to Earth.

Dr Floor van Leeuwen, also based at the IoA, is project manager and co-ordinator of the consortium that will process the Gaia photometric data, which involves 60 scientists across Europe of the 400 in total in the Gaia project. "We installed our major computer processing capability last month, supported by a special £750,000 grant from the UK Space Agency, which provides our funding support," he said.



Artist's impression of the Gaia satellite

Added Gilmore: "By creating a precise 3D chart of our galaxy, Gaia will help scientists understand an enormous range of complexities related to its origin, structure and evolution, as well as answer some fundamental questions such as the structure of space-time."

For more information, please contact Professor Gerry Gilmore (gil@ast.cam.ac.uk) or visit www.esa.int/esaSC/120377_index_0_m.html

New test to detect arsenic contamination in drinking water

An economical and easy-to-use biosensor could reduce the chance of being poisoned by arsenic – a common contaminant of wells in parts of Asia.



Pigments expressed by bacteria

Arsenic is one of the most common elements on Earth and is present as arsenic salts in all water. The World Health Organization sets the safe level for arsenic in drinking water at 10 parts per billion. From the Himalayas to Southeast Asia, arsenic levels in drinking water can be more than 10 times that amount, yet the wells are rarely tested. The problem has been termed "the largest mass poisoning of a population in history", with calls for a reinvigoration of moribund well-testing campaigns.

For instance, of the more than 400,000 shallow tube wells in Nepal, it is estimated that nearly 10% of them are contaminated

with arsenic, which can cause a variety of health problems, including skin lesions, diseases of the blood vessels of the hands and feet, and cancer of the skin, bladder, kidney and lung.

Several arsenic testing kits are available on the market, but they require expensive machinery to read the outputs, and almost all of them use mercury bromide, which is extremely toxic.

Dr Jim Ajioka from the Department of Pathology, along with Dr Jim Haseloff from the Department of Plant Sciences and colleagues from the University of Edinburgh, has designed a whole-cell arsenic biosensor

that is cheap, non-toxic and easy to use.

Some species of bacteria are natural arsenic biosensors: in the presence of less than 10 parts per billion of arsenic, they initiate the production of enzymes and an efflux pump for the detoxification and removal of arsenic. For the sensor, the team will take the genes that detect arsenic and combine them with bacterial genes that produce coloured pigments. The modified bacteria will turn green when arsenic levels are safe, and purple when arsenic levels are unsafe. The test uses a harmless strain of the soil-dwelling bacterium *Bacillus subtilis*, which poses no threat to human health or the environment.

The extremely simple visual output combined with the low cost (estimated at around \$0.50 per test) and the lack of need for any expensive monitoring equipment make the whole-cell arsenic biosensor ideal for use in the rural areas where arsenic contamination of drinking water is widespread.

With the assistance of Cambridge Enterprise, the University's commercialisation arm, the team has received a translational grant from the Wellcome Trust. It is anticipated that a functioning device can be built within the next 18–24 months, with field testing to follow.

For more information, please contact Dr Rachel Atfield at Cambridge Enterprise (rachel.atfield@enterprise.cam.ac.uk).

New Centre for Carbon Reduction in Chemical Technology

The University of Cambridge and the National Research Foundation, Singapore, have announced plans for a collaborative research centre specialising in energy-efficient, low-carbon chemical process technology.

As world energy demand rises, finding more energy-efficient ways to produce chemicals will be a critical area of global concern in the decades to come, but the need to cut carbon emissions has also become more pressing.

The new Centre for Carbon Reduction in Chemical Technology, which will be based in Singapore as part of its international Campus for Research Excellence and Technological Enterprise (CREATE), will focus on minimising the carbon footprint of industrial-scale chemical processes.

In particular, the Centre will examine ways of improving energy efficiency, and explore strategies for carbon capture and use in the petrochemical and refining technologies. In a wider context, the assessment and abatement of the carbon footprint of the integrated petrochemical plants and electrical network on Jurong Island in Singapore will be addressed.

The CREATE campus brings together top universities to develop world-leading research projects on issues of global importance. The new Centre will aim to become an 'innovation hub', involving researchers from the University of Cambridge and two partner institutions, the Nanyang Technological University (NTU) and the National University of Singapore (NUS).

Professor Sir Leszek Borysiewicz, Vice-Chancellor of the University of Cambridge, said: "Energy is a research theme of strategic importance at the University of Cambridge, where we have more than 200 academics working on energy-related projects and strong links with a range of industry partners. The Centre for Carbon Reduction in Chemical Technology is an opportunity to bring our own cutting-edge research into a world-class partnership aimed at helping to secure a low-carbon future."

Rainforest remedy could spell end of dental pain

An ancient Incan toothache remedy – for centuries handed down among an indigenous people in the rainforests of Peru – could revolutionise worldwide dental practice.

The toothache remedy, made from varieties of an Amazonian plant species of *Acmella oleracea* and turned into a gel for medical use, has proved successful during the first two phases of clinical trials and may hasten the end of current reliance on local anaesthetics in dental use and non-steroid anti-inflammatory drugs (NSAIDs) in specific applications.

Cambridge University anthropologist Dr Françoise Barbira Freedman, the first westerner to be invited to live with the Keshwa Lamas in Amazonian Peru, is leading efforts to bring this wholly natural painkiller to the global marketplace as an organic alternative to synthetic painkillers.

In doing so, the spin-out company she has founded, Ampika Ltd, will be run according to strict ethical guidelines. Through Cambridge Enterprise, the University's commercialisation arm, the company will channel a percentage of any future profits back to the Keshwa Lamas community who agreed to share their expertise with her.

The painkiller has shown no known side-effects during the past five years of Phase I and II trials, and Freedman, who has continued to visit and live among the Keshwa Lamas over the past 30 years, is confident the stringent Phase III trials (multi-location trials across a diverse population mix) will be the final hurdle to clear. If successful, Ampika's plan is to bring the product to market in 2014/15.

"This treatment for toothache means we could be looking at the end of some



Acmella oleracea

DR FRANÇOISE BARBIRA FREEDMAN

injections in the dentist's surgery," explained Freedman. "We've had really clear results from the tests so far, particularly for periodontological procedures such as root scaling and planing, and there are many other potential applications."

The Keshwa Lamas' remedy represents the first clinical trial of a natural product in Peru using the International Convention of Clinical Trials, of which Peru is a signatory, the gold-standard for clinical trials that is recognised across the Pacific and Atlantic regions.

Dr Freedman has already been able to channel some early funding to the Keshwa Lamas to help in the creation of a medicinal plant garden to conserve plants and plant knowledge related to women's health and maternity care – with the express aim of preserving wisdom for future generations.

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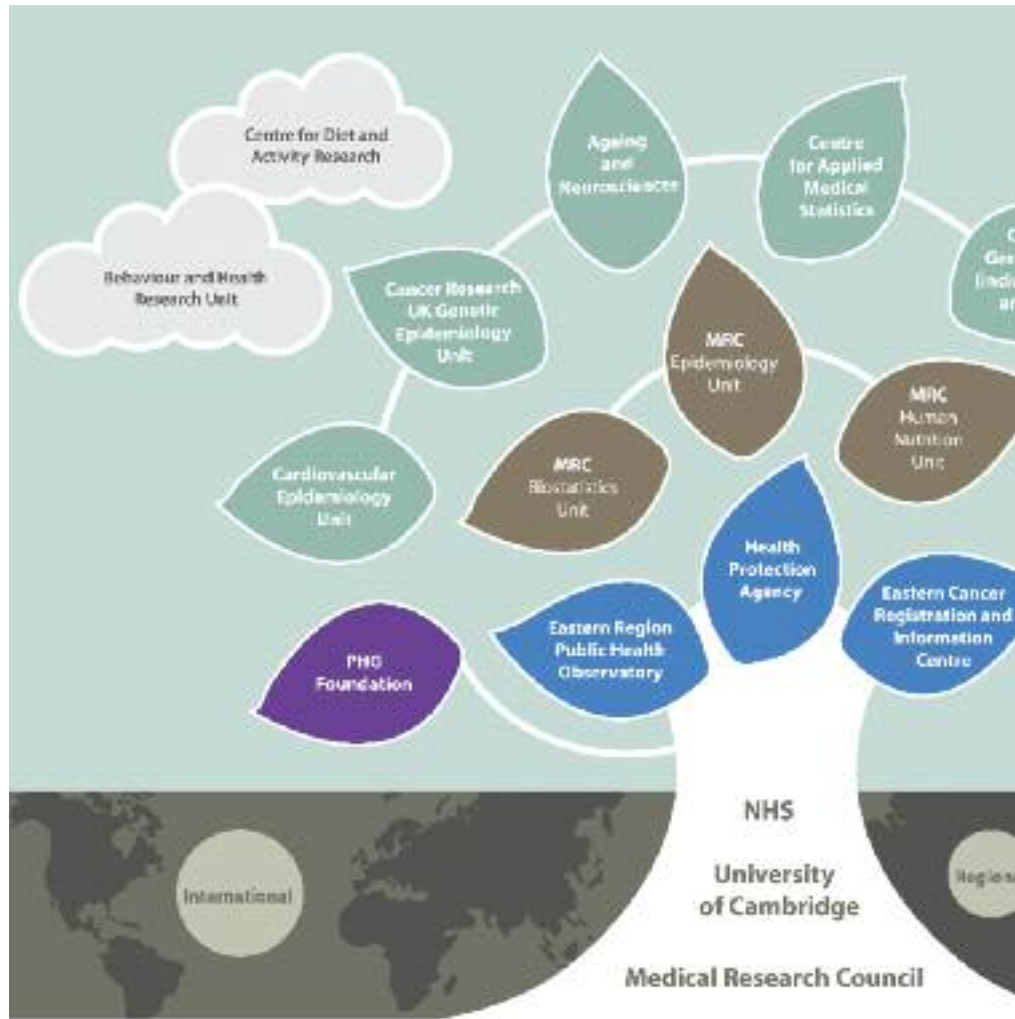
Our Consultancy Services team can connect your company with the expertise you require. For more information, visit www.enterprise.cam.ac.uk/consultancy

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Rooted in evidence: a public health response to dementia

Research programmes at the Cambridge Institute of Public Health focus on common chronic disorders. Currently under the spotlight is dementia and a major new project that will underpin improved prevention, screening and patient care.



Cambridge Institute of Public Health

Today, more than 600,000 people in England are affected by dementia – a progressive and terminal brain disease that, as more people live longer, is predicted to affect twice this number within 30 years. It’s an escalating public health problem that the Department of Health has stated is a national priority.

However, according to a report published by the National Audit Office in 2010, there is too little joined-up working between health and social care services for people with dementia, a situation echoed by Professor Carol Brayne, Director of the Cambridge Institute of Public Health (CIPH): “What patients and families tell us is that there are problems with fragmentation of care for dementia, with not enough information about what’s available and what pattern of services works best.”

Brayne and colleagues within CIPH (see panel), together with collaborators from Cambridgeshire and Peterborough NHS Foundation Trusts and partners from the Cambridge University Health Partnership, realised that a new approach was needed to underpin the delivery of improved dementia care, as well as to further research on dementia screening, treatment and prevention. Their aim is to

build a dementia registry to support both service and research.

Evidence road map

“Until now, not enough of the research evidence cited in dementia guidelines has been generated on the populations to whom the treatments will be applied – the older old, aged 80 and above,” explained Brayne. “This could be resolved by an up-to-date dementia registry based on the systematic collection of all data relating to individual patients with dementia combined with a road map of evidence, both qualitative and quantitative, right the way through from prevention to palliative care.”

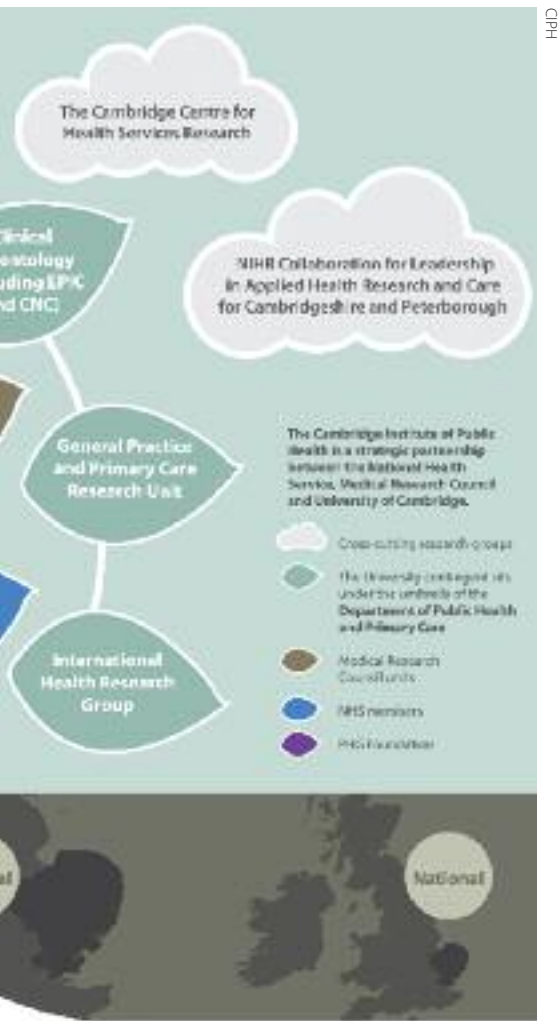
Physicians and public health specialists need accurate and up-to-date data to compare therapies, reduce risks and set standards, and in recent decades registries have become a key part for monitoring illnesses such as cancer, infectious disease and diabetes. Because registries contain information on patient history, diagnosis, treatment and social care, they are valuable not only for making important public health decisions about treatment and co-ordinated care but also for identifying gaps that require further research.

The complex process of designing and delivering a registry for dementia in Cambridgeshire and Peterborough has now

begun. It aims to be the first truly population-based register nationwide to link all services in the area. Developing a registry is not without its challenges, as Brayne, who chairs the steering committee, explained: “There are very important data governance and social and ethical issues to address, including the label itself – not everybody who might meet the criteria for dementia would wish to call themselves demented. It’s a very emotive label and there’s a lot of fear. One of things we want to do is help with destigmatisation.”

After a scoping study commissioned by the Collaboration for Leadership in Applied Health Research and Care for Cambridgeshire and Peterborough (CLAHRC CP, see page 16), work began last year to develop the system and the first phase of the registry is under way, working with primary and secondary care.

Two phases that will sit alongside each other have been planned: one (now in active development) is a care pathway registry to link data directly from GPs relating to various stages in the patients’ journey through inpatients, outpatients, community care and related services; and another will create a research registry of people with dementia who are suitable, and would welcome the opportunity, to participate in research. Both phases have the backing of the National Institute for Health Research (NIHR)



HdH

Cambridge Institute of Public Health

In just 20 years, Cambridge's Institute of Public Health (CIPH) has grown to encompass so many partnerships that a 'tree of life' diagram (see left) is needed to make sense of the Institute's scope. In April it was selected as a member of the National Institute for Health Research School for Public Health Research (NIHR SfPHR).

Through the establishment of large-scale population resources, CIPH's individual partners investigate the influences of genetic and lifestyle factors in chronic diseases and then translate this evidence into the development and evaluation of preventative interventions.

In April this year, CIPH was selected as one of eight leading academic centres to collaborate as part of the new NIHR SfPHR, which will place emphasis on what works practically, can be applied across the whole country and better meets the needs of policy makers, practitioners and the public.

"Public health must connect with all relevant areas affecting health," said Professor Carol Brayne, Director of CIPH. "It's about seeing the large picture by piecing together the component parts. Above all it's about creating, assessing and working out how to implement the best possible evidence.

"Decisions on the shape and content of health services aren't easy," she continued. "Public health can help by providing the distance and independence required, and can then link these to the commissioning of the appropriate services for populations."

CIPH is a strategic partnership between the NHS, the University of Cambridge Department of Public Health and Primary Care, and three Medical Research Council units: the Biostatistics Unit, the Epidemiology Unit and the Human Nutrition Unit. The NHS members are the Eastern Region Public Health Observatory, the Regional Epidemiology Unit of the Health Protection Agency, and the Eastern Cancer Registration and Information Centre. The Foundation for Genomics and Population Health is the first charitable status member of CIPH.

CIPH has also supported several initiatives that span the Institute: the Cambridge Centre for Health Services Research, the Centre for Diet and Activity Research (page 12), the Behaviour and Health Research Unit, and the Collaboration for Leadership in Applied Health Research and Care for Cambridgeshire and Peterborough (page 16).

For more information, please visit www.iph.cam.ac.uk/

Public Health

Dementias and Neurodegenerative Diseases Research Network, which is also actively supporting the development of registers nationwide, and now endorsed through the Prime Minister's Challenge.

"The previous lack of a dementia register across the Cambridgeshire and Peterborough areas has meant there has been limited information for planning services," added Brayne. "Going forward, stakeholders will be able to monitor trends and plan ahead for the ageing population. We hope this initiative will also improve safety and efficacy of day-to-day clinical management for people with dementia, improve outcomes and maximise efficiency."

Data for health

The dementia registry is one element of a more ambitious vision: to integrate data with health care planning and research for a whole range of common chronic diseases "so that doctors have the right information at the right level in front of them, and researchers have the appropriate permission to recruit patients for research studies."

Dementia is a current priority but, long term, what Brayne and colleagues are calling Data4Health Cambridgeshire will draw from CIPH's work on conditions such as cancer, cardiovascular disease, neurodegenerative diseases, osteoporosis and metabolic diseases,

and hope to join this all the way through to local authorities and voluntary sectors. The work of CIPH partners such as the Eastern Region Public Health Observatory and Eastern Cancer Registration and Information Centre will be crucial to push forward health information sharing for care policy and research.

"The key benefit of this approach is that results from world-class researchers are immediately open to the assessment of their impact on a population," explained Brayne. "For instance, for dementia, we have a well-established programme of ageing and neuroscience research across the University. Data4Health will feed into these programmes and be fed by them."

Examples include research in the Biomedical Research Unit in Dementia and the Cambridge Centre for Brain Repair on the molecular basis and potential for screening and treatment of neurodegenerative diseases; research at the Cambridge Centre for Ageing and Neuroscience on how individuals can best retain cognitive abilities into old age; and longitudinal studies, some of which began running in the 1980s, led by Brayne at CIPH and colleagues in the Department of Psychiatry to investigate depression, physical disability and early detection of dementia. In addition, researchers in the Behaviour and Health Research Unit and in the Centre for Diet and Activity Research (see page 12) are

gathering evidence on life-course behaviours that optimise the chance of a healthy old age.

"Crucial to the success of the registry," added Brayne, "is allowing the whole population to become part of the enterprise. They can become more familiar with the benefits of a research and experimental approach to generating knowledge, and ultimately they can seek to drive it themselves – as true partners in the process of public health research and action."



Professor Carol Brayne

For more information, please contact Professor Brayne (cb105@medschl.cam.ac.uk), Director of the Cambridge Institute of Public Health (www.iph.cam.ac.uk/).

Each year melioidosis – a soil-borne disease dubbed the ‘Great Mimicker’ because of its frequent misdiagnosis – kills as many people in some regions of Southeast Asia as does tuberculosis. Now researchers are compiling the first public health guidelines to reduce the incidence of this disease.

Melioidosis: exposing the ‘Great Mimicker’

It is, to quote poet T. S. Eliot, “fear in a handful of dust”. Not an allusion to mortality as the poet himself meant, but a killer that lives in the soil itself.

Melioidosis is caused by *Burkholderia pseudomallei*, a bacterium that resides in the soil of Southeast Asia and northern Australia. In some locales, the number of people who die after developing melioidosis is as high as 40%, and in northeast Thailand it causes as many deaths as does tuberculosis. What makes the disease so menacing is that not only is the bacterium resistant to all but a narrow range of antibiotics but it is also frequently under- or misdiagnosed, with fatal and often rapid consequences.

Yet, according to Cambridge scientist Professor Sharon Peacock, a world expert on melioidosis, this infection and its related deaths are potentially preventable. Not through vaccination (indeed, none exists) but through simple public health measures. “Because individuals acquire infection after contact with soil containing the pathogen, and not from person-to-person contact, it’s potentially avoidable through behavioural changes,” explained Peacock. “Simple guidelines that make people aware of the risks associated with certain activities could ease a major disease burden.”

Although much progress has been made in the past decade towards understanding how the bacterium causes disease, little is known about the global distribution of the bacterium in the environment, and therefore where people (including travellers) are at risk. In addition, the US Centers for Disease Control and Prevention has classified the bacterium as a Category B ‘select agent’ (potential biological weapon). Preparedness against melioidosis in the event of a



Melioidosis can take up to a week to diagnose following culture of the bacterium in a microbiology laboratory

deliberate release has therefore become a security concern.

Peacock has been working in collaboration with a team led by Dr Direk Limmathurotsakul, Deputy Head of Microbiology at the Wellcome Trust Major Overseas Programme in Thailand, to trace the routes of infection for melioidosis. Their aim has been to drive down the incidence of disease by providing the first evidence-based guidelines worldwide for its prevention.

‘Tip of the iceberg’

Although melioidosis was first described in 1911 in Burma, the disease has been little studied over the past century. Not until US soldiers returned home infected with the bacterium after their service in Vietnam did the disease begin to attract attention in the West. Even then, the disease was largely regarded as chronic rather than acute – patients tended to develop symptoms so long after acquiring the infection that it became known as the ‘Vietnamese time bomb’.

Only since the 1970s has melioidosis begun to be taken seriously as a public health threat in Southeast Asia, said Peacock: “It’s been a hidden disease – we’re only really now seeing what many believe is the tip of the iceberg in terms of numbers of people infected.” Under-reporting, she believes, is the consequence both of it taking up to a week to diagnose the disease by culturing the bacterium in a microbiology lab, and of the

scarcity of such diagnostic facilities across the region.

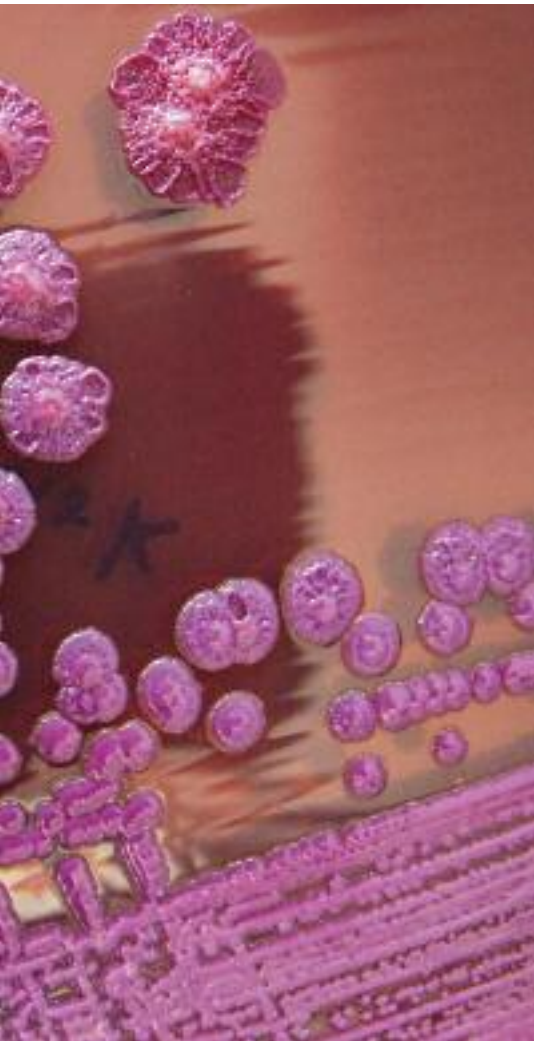
Misdiagnosis is common because melioidosis can cause infected individuals to present with a wide range of clinical manifestations. Unhappily, in the absence of an accurate diagnosis, the specific and long-term antibiotic treatment the patient requires is rarely given, and death occurs swiftly from severe sepsis and associated organ failure. “The single most important objective therefore has to be to prevent people from acquiring the disease in the first place,” asserted Peacock.

Inoculation, ingestion, inhalation?

Peacock, Limmathurotsakul and colleagues have now completed the first prospective hospital-based case-control study in Asia to identify what aspects of daily living put individuals at risk of *B. pseudomallei* infection.

“Current advice in northern Australia, where melioidosis is also common, includes avoiding contact with soil and washing hands and feet. But this is largely based on common sense rather than evidence, and compliance and efficacy are unknown,” explained Peacock, whose research was funded by the Wellcome Trust. “In Asia, no advice is given to people living in melioidosis-endemic areas. A programme of prevention could be relatively inexpensive, readily implementable and applicable to all.”

Over an 18-month period, patients



PROFESSOR SHARON PEACOCK

presenting to hospital with melioidosis were recruited to the study. Using a questionnaire and home visits, the team have been tracing the route of infection – investigating whether disease has resulted from inoculation through abrasions in the skin, ingestion of water and food, or inhalation of aerosols – and using genotyping to define the bacterial strains present in the patients and environment.

“There are major knowledge gaps in Asia regarding the frequency with which water supplies are contaminated with *B. pseudomallei* simply because no-one has looked before,” explained Peacock. “We are also uncertain whether being outside during severe weather could be a risk factor associated with inhalation of the bacterium.”

The results of the research have been collated and a set of guidelines will be developed and disseminated to a network of public health officials. The main recommendations are likely to be to not drink untreated water, to avoid exposure to severe weather, and for agricultural workers to use protective clothing and footwear. Now, Limmathurotsakul and colleagues are developing a public engagement campaign to raise awareness of melioidosis in Thailand.

A previous study by Peacock and colleagues has shown that another strong risk factor for melioidosis is diabetes, which puts individuals at a vastly increased risk of *B. pseudomallei* infection. Given that the prevalence of diabetes is rising in Thailand, an additional aim is to provide public health guidance targeted towards education programmes in diabetic clinics.

from the soil in 1998. Once detected, a study was carried out in the capital and within a few years several hundred cases had been diagnosed.”

“We predict that melioidosis will become recognised as a major pathogen throughout this region in the wake of laboratory strengthening and use of standard guidelines,” she added.

Worldwide, the paucity of information about the geographical distribution of the organism has meant that there is an incomplete global risk map, with vast regions of the world completely unmapped, including Indonesia, India, Africa and most of South America. Peacock and colleagues have initiated an international working party that will facilitate the mapping process. First, however, they had to devise consensus guidelines on how to carry out soil sampling using the simplest and cheapest of techniques, to maximise use in resource-poor settings. Guidelines have now been agreed and the team is in the process of developing a website (www.melioidosis.info/) from which protocols for sampling can be downloaded, and complete data from sampling studies can be deposited to build a global map of the distribution of environmental *B. pseudomallei*.

Melioidosis has recently been described in southern India, and soil-sampling studies are under way there. With the support of the Cambridge-Hamied Visiting Lecture Scheme, Peacock has been working with researchers at Kasturba Medical College, Karnataka, India, to provide practical advice and knowledge on environmental sampling. Local initiatives will enable researchers in the region to monitor, manage and reduce the effects of an emerging infectious disease.

“These initiatives in Thailand and India have the potential to reduce the impact of an emerging infectious disease,” Peacock explained. “While the true incidence of melioidosis is unknown, it is likely that many millions of people are repeatedly exposed to *B. pseudomallei*.”

“It’s been a hidden disease – we’re only really now seeing what many believe is the tip of the iceberg in terms of numbers of people infected.”

Inoculation through skin from soil is one of the most common routes for acquiring the bacterium that causes melioidosis

Thinking globally

The team are now widening their scope to consider other regions of Asia and the world. Melioidosis is known to occur in areas of Southeast Asia such as Laos and Cambodia, but incidence rates are poorly defined and may be grossly underestimated, as Peacock highlighted: “It was very telling that the first time it was realised that melioidosis was in Laos was when the bacterium was cultured



VANAPORN WUTHIEKANUN



Professor Sharon Peacock

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New research will bring social scientists closer to uncovering the economic basis of a “gigantic human catastrophe” that followed the fall of communism in the former Soviet Union.

The human cost of economic policy

As scenes of violence and anger unfolded on the streets of Greece this year, the effects of radical economic change on society became all too evident. Across the European Union, government austerity programmes have been met with public protest against tough public sector cuts and raised taxes aimed at cutting deficits.

Not only do certain economic policies trigger anger and unrest, but they can also have a much deeper effect on society, drastically affecting the health and mortality of ordinary people. This is the conclusion of Cambridge social scientists Dr Lawrence King and Dr David Stuckler, based on a decade of ground-breaking research on the political economy of public health.

Now, a project led by King has commenced that will look in depth at the human health cost of economic policy. The study – the first to look at this on such a scale – will interview 110,000 people across the former Soviet Bloc to understand how rapid privatisation affected the health of individuals, an economic crisis that the researchers describe as a “gigantic human catastrophe”.

Previous studies of the health impact of economic decisions have relied on cross-national analyses at the country level. Although this type of research is crucial, by taking the research to the level of the individual, the new project will generate

decisive evidence on the role of privatisation in the post-communist mortality crisis. “Earlier studies have been a bit like flying on a space shuttle looking down. We want to generate micro-level data to make sure that our correlations are correct,” explained King.

The study follows research by King and Stuckler published in *The Lancet* in 2009 that sought to explain why the former Soviet Union underwent dramatic mortality fluctuations following the fall of communism (see graph). Between 1990 and 1995, an estimated 7 million premature deaths occurred in the countries that emerged from the USSR, rivalling the number of deaths attributed to Stalin’s politically induced famine in 1932–1933. Mortality rates rose by 12.8% in men and life expectancy fell to 64 years in 1994, the lowest level in the post-war period.

“The magnitude of this disaster was completely unexpected,” said King, who has been awarded a five-year European Research Council Advanced Investigator Award to lead the research. “And the puzzle was compounded by the dramatic variation in the mortality experience both within countries as health inequalities emerged and between countries.”

Investigating national-level data, King, Stuckler and Professor Martin McKee, from the London School of Hygiene and Tropical Medicine, previously reported that a greater



“Policies that are being promoted to create a unified global market, if not paired with social policies to protect people, can have negative health outcomes.”

Mass privatisation and adult mortality rates
Belarus and Russia





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Abandoned Russian hospital

speed and scale of mass privatisation, a component of so-called shock therapy, was one root cause of the rise in post-communist mortality rates.

Russia, for instance, pursued a programme designed to achieve super-rapid privatisation of huge sections of the economy by giving vouchers to citizens that could be exchanged for share ownership – creating a class of ‘owners’ overnight and aiming to make the transition to capitalism irreversible. In as little as two years, almost 80% of the industrialised sector of Russia was privatised. By contrast, in countries such as Belarus, privatisation was rare and, where it did occur, the voucher system was not used. The drop in life expectancy in Russia between 1990 and 1994 was twice that observed in Belarus.

“Unemployment and the associated stress translated into increased alcohol abuse and violence, and loss of firm-provided medical care and reduced fiscal spending on health led to decreased access to and quality of health care,” said Stuckler.

Their results attracted much debate in the global media. Critics proposed that factors other than privatisation might correlate with mortality rates and that cross-national data might conceal the true cause. The new study will provide decisive evidence on the debate by adopting a new methodology not previously used in such analyses: using interviews with random

population samples to collect data on the deaths of relatives to estimate the key factors underlying mortality. The study will also examine the importance of occupation and education on mortality, and how this has changed over time.

The research teams led by King and Stuckler have also undertaken several other studies that trace links between economic programmes and health, including the link between the Greek financial crisis and an increase in HIV, heroin use, prostitution, homicides and suicides. Their teams’ work has also assessed the role of economic policies of the International Monetary Fund in the rapid spread of tuberculosis in Eastern Europe and the former Soviet Union; and the role of financial crises worldwide and the transmission and control of infectious diseases.

On the basis of their studies, they argue that political and economic policies and processes can affect the lives of millions. “Economic policies can ‘get under the skin of individuals’ and have a huge impact on public health,” said King. “Not just privatisation but also freeing up markets, austerity programmes and deregulation. Policies that are being promoted to create a unified global market, if not paired with social policies to protect people, can have negative health outcomes. We want to understand why some communities and individuals are more vulnerable than

others to economic upheaval and how governments can plan ahead.”

As Europe remains in the grip of economic hardship and punishing public sector cuts – the societal effects of which might well be felt beyond economic recovery – what steps can be taken to mitigate putting lives at risk through government spending cuts? “Strong social support networks,” said Stuckler. “Putting in place protective social and public health policies during, and in advance of, economic shocks appears to be key to avoiding ordinary people paying the ultimate price.”



Dr Lawrence King (right) and Dr David Stuckler

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Ethical dilemmas and global health

Just as a nation's health can be affected by its economic programmes, global health can be affected when unresolved societal tensions slow down the process of combating disease.

In September 2011, delegates from every country worldwide met at the United Nations (UN) to discuss the worrying global rise in non-communicable diseases (NCDs). NCDs, which include cancer, diabetes, heart disease and chronic lung diseases, are responsible for 63% of deaths annually, with the greatest burden shouldered by developing countries. Although cost-effective health interventions exist, such as tobacco and alcohol legislation, too few countries are implementing measures to a sufficient level.

As the UN prepares to report on the situation at the General Assembly in September 2012, researchers at the University of Cambridge and the London School of Hygiene and Tropical Medicine (LSHTM) have identified four “ethical tensions” that must be resolved to speed-up the process of fighting NCDs globally.

The research led by Drs Sridhar Venkatapuram and David Stuckler reviewed global health documents to map out dilemmas arising from policy approaches involving human rights, social determinants, funding and disease prioritisation. Their research was published recently in the *Bulletin of the World Health Organization*.

“These ethical tensions are not exhaustive or mutually exclusive but provide a framework for debate,” explained Venkatapuram. “The UN declaration is a great step forward but deep ethical tensions are evident in all the regional declarations on NCDs. We must address these issues if we are to move from high-level commitments to effective action.”

Dr Venkatapuram and Dr Stuckler describe their findings in more detail in an article on our website: www.cam.ac.uk/research/discussion/ethical-dilemmas-and-global-health/



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MRC EPIDEMIOLOGY UNIT

Unhealthy diet and physical inactivity: understanding these silent killers

Population-based interventions for tackling unhealthy diet and physical inactivity could save millions of lives. An ambitious research programme is providing evidence for how best to deliver the goal.

Living a healthy lifestyle might seem like common sense, but the environment we live in can make healthy choices more difficult. Whether it's how much access we have to green spaces, the transport we take to work, or our diet, each can have an impact on leading a long and healthy life.

Diet and activity behaviours, together with alcohol and tobacco, are risk factors for the world's fastest growing health epidemic: a group of 'silent killers' that often develop slowly over many years and are known as the non-communicable diseases (NCDs).

NCDs, so-called because they are not transmitted person to person, include diabetes, cardiovascular disease, chronic respiratory disease, cancer and mental health disorders, and are by far the leading global cause of death. Of 57 million deaths recorded worldwide in 2008, NCDs were responsible for 36 million, 80% of which were in low- and middle-income countries. By 2030, the total number of NCD-related deaths could rise to 52 million and result in a cumulative loss in global economic output of \$47 trillion.

The statistics are deeply shocking. But, as Professor Nick Wareham, Director of both the Medical Research Council (MRC) Epidemiology Unit and Cambridge's Centre for Diet and Activity Research (CEDAR), explained there are potential solutions: "Behaviour is a key risk factor for NCDs, often closely connected with biological, environmental and social factors. With a more supportive environment and the right incentives, individuals might be more able to change their behaviour to look after their own health: taking exercise, eating a healthy diet, not smoking and limiting alcohol consumption."

"As well as ensuring that high-risk individuals get the right support, we need effective strategies for targeting whole populations," he added. "The challenge is to

discover what determines the population distribution of health-related behaviours so that we can understand how those distributions can be shifted."

Research in a changing world

CEDAR is intent on building the evidence base on which to move populations in the right direction. Hosted by the Cambridge Institute of Public Health, the Centre is a partnership between the Universities of Cambridge and East Anglia, and the MRC Epidemiology Unit, the MRC Biostatistics Unit and the MRC Human Nutrition Research Unit. Created in 2008, it is one of five UK Public Health Research Centres of Excellence funded with a total of £20 million over five years by the UK Clinical Research Collaboration.

One of the efficiencies of the CEDAR approach is that it enables new studies to be overlaid on the foundations of some remarkably long-running, large-scale epidemiological studies carried out by the University and embedded MRC Units. The European Prospective Investigation of Cancer (EPIC)-Norfolk study, for instance, has been studying 25,000 individuals for almost 20 years to understand not only the connection between diet and cancer but also the factors that are most often present when people stay healthy throughout life. "Many of these factors might be obvious but you actually have to demonstrate their benefit or their risk so that interventions are based on empirical data," explained Wareham.

Measuring the determinants of behaviour and evaluating interventions lie at the heart of the portfolio of projects at CEDAR. One study, SPEEDY, has been focusing on the factors that determine diet and physical activity in childhood and adolescence, a period that shapes behaviours that can last a lifetime. Among the findings of the project, which is funded by the National Prevention



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Previously in Research Horizons...

With the aim of improving the prediction and prevention of common chronic conditions such as cardiovascular disease (CVD) and cancer, some of the largest population studies to date are being analysed by the University's Department of Public Health and Primary Care.

Led by Professor John Danesh, the Department brings together unique expertise in epidemiology, biostatistics, large-scale genetic analysis and public health medicine. The goal is to translate evidence on the role of genetic and lifestyle factors into the development and evaluation of preventative interventions.

Learn more about how two studies – part of the portfolio of research within the Department's Cardiovascular Epidemiology Unit – are helping to understand why CVD is increasing at a greater rate in South Asia than in any other region globally: www.cam.ac.uk/research/features/high-risk-hearts-a-south-asian-epidemic/ ...and how scientists at the Department's Genetic Epidemiology Unit are leading the search for the 'genetic cards' that, together with lifestyle, determine an individual's risk of cancer: www.cam.ac.uk/research/features/cancer-what's-on-the-cards/

"It might be that the biggest influences on the population's diet and activity won't just come from simply urging people to change. Instead, major whole-scale restructuring of the way society operates might be necessary."

Research Initiative (NPRI), is the importance of the 'physical activity friendliness' of the school environment. One, perhaps counter-intuitive, finding is that allowing children to play outside in wet weather during school break times is associated with lower activity levels than keeping them indoors and providing opportunities for physical activity. This has implications for school policies on indoor play and the design of school grounds for wet weather.

Through systematic reviews of the evidence and a new randomised trial, CEDAR and the MRC Epidemiology Unit is also learning about how we can prevent childhood obesity by intervening during infancy. UK surveys have shown that more than one in five children are overweight or obese by the time they start school. "Little research has looked at how best to protect the health of bottle-fed babies, who gain weight rapidly and tend to be at higher risk of childhood obesity," said Wareham. It turns out that many mothers lack information about how best to bottle-feed their babies and mistakes in feed preparation are common. CEDAR has developed a behavioural intervention aimed at parental feeding which is undergoing evaluation in a randomised controlled trial funded by the NPRI.

Some aspects of behaviour are shaped by the environment, including the layout of the buildings we work in or the infrastructure that determines how we travel to work. CEDAR researchers are interested in so-called natural experimental studies, which examine the effects of changes in the environment and policy on physical activity. The Commuting and Health in Cambridge study, funded by the National Institute for Health Research, is assessing whether the provision of new transport infrastructure such as the Cambridgeshire Guided Busway has any effect on travel behaviour and physical activity in the

commuting population. The Busway only opened in summer 2011 but results gathered during the 'before' period are already providing insight into the factors that influence people's travel behaviour.

"It might be that the biggest influences on the population's diet and activity won't just come from simply urging people to change," explained Wareham. "Instead, major whole-scale restructuring of the way society operates might be necessary – from increasing access to green spaces, changing schools' food policies to rethinking the physical structure of road networks."

Capacity, research, translation

Building research capacity is a key aim of CEDAR, and currently 35 researchers with expertise in biostatistics, epidemiology, behavioural science, health economics, health geography and public health nutrition contribute to the work of the Centre. Another aim is to make evidence available in a form that is most usable to policy makers, through physical products such as evidence briefs and evaluation toolkits, and through developing relationships in policy and practice arenas.

Helping to facilitate the translation of research to policy, CEDAR works closely with the Eastern Region Public Health Observatory, which provides information, data and intelligence on people's health and health care for practitioners, policy makers and the wider community.

Some CEDAR investigators also work as part of the newly formed Behaviour and Health Research Unit (BHRU), which is funded by the Department of Health Policy Research Programme to contribute evidence on effective ways of changing behaviour in populations to improve health and reduce health inequalities. Policy makers are currently showing great interest in 'nudge' approaches – altering environments to prompt healthier

behaviour, without banning particular choices – and last year the BRHU questioned whether such an approach stands up to scientific scrutiny. We know from past examples that firmer legislative approaches can reap dramatic health rewards: when Scotland first imposed a ban on smoking in public places in 2006, a 17% reduction in admissions for heart attacks was recorded within a year across nine Scottish hospitals. But questions remain about which interventions are the most cost-effective and worthwhile – the so-called 'best buys'.

"The increasing number of people with NCDs is a vast public health and economic problem. Although it is widely accepted that something needs to be done, there is uncertainty about how this epidemic can be stemmed," said Wareham. "At the moment, the sound base of research underpinning solutions is largely lacking. There may be some policies that could be put in place now but we believe that interventions should be better evaluated. Going forwards, the scale of the task we face globally is huge. CEDAR has already made a good start."



Professor Nick Wareham

For more information about CEDAR, please visit www.cedar.iph.cam.ac.uk/

Winds of change for pollution sensing

A new system of pollution sensing, currently being tested at Heathrow Airport, could revolutionise monitoring air quality and predicting its health impacts.

The Great Smog of London is often upheld as a time when pollution reached appalling levels: over a four-day period in December 1952, the capital came to a standstill, cars were abandoned, airports closed and over 4,000 people died due to respiratory or cardiovascular problems. But what might come as some surprise is that roughly the same number of people died as a result of pollution in London in 2008.

The pollutants may have changed – then it was smoke and sulphur dioxide from coal fires, now it's principally ozone, nitrogen dioxide and fine particulate matter, mostly from vehicular emissions – but, according to a recent report by the government's Environmental Audit Committee, 30,000 people died in the UK as a result of pollution in 2008, and life expectancy was reduced by as much as nine years in the worst-affected areas.

With calls for the government to meet European Union standards on air pollution, the provision of accurate, real-time monitoring of air quality is crucial to understanding the factors that influence pollutant concentrations. A new study led by the University of Cambridge has begun testing instruments that could revolutionise not just pollution sensing but also relating actual exposure to medical impacts.

The small, portable, low-cost instruments contain a series of sensors that measure six gases, volatile organic compounds and airborne particulates. "Some of the sensors were developed for use indoors as gas alarms but working with project partner Alphasense we've been able to push the sensitivity a thousand-fold for use in an urban environment," explained the project leader, Professor Rod Jones, from the Department of Chemistry. "Our portable instruments, capable of taking measurements in a wide range of

environments, will complement the government's pollution monitors which operate at fixed sites across the UK."

The project, which has been funded by the Natural Environment Research Council, follows a proof-of-concept study carried out in Cambridge in 2009. Sensors deployed around the city monitored the levels of carbon monoxide and nitrogen oxides in the air, and GPRS functionality allowed the data to be transmitted via the mobile phone network back to a central server from where the data are accessible via web interfaces. Using visualisation tools such as Google Earth, the researchers were able to monitor pollution levels on a street by street basis.

An improved version of these devices is now being deployed at 60 locations around Heathrow Airport. The units, which are wireless and battery powered, also contain a miniature counter that measures tens of thousands of airborne particles per second developed by the University of Hertfordshire with support from the University of Manchester.

"Over 12 months, the sensors will gather data from around the airport to correlate pollution with the factors that cause it," explained Dr Iq Mead, who is responsible for the sensor node design, construction and deployment. "We couldn't do this without the support of the British Airport Authority and British Airways, who are providing a record of the movement of planes and their specific thrust levels." In addition, researchers at Imperial College London are providing valuable input on modelling transport and deployment of the units, with the National Physical Laboratory assisting with aspects of the network calibration.

The study will generate a complex dataset, and one of the challenges has been to create software that correlates pollutants with the movement of cars and planes, and with the time, location and weather. The

software design, which has been led by Mark Hayes, Director of the Cambridge eScience Centre, will also enable modelling of future changes, such as what effect the building of a third runway at Heathrow could have on pollution levels.

The team is working with Cambridge Environmental Research Consultants – a world-leading urban air-quality modelling group – who will use the unprecedented level of data created by the study to test their models of air quality.

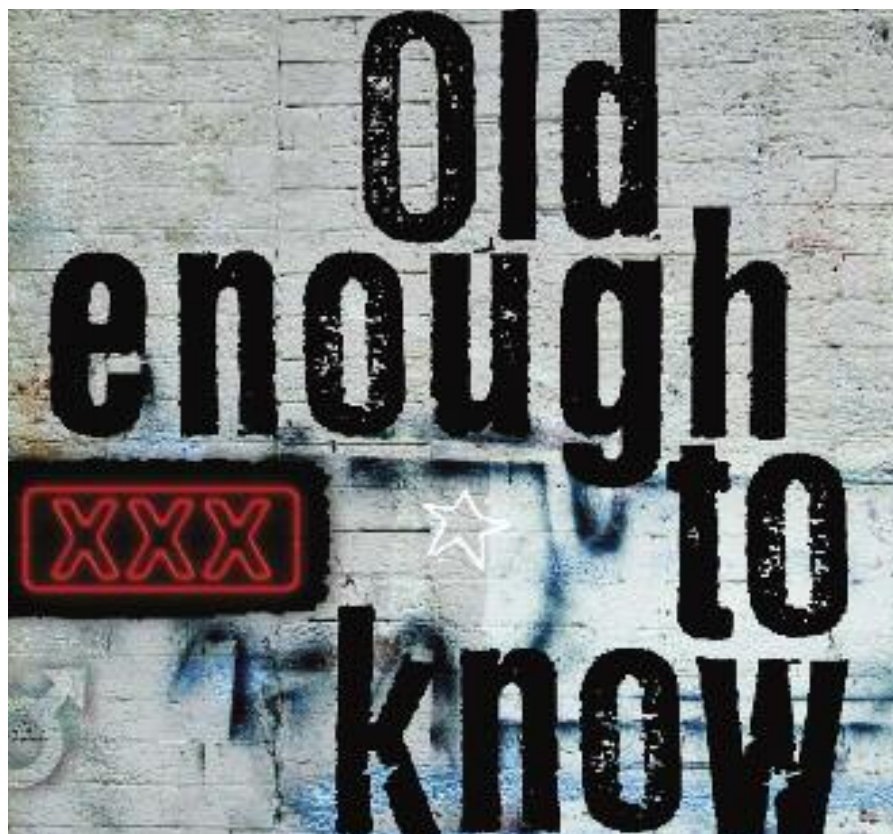
Moreover, as Jones explained, the new system could be the beginning of a new means of pollution monitoring for health: "These sensors could eventually be small enough to pin to the lapel and cheap enough to be used in parts of the world that can't afford expensive kits. We'll be able to relate actual exposure to particular pollution events to medical impacts. In a sense this is a disruptive technology. It's going to change the way that people monitor individual exposure."



Professor Rod Jones (left) and Dr Iq Mead

For more information, please contact Professor Jones (rlj1001@cam.ac.uk) at the Department of Chemistry (www.ch.cam.ac.uk/) or visit www.snaq.org/





DETAIL FROM BOOK COVER WITH PERMISSION FROM HSRC PRESS

Asked to give their perceptions of current AIDS education classes and how they desired these classes to be, the children described how the curriculum centred on the giving of factual information – facts that they found difficult to connect to the confusing and mysterious world around them. Moreover, they felt that they couldn't share their own knowledge with adults.

"When the teachers, parents and members of the community were presented with the findings, they were surprised and concerned at the extent of the young people's knowledge," explained researcher Dr Susan Kiragu. "They thanked us for coming because it gave them a kind of 'permission' to talk about this sensitive, almost taboo, area, without feeling they were corrupting the children."

The project created what the researchers call a dialogic space; an opportunity for the children to ask questions based on what they already know, and for the teachers and the parents to respond openly and honestly. "The format we devised for the dialogues was engaging, interactive and rooted in the reality of the children's experience – what is in fact simply a model of good sex education," explained McLaughlin. "Because we want this to be a sustainable programme that will continue long after the duration of the project, we packaged the findings as a toolkit to support teachers through the process."

The toolkit and a process for curriculum development is now being trialled in Botswana, Ghana, Kenya, South Africa, Swaziland and Tanzania. As the researchers gather the results of the trial over the next few months, the hope is that their innovative programme has offered the means to deliver the 'social vaccine' by transcending cultural barriers to learning.



Dr Colleen McLaughlin (right) and Dr Susan Kiragu

For more information, please contact Dr McLaughlin (cm10009@cam.ac.uk) at the Centre for Commonwealth Education, Faculty of Education (www.educ.cam.ac.uk/). The Centre is funded by the Commonwealth Education Trust.

Old Enough to Know: Consulting children about sex and AIDS education in three African countries, by Colleen McLaughlin, Sharlene Swartz, Susan Kiragu, Mussa Mohamed and Shelina Walli, is published by HSRC Press: Cape Town, South Africa.

Educating young people about HIV/AIDS has been hailed as a 'social vaccine' in public health but the question of how best to do this has long been debated. Now, innovative research focused on Africa is providing some answers.

"The teachers are careful with us because they think we are still young... They think we are going to be naughty or sometimes experiment what they told us... [but] who wants to experiment with AIDS?" These words, spoken by a grade 6 South African schoolboy to a team of researchers at the Centre for Commonwealth Education, capture the essence of the conflicts inherent in educating children about sex and HIV/AIDS. What do they know, what do they need to know and how best to tell them?

In the absence of a cure or vaccine for HIV/AIDS, education about safe sex is regarded as one of the primary means for prevention. Despite a falling incidence of HIV infection, the need for such efforts remains acute: in the three decades since AIDS cases were first reported in sub-Saharan Africa, an estimated 14 million children have been orphaned in the region.

"HIV/AIDS education programmes already exist in African schools," explained Dr Colleen McLaughlin, "but deep-rooted socio-cultural, religious and moral constraints make it difficult for teachers to speak to children about sex. Moreover, preparing teachers to do this, and providing them with appropriate resources, is not necessarily driven by evidence-based understanding." The ASKAIDS project that McLaughlin leads in the Faculty of Education hopes to remedy the situation.

Over a two-year period, the team of researchers in the UK and three countries in Africa first took a step back from what works in the classroom, and asked two fundamental questions: how much do children know already and how does this knowledge intersect with what they learn in the classroom? Their results have just been published in a book entitled *Old Enough to Know*.

"We worked with children at grade 6 in primary school [median age 12] because this is the final year of compulsory education in the countries we were working in, Kenya, Tanzania and South Africa, and also because of a common perception that primary age is too young – that educating this age group is a risk rather than a protective factor," said McLaughlin. "Perhaps one of the more surprising findings was that their sexual knowledge was already wide-ranging."

When the team asked the children to use cameras to make a record of the people, places and things from which they learned about sex, love, AIDS and relationships, the resulting images were unbelievably powerful. "The young people have a vigilant awareness of a highly sexual world around them, including prostitution, pornography and drug-related sex, and a fairly sophisticated knowledge of adults' sexual practices," McLaughlin said. "So much so, that it's clear that children are at risk if treated as innocents in HIV/AIDS education."

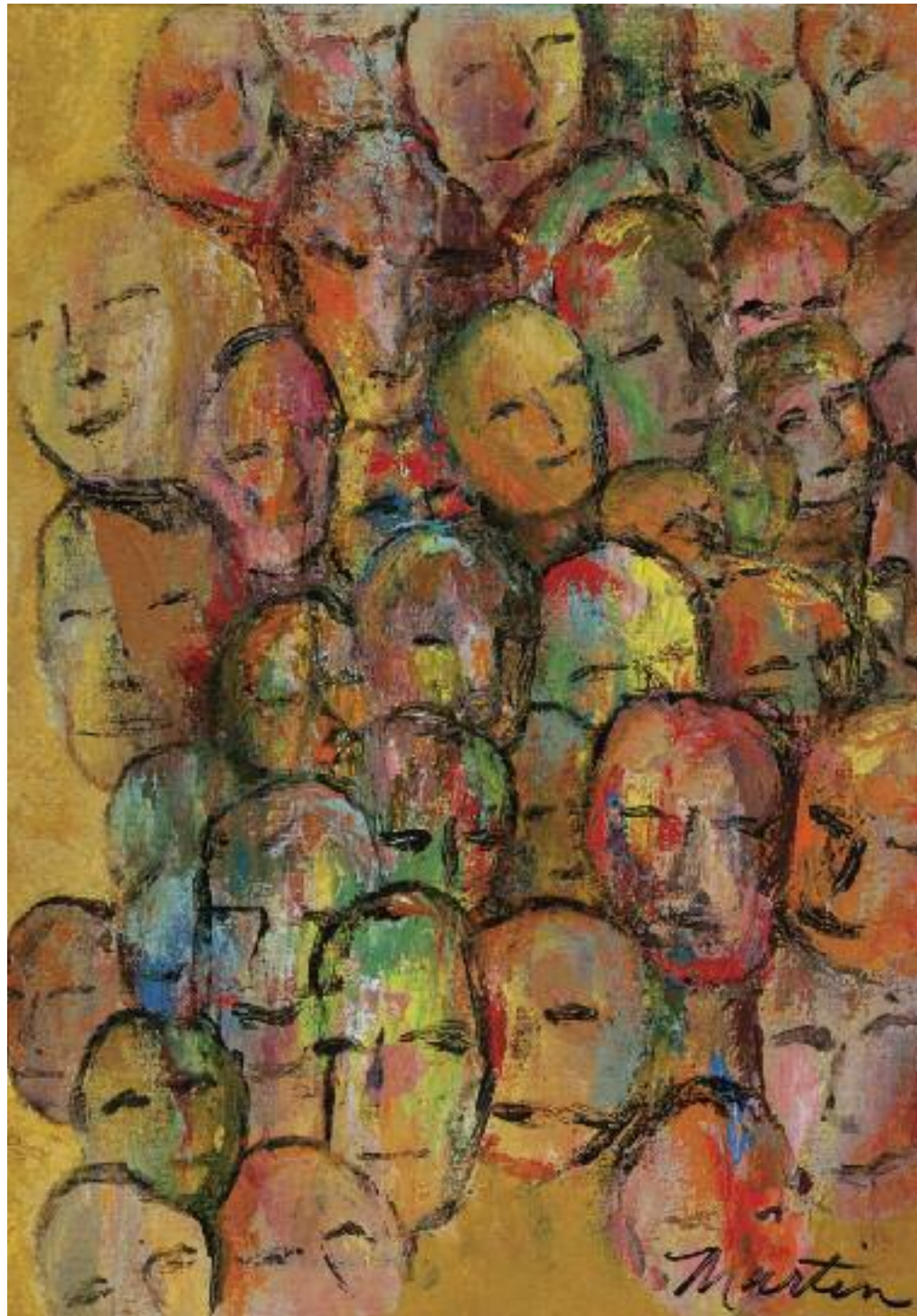
With the people, for the people: applying mental health research

From campus to community, the worlds of mental health research and medical practice are being brought together by a collaboration involving researchers, health and social care providers, and the patients themselves.

Imagine a 17-year-old man with a learning disability arriving in A&E with suspected appendicitis. By the time he's been treated, he will have navigated a system complex enough to challenge anyone. A web of interactions will have been woven involving A&E, surgery, social services and mental health services, and complicated by the fact that, at 17, the young man faces transition from adolescent to adult services.

Professor Peter Jones, Director of the Collaboration for Leadership in Applied Health Research and Care for Cambridgeshire and Peterborough (CLAHRC CP), cites this young man as an example of one of the many highly vulnerable people who must traverse what he describes as pinch points in mental health services: "such gaps, despite vast efforts on the part of those carrying out the services, can sometimes place individuals with mental health problems in an impossible situation."

Each year, around one in four adults in Britain will experience some kind of mental health problem, a condition that also affects children and the elderly. CLAHRC CP, a five-year, £23 million collaboration between the University of Cambridge, the National Institute for Health Research (NIHR) and six health and social care providers (see panel), is focusing applied health research on the urgent needs of patients at the front end of mental health service delivery. Three years into the CLAHRC, the work is having demonstrable beneficial outcomes to patients and clinicians.



Found in translation

CLAHRCs (there are nine around the country) have their origins in the 2006 Cooksey Review commissioned by the UK government, which identified two major gaps in the translation of health research into health care: the translation of basic research into products (often called 'bench to bedside' or type 1) and the implementation of these products into clinical practice (type 2). CLAHRCs, funded by the NIHR, were established to bridge the type 2 gap.

It's not a straightforward matter, as Jones explained: "The type 2 gap involves a great many players and an understanding of how to move ideas around a system. In fact, it's a sophisticated systems engineering and management problem."

No wonder that Jones attributes a crucial part of the success of CLAHRC CP to the involvement of Cambridge's Engineering Design Centre (EDC), Judge Business School (JBS) and Institute of Public Health: "We can look back now and see that much of our thinking began to change in the early stages as a result of these cross-cutting conversations. What we've learned is that there are principles to short-circuiting having an idea and getting it into the hands of people who can use it."

Invention to innovation

The research strands of CLAHRC CP focus on the mental health of children and adolescents, adults with disorders, and old-age and end-of-life care (see panel). "Much of the research is highly technical but with

close co-operation between researchers and the consumers – patients, clinicians and service managers – we've been able to make sure the findings are rapidly available and implemented," explained Jones. "You could say that co-production is the essence of CLAHRC."

Many of the research projects (26 at last count) demonstrate how involving consumers at an early stage not only helps to shape the work but also enables the consumers to plan for implementation. Jones likens the situation to a process in which the research is 'pulled through' by the end user: "When you have liaised with the consumer very early on, you know that their question is your question and they're eager for your results."

One example has been the Transfer of Care at 17 (TC17) study led by Professor Ian Goodyer, aimed at understanding the factors that facilitate or hinder successful outcomes when young people leave the care of the local authority. Adolescence is a complex period of rapid change for all young people but it's also a critical period of vulnerability for developing mental health problems: approximately 50% of all lifetime mental disorders begin in the middle teenage years and 75% by the mid-twenties.

After discussion with Cambridgeshire Social Services, the TC17 researchers realised that describing the mental health needs of children in care was almost completely uncharted territory. Little was known of mental illness influences on personal and social adjustment in those leaving care, and adolescents revealed a reluctance to seek help. In association with young people, the team developed a tool to assess barriers to care and, partly in response to the findings, Cambridgeshire Social Services are undergoing a restructuring exercise to cater for 44 new units with an emphasis on family well-being and mental health.

The project has also led to the development and piloting of a new mental health training package for foster carers to help them identify core symptoms of emotional distress through close observation during a child's first two weeks in care. "Both Cambridgeshire County Council and Peterborough County Council are enthusiastic about the pilot, along with the Looked After Children Psychology Service," explained Goodyer. "If the results are positive it could lead to a fundamental change in how the foster carers are educated and supervised to help children in their care."

"The greatest impact of the CLAHRC to date has been, and continues to be, the gradual enlightenment on the part of our local authority, voluntary sector and clinical colleagues of the potential value of high quality research to their work," added Jones.

The main aim of CLAHRC-CP is to increase the value of services and what they can do for patients and their families. Often, improved services also result in cost savings,

CLAHRC CP research and implementation themes

Research themes (led by the Department of Psychiatry):

- **Child and adolescent mental health:** Professor Ian Goodyer, with Professor Simon Baron-Cohen and Dr Paul Wilkinson
- **Adult disorders:** Professor Tony Holland, with Dr Isabel Clare and Dr Howard Ring
- **Old-age and end-of-life care:** Dr Tom Dening and Dr Stephen Barclay

Implementation themes:

- **Linking research outputs with public health policy analysis and evaluation of health interventions:** Professor Carol Brayne, with Dr Christine Hill, Institute of Public Health
- **Design of health and social care systems:** Professor John Clarkson, with Dr Terry Dickerson, Engineering Design Centre
- **Knowledge translation and service innovation:** Professor Michael Barrett, with Dr Eivor Oborn, Judge Business School

CLAHRC-CP brings researchers together with Cambridgeshire and Peterborough NHS Foundation Trust, NHS Cambridgeshire, Cambridgeshire Community Services NHS Trust, NHS Peterborough, East of England Strategic Health Authority and Cambridgeshire County Council.

For more information, please visit: www.clahrc-cp.nihr.ac.uk/

as is the case for the outcome of a research project on Improving Access to Psychological Therapies (IAPT).

The IAPT programme, provided by the NHS, offers psychological therapy to people suffering from mild to moderate depression and anxiety disorders, where previously medication and a long wait on a list for a counsellor had been the only option for GPs. Each year in England, mental health conditions cost approximately £105 billion due to loss of earnings and associated treatment and welfare costs.

Working with the East of England Strategic Health Authority, CLAHRC researchers, led by Jones, investigated whether the programme was meeting the needs of the local population. Having analysed data from over 100,000 consultations, the team showed that simply offering therapy by telephone rather than face to face was just as effective and yet much more cost-effective and convenient. It also opened up the service to people otherwise unable to access support owing to their remote location, physical disability, employment status or their avoidance of talking about their condition in person.

Alison Watson, IAPT Research Associate, explained the impact of the study: "It's definitely a case of invest to save. For every patient who recovers from depression or anxiety, the NHS is saving over £1,000. IAPT is designed to prevent that 'revolving door syndrome'. People are taught the skills to self-manage their condition, which leads to long-term sustained recovery. Access to the talking therapies over the telephone has been a real innovation in service delivery, which has helped services meet the needs of their local population."

Boundary spanners

Ultimately, the key to translating invention into innovation sustainably, believes Jones, are boundary spanners – individuals who

can understand both research and clinical practice. The CLAHRC Fellowship scheme, developed over the past year, has now trained 27 individuals from health and social care in research methodology, service redesign and change management. Already CLAHRC Fellows are making an invaluable contribution, acting as local 'research champions', and helping the CLAHRC connect with health care practitioners in the community.

Looking forward, Jones reflected on what he finds most exciting about the CLAHRC: "It's the ability to be reactive to co-production and to be flexible enough to take on emerging areas in mental health, because if the consumers really want an answer, then it will happen more quickly and you'll have more impact."

"When you have liaised with the consumer very early on, you know that their question is your question and they're eager for your results."



Professor Peter Jones

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In tracing the modern history of Germany's policy on intoxicant and drug use, which favours therapy rather than punishment, Cambridge historian Dr Victoria Harris highlights that criminalisation may not be the only route.

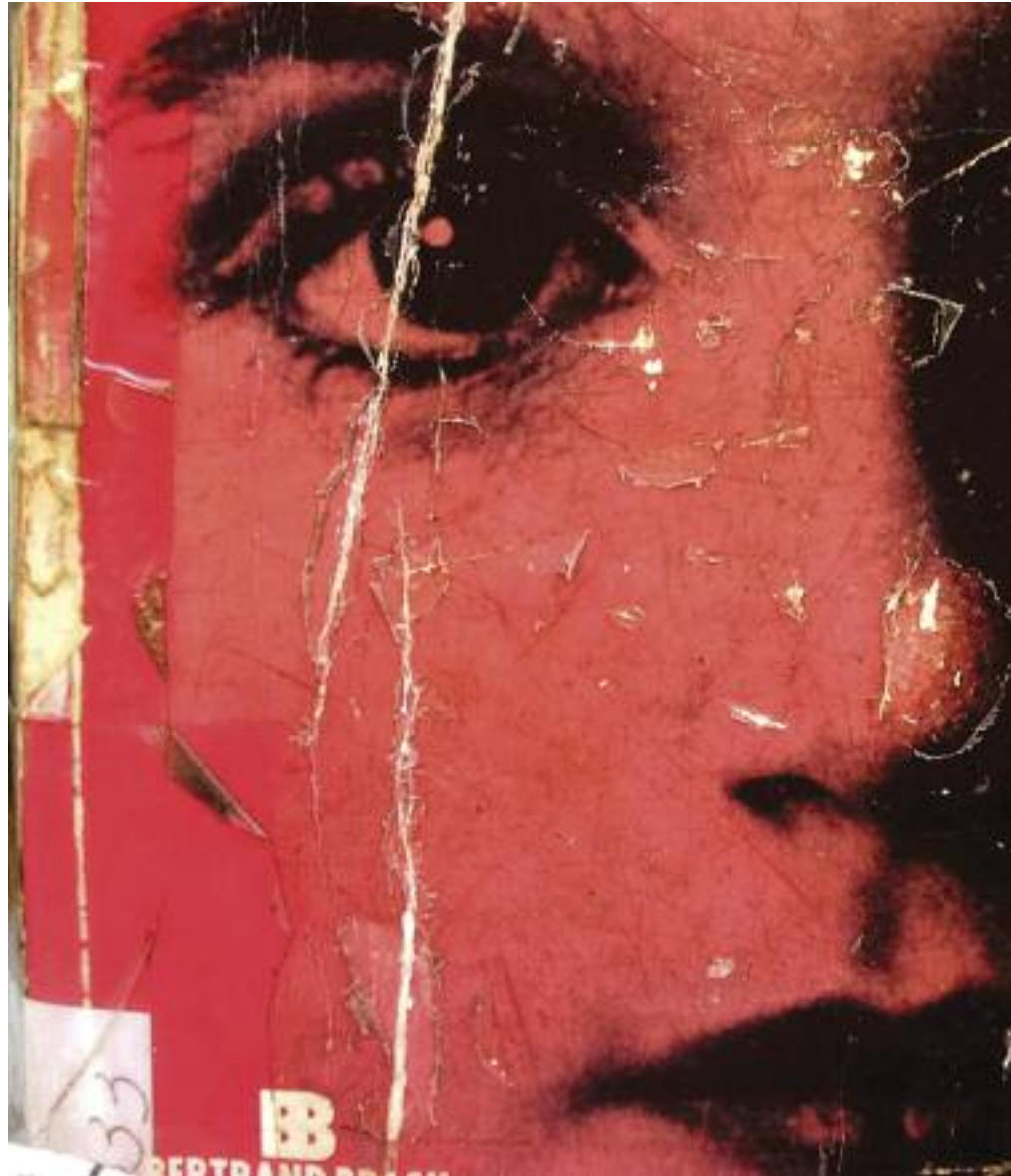
Intoxicating history

As the Department of Health gears up to publish its alcohol strategy for England later this year, it does so amidst newly published figures estimating that a failure to reform alcohol laws could lead to 210,000 preventable deaths in England and Wales in the next 20 years.

Substance abuse too is recognised as an increasing threat to public health. Although the first international drug treaty was signed a century ago in efforts to halt the opium, morphine and cocaine trade, last year the Global Commission on Drug Policy concluded that the global war on drugs had failed. According to estimates by the United Nations (UN), opiate use increased worldwide from 1998 to 2008 by 35%, cocaine by 27% and cannabis by 8.5%.

How should governments respond? What is the best policy to safeguard public health against the dangers of intoxicants? Should policy makers treat these substances as separate or related? While scientific risk assessments provide one answer, we can also learn valuable lessons for policy making by looking at how society has tackled the issue in the past. If we want to understand how to design more appropriate international policies we need to understand how current policies developed and why they have failed.

In many respects, our understanding of this historical context has been distorted by the dominance of the prohibitionist and criminalisation models of intoxication management. But, if we look at the policies of Germany – a country which deviated from the more common model of increased criminalisation favoured by the West over the past century – we can see that prohibition was not the only history of intoxication management, and can gain new insights into how these alternative strategies managed the public dangers (and benefits) of intoxicants.



Rauschmittel

On 21 August 1883, *The New York Times* reported the emergence of a new temperance movement in Germany. Previous attempts to instil in Germans the desire to abstain from alcohol had been an utter failure. Alcohol had a central ritual and nutritional function, and the brewing industry was powerful.

The new movement was savvy, no longer urging Germans to pledge 'total abstinence'. Nor did it any longer condemn politicians drinking beer while talking politics. Nor even the 'jovial drunkenness' of students. This contrasted sharply with Britain's temperance movement which, by the late 19th century, urged abstinence. Teetotalism reached its most extreme legislative incarnation in the USA, where alcohol was illegal between 1920 and 1933.

When compared to American prohibition, German temperance activists' acceptance of drunkenness seems bizarre. But not when compared to Germany's treatment of other intoxicants. Germany introduced the world to cocaine, heroin, amphetamines and MDMA; it was also reluctant to criminalise them. Even with tobacco, Germans have been permissive,

refusing to implement a European Union directive banning smoking in public spaces in 2008. In fact the German language treats intoxicants together: the word *Rauschmittel* describes alcohol, medicines, illicit drugs and cigarettes, and means 'articles of intoxication'.

My research explores why and how Germany took this approach to managing *Rauschmittel*. It connects political and everyday history, examining how cultures of intoxication shaped and were shaped by policy, and what this tells us about German society. It asks: why was a country famous for its repressive dictatorship and its obsession with national health also so permissive?

Given smoking's well-publicised dangers, it is initially hard to view Germany's intoxicant policy as public health orientated. However, its approach to temperance demonstrates an early preference for recognising a user's positive experiences and negative abuses of a substance, rather than treating a substance as inherently problematic. This attitude has informed Germany's intoxicant policy and its treatment of users throughout the modern period. By closely regulating users' activities, one could reduce a substance's potential harm rather than criminalise it and, by extension, its users.



PHOTO OF THE BRAZILIAN EDITION OF THE BOOK EU, CHRISTIANE F., 13 ANOS, PROGADA PROSTITUIDA... (PUBLISHED BY BERTRAND BRASILI BY KARINA JUNQUEIRA ON FLICKR)

Christiane F., perhaps Germany's most famous 'heroin statistic', who started using the drug aged 13 in 1975

"If we want to understand how to design more appropriate international policies we need to understand how current policies developed and why they have failed."

Christiane's story

Despite its success in regulating alcohol consumption in a culturally acceptable manner, Germany was not immune to the destabilising effects of new 'trends' in intoxicant use. The most famous example is heroin which, although first produced in Germany in the late 19th century, was relatively well controlled until the late 1960s, despite (or perhaps because of) its legality. Addiction was a problem, but it was limited to doctors, their patients and their social circles.

This changed when younger, poorer, West Germans gained a taste for the drug. In 1967, the West Berlin police reported 57 drug offences; in 1970, 858; and in 1980, 4,429. By 1971, heroin was criminalised in Germany via a UN treaty.

But perhaps Germany's most famous 'heroin statistic' is Christiane Felscherinow, who started using the drug aged 13 in 1975. Her experiences, recorded by two journalists and later made into a film, demonstrated to Germans the Berlin authorities' lack of expertise in treating heroin. Individuals like Christiane were visible manifestations of a serious social ill, and less easy to stereotype as devilish deviants because of their youth and vulnerability. As a result, the authorities began to treat heroin use as a threat to public health, not as a criminal problem.

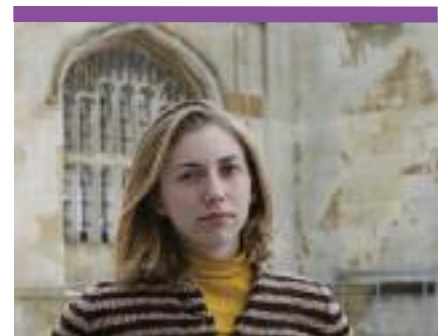
The Berlin authorities implemented a tightly regulated therapy chain, which followed users from the street through their social reintegration, and by 1981 Germany had changed its drug policy to legally favour therapy not punishment. Needle programmes were established in 1984, and today Germany has the largest number of needle vending machines in the world. Methadone treatment for addicts began in 1992; since 2003, Germany has also treated addicts with heroin. Switzerland and the Netherlands, which have

similar intoxicant histories, have done likewise. Four cities from these three countries declared the 'war on drugs' a failure in 1990, calling most drug use a 'temporary' part of most users' biography, best regulated, not criminalised – and 21 years later much of the world has followed suit.

Lessons from history

When the Global Commission on Drug Policy declared in 2011 that attempts to reduce drug use through supply-side prohibition had failed, they urged a science-based debate to develop ideas for new international policy. My research emphasises the importance of also taking a historical approach, one that does not base its exploration of substances on their current criminal or cultural status, but instead takes as its focus the entire category of intoxicants.

This historical approach demonstrates the importance of connecting policy to everyday experience. Doing so prevents the marginalisation of users in discussions of intoxicant policy and allows for a better understanding of intoxication's dangers *and* enticements.



Dr Victoria Harris

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By contrast, prohibitionist-based policies and their corresponding histories have focused on the path to and from criminalisation and rarely on individual users and the society in which they lived. Because prohibitionist-orientated histories classify substances by their legal position, past trends in intoxicant use have become distorted by present-day legal realities. This is equally problematic for illegal drugs as for substances like alcohol and cigarettes, for which the lines of acceptability or taboo are more fluid, and for which a defensive justification for their legality in the West has developed.

Of course, effective regulation necessitates public acceptance of governmental interference. This might not have worked in the UK, with its history of liberal individualism. But in Germany, a country with a highly interventionist state, which boasted numerous positive and negative regulations that did not exist in the UK, intoxicant regulation was more culturally acceptable. However, it did not proceed smoothly. International treaties, which Germany chose or was compelled to support, increasingly favoured supply-side prohibition, undermining Germany's preference for consumption-side regulation.



Frugal innovation

Co-author of recently published book *Jugaad Innovation*, Professor Jaideep Prabhu argues that a frugal and flexible approach to innovation can generate breakthrough growth not only in the developing world but also in the West.

Innovation is a major imperative for companies and governments worldwide. But post-downturn we can't solely rely on the tried-and-tested formula which has sustained innovation efforts in the West for decades: highly structured R&D processes that result in expensive top-down projects. Instead, how can we do more for less, while serving broader markets?

One solution is for the West to look to places like India, Brazil and China for a new, flexible approach to innovation – to the activities of individuals like Dr Mohan, a resourceful innovator in Chennai, India, who has created a highly frugal and effective solution to a major public health problem. Or Harish Hande from Bangalore, India, whose Solar Electric Light Company (SELCO) offers affordable, sustainable lighting solutions for those who live outside the electricity grid.

Despite their remarkable work, such individuals are not an exception. Emerging markets are teeming with frugal and flexible innovators like these. In the nearly four years that my co-authors and I have been researching the phenomenon of *jugaad* (a Hindi term that roughly translates as 'overcoming harsh constraints by improvising an effective solution using limited resources'), we have encountered hundreds of entrepreneurs in resource-constrained

Entrepreneur Harish Hande saw providing lighting to rural homes in India as an opportunity for *jugaad* innovation; here a vegetable vendor in Bangalore uses a solar lamp to light her stall

circumstances worldwide who have innovated in areas as diverse as health care, education, financial services, energy and entertainment.

The self-expanding diabetes clinic

India has the dubious distinction of being the diabetes capital of the world. In many cases, rural patients don't know what diabetes is, let alone that they may be suffering from it. Even when they do know, the lack of good rural health care means travelling to distant cities and taking time away from work to get the necessary medical attention. Given that 70% of India's 1.2 billion people live in villages, this situation has all the makings of a public health disaster.

Enter Dr Mohan, Director of the Madras Diabetes Research Foundation and Chairman of Dr Mohan's Diabetes Specialities Centre in Chennai, capital of the South Indian state of Tamil Nadu. Deeply concerned about the consequences of a looming public health crisis, and aware of India's socioeconomic realities, Mohan engaged in a frugal and flexible piece of thinking: what if physicians could remotely consult patients without either group having to travel?

“Jugaad innovators have a mindset that encapsulates several attitudes and practices, including the ability to seek opportunity in adversity, do more with less, think and act flexibly, keep things simple, include the margin, and follow the heart.”

After much trial and error, he brought to life a mobile clinic, housed in a satellite-enabled van, which visits some of the remotest parts of Tamil Nadu and links urban doctors to rural patients and community health workers. The van has telemedicine technologies to conduct diagnostic tests and transmit them via satellite even from areas too remote for internet connectivity. From their offices in Chennai, Dr Mohan and colleagues can see and communicate remotely, in real time, with rural patients through video monitors, while tests such as retinal scans are transmitted within seconds for immediate evaluation.

To avoid straining the frugal business model, improvisations were made such as partnering with the Indian Space Research Organization to obtain free satellite communications for his telemedicine service, and recruiting young volunteers from small towns to run most of the operations in the mobile clinic. Already Dr Mohan and colleagues have screened more than 50,000 people across over 40 villages in Tamil Nadu and provided treatment to thousands of patients.

Here comes the sun

Providing lighting to rural homes in India is also a challenge. Over 40% of India's population live outside the electricity grid and many have to rely on kerosene lamps for lighting. Kerosene is expensive and not always available, and produces a poor quality of light and unhealthy fumes.

Harish Hande saw this problem as a potential opportunity for *jugaad* innovation. In 1995, he founded SELCO to provide affordable solar energy to India's rural poor. To do so, he had to rethink how he financed his business, priced his services, and distributed and maintained his solution.

He started with \$30 seed money. Banks were hesitant to lend and venture capitalists deemed his unproven business model too risky to invest in. So Hande bootstrapped SELCO: he used the \$30 to buy his first solar home lighting system, which he then sold. With the revenues, he purchased additional systems, which he also sold, and so on.

As Hande penetrated deeper into rural areas, he learned that his potential customers – many of whom earned \$1 to \$2 a day – could not afford the up-front costs of buying and installing his solar lighting systems, and there was no economical way to maintain them across multiple villages. His solution was to create a rural network of small-scale entrepreneurs who own and maintain the solar panels and batteries, and rent them out to consumers on a pay-per-use basis.

This business model made SELCO's solution affordable and accessible to scores

of rural customers, including corner-shops, small-scale farmers and women working from home. It also created an incentive for local entrepreneurs to distribute and maintain the equipment over time. Within a few years, 125,000 households have already taken up the solar lighting system.

A universal solution to universal challenges

The fruits of *jugaad* innovation include the \$2000 Tata Nano car, \$50 Aakash tablet PC, 1 cent/minute mobile phone calls, £500 electrocardiography (ECG) machines (and \$1 ECG scans), \$25 water purifier, \$70 fridge that runs on batteries, and so on.

In the course of our research we learned that the entrepreneurial spirit of *jugaad* is not limited to India. It is widely practised in Argentina, Brazil, China, Costa Rica, India, Kenya, Mexico, the Philippines, and other emerging economies. Brazilians call it *gambiarra*; the Chinese, *zizhu chuangxin*; and the Kenyans, *jua kali*.

A resource-constrained and unpredictable environment makes frugal and flexible innovation necessary, even vital. *Jugaad* innovators have a mindset that encapsulates several attitudes and practices, including the ability to seek opportunity in adversity, do more with less, think and act flexibly, keep things simple, include the margin, and follow the heart. Specifically, *jugaad* entrepreneurs are resilient, frugal, adaptable, inclusive, empathetic and passionate. All these traits help them to compete and succeed in the complex world of emerging markets.

But the *jugaad* mindset, and the innovations that result from it, not only hold promise for the poor in emerging markets. Increasingly, such a frugal and flexible approach has relevance to Western economies that are reeling under the pressures of economic recession and budget constraints.

Unsurprisingly, we have found that many Western firms, faced with resource constraints of their own, and recognising the limits of the expensive, rigid and insular structured approach to innovation, have begun to apply *jugaad* and its principles within their organisations. For example, GE has applied *jugaad* to develop radically affordable ECG machines not only for India and China, but also for the USA and Europe; other firms applying *jugaad* include 3M, GM, PepsiCo, P&G and Renault-Nissan.

Yet, while *jugaad* offers an interesting and useful counterpoint to more structured approaches to innovation, it isn't necessarily a substitute for the latter. Rather, *jugaad* can be an effective complement. For instance, as in the example of Dr Mohan, although his

jugaad approach has been successful in delivering diabetes care in an affordable and effective way for some people, it has yet to achieve scale. Scaling the solution will probably require a more systematic application of resources around the basic model he has developed.

In summary, for firms and governments around the world struggling to deal with scarcity and complexity, our research suggests that *jugaad* and the emerging markets it comes from offer a solution not only in the developing world but also in the increasingly resource-constrained and complex West. Innovators like Dr Mohan and Harish Hande, and their relentless pursuit of frugal and flexible solutions, could be just the thing the world needs to grow without depleting the planet's resources.



***Jugaad Innovation: Think Frugal, Be Flexible, Generate Breakthrough Growth* by Navi Radjou, Jaideep Prabhu and Simone Ahuja was published by Jossey-Bass in April 2012 (www.jugaadinnovation.com/)**



Professor Jaideep Prabhu

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A new dimension to DNA and personalised medicine of the future

By investigating the existence of an unusual four-stranded structure of DNA in human cells, scientists have opened the door to novel cancer therapeutics and a new era for personalised medicine.

When Watson and Crick discovered the double helix structure of DNA in 1953, they declared they had “found the secret of life”. However, as in all pursuits of science, the story did not end there. Less than 60 years later, a team led by chemist Professor Shankar Balasubramanian and cancer biologist Professor Steve Jackson has found that an unusual four-stranded configuration of DNA also forms at sites across the human genome in living cells.

Although known about by scientists for decades, the structure was considered to be something of a structural curiosity rather than a feature found in nature. It forms in regions of DNA that are rich in one of its building blocks, guanine (G), when a single strand of the double-stranded DNA loops out and doubles back on itself, forming a four-stranded ‘handle’ in the genome.

G-quadruplexes have been known to occur at the ends of chromosomes in the regions known as telomeres, but it wasn’t until a strong association had been noticed with genes responsible for cell proliferation that Balasubramanian and others began to suspect that G-quadruplexes might be a

potential target for cancer therapy. “If you synthesise a quadruplex-binding molecule and put it into cancer cells, it can impair the growth of these cells,” he said. “We’ve come such a long way from thinking that we understand the genome – and it appeared that this structure could tell us something new.”

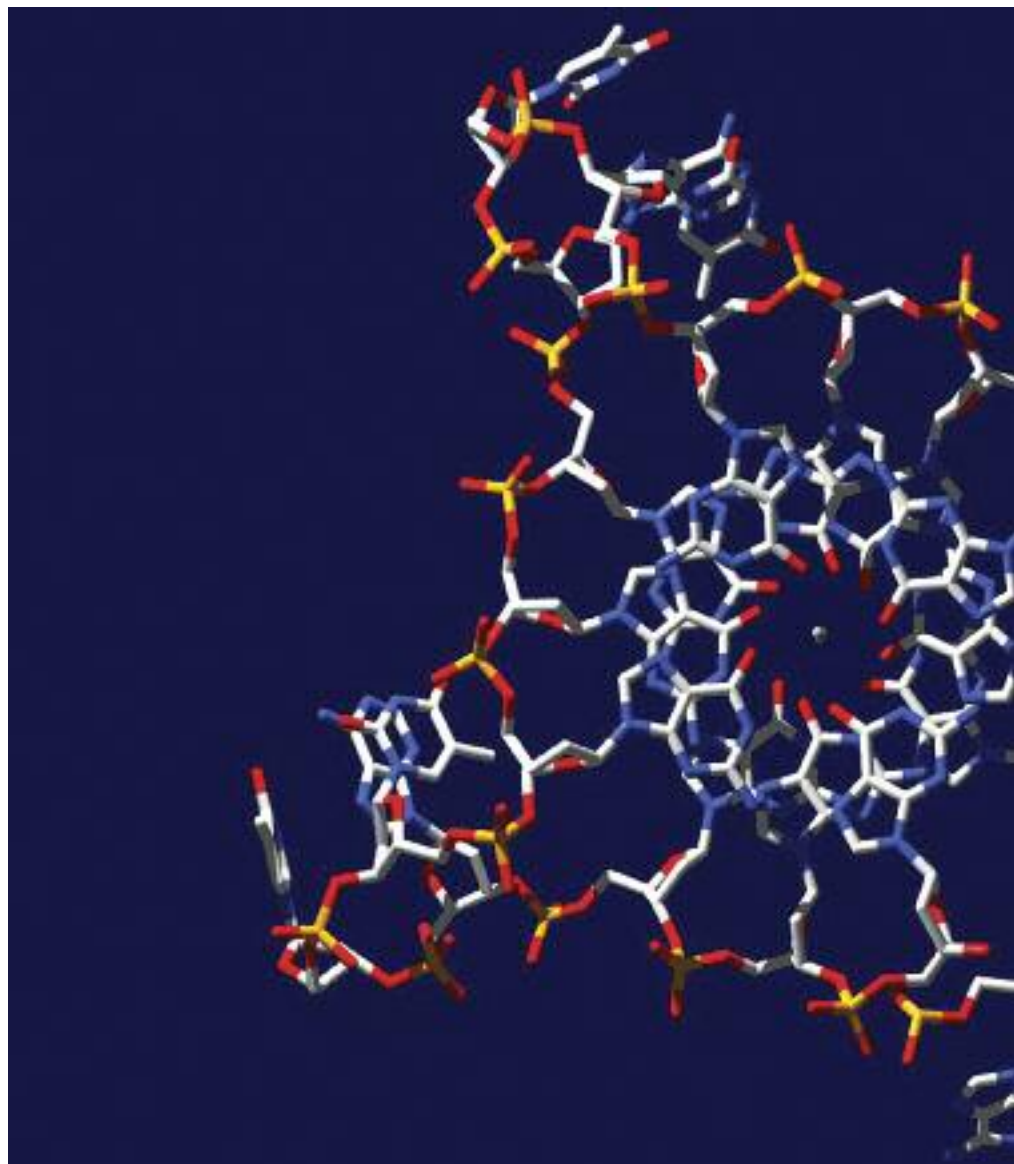
Dr Raphaël Rodriguez, a Senior Research Associate who has worked with Balasubramanian for the past seven years, developed a small synthetic drug called pyridostatin to target G-quadruplexes. Two years ago the pair joined forces with Jackson, whose lab is studying the fundamental biology of cancer. In a recent article published in *Nature Chemical Biology*, they showed that not only do these structures form in cancer cells – the first time this has been demonstrated – but that pyridostatin can actually interact with G-quadruplexes to prevent proliferation of these cells. Although the function of G-quadruplexes remains a mystery, the discovery holds great potential for new, more selective approaches to treating cancer via interference with the genome, as well as offering a new dimension to personalised medicine.

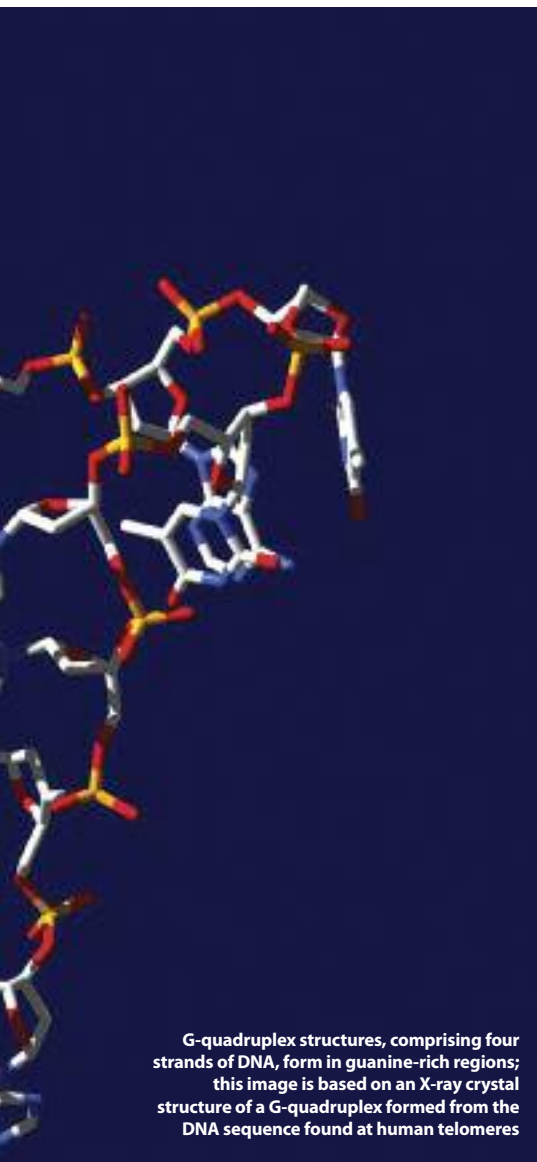
Protecting the genetic code

At the heart of the new discovery is an innovative way of locating the structures in living cells and then ‘capturing’ them for further examination. The scientists discovered that when pyridostatin binds to G-quadruplex DNA it causes a double-strand break in the double helix when the cell tries to replicate and copy its genes: “Pyridostatin binding to G-quadruplexes is a major impediment to copying the genome – so if a cell tries to replicate, this will generate breaks in the DNA,” said Jackson.

Over the years, Jackson’s lab has found that there are certain proteins in the cell that act as molecular policemen, patrolling the nucleus of the cell looking for damaged DNA. If they detect damage, they start making repairs, and at the same time set off alarm signals to alert the rest of the cell that there’s a problem.

When there is no DNA damage, these molecular policemen are distributed evenly throughout each cell’s nucleus. But when cells are treated with pyridostatin, they congregate in specific locations on the DNA, indicating regions of damage, and showing up as dots under the microscope. “The field really





jumped on the idea that these dots represent telomeres that have G-rich sequences and *in vitro* have the potential to form G-quadruplexes," said Jackson. "But we stained the dots for telomere proteins and found there was only a small amount of overlap. So clearly, this pyridostatin compound is inducing DNA damage in lots of other places, and we were faced with the issue: 'if they are not telomeres, what are they?'"

This confirmed an earlier finding in Balasubramanian's lab by Julian Huppert, then a PhD student, who devised a computational search algorithm to map out every spot in the entire human genome that had potential to fold into a G-quadruplex. He found there were close to 350,000 of them.

Next-generation genome sequencing

For several years, it seemed that accurately locating the specific DNA regions that were being damaged by pyridostatin was theoretically possible by breaking up the cells, drawing out the molecular policemen that were bound to the damaged DNA, and sequencing the DNA to find its location within the genome. However, with millions of genome sequence reads required for an

accurate result, finding the answers seemed a long way off.

But a new technology has changed all of this. In collaboration with colleagues in the Department of Chemistry, Balasubramanian pioneered a faster, cheaper method of decoding DNA called Solexa sequencing, which was taken up commercially a few years ago by Illumina Inc.

Using Solexa sequencing to look across the whole genome, Rodriguez together with researchers in Jackson's lab found certain hotspots of pyridostatin-induced DNA damage, indicating the locations where the drug was acting. "These hotspots were exclusively in the parts of the genome that Julian's algorithm had predicted as predisposed to folding into quadruplex structures – so it wasn't random," said Balasubramanian.

One of the key differences between cancer cells and normal cells is cancer cells are generally more vulnerable to DNA-damaging drugs. Using high-throughput sequencing, the collaboration identified that SRC, a major gene associated with breast cancer, is one of several hotspots on the genome targeted by pyridostatin. This supports the idea that certain cancer genes can be interfered with by small molecules designed to bind to specific DNA sequences. "For the very first time we're able to map structures in DNA with high resolution, in a functional context," added Balasubramanian.

"With Shankar's new technology, together with our knowledge of DNA repair, we have been able to do something that neither his nor my lab would have been able to do on its own," said Jackson. "It's a wonderful paradigm for chemical biology – we are bringing chemistry and biology together to learn more about this unusual DNA structure and its potential as a target for cancer therapeutics."

A new approach to personalised medicine

Jackson has established two local spin-out companies, MISSION Therapeutics and KuDOS Pharmaceuticals, which have used knowledge of DNA repair to develop new anti-cancer drugs. He feels that existing and future chemicals developed by Balasubramanian and colleagues have exciting potential as anti-cancer agents, particularly if compounds can be made that hit even fewer DNA targets than pyridostatin and are thus more selective in their actions. "If drugs can be developed that only target a small number of sequences in the genome, that could be fantastic in terms of switching off a tumour-driving gene, or targeting HIV or other viral DNA," said Jackson. "It's not simple to develop these drugs, but that's the long-term goal."

For Balasubramanian and Rodriguez, this work holds potential for a new approach to testing the interaction of molecules with potentially any structure in DNA and could

hail a new era for personalised genomic medicine. "There are a significant number of drugs today that work by targeting DNA," said Balasubramanian, "but we don't actually know exactly which parts of the genome they target, and how this may vary between cells or patients. Our approach could be applied to give a better understanding of why certain drugs work, or don't work, in different patients."

If the structure of the genome differs between individuals, as they believe it does, then a patient's predisposition to the effectiveness of DNA-interacting drugs might also differ. "You can imagine a day when physicians would look at the set of drugs available and decide which of these would be most suited to the patient, simply by predicting whether or not the structural hotspots for each drug exist in the patient," said Rodriguez. "They could then choose the drug that has the best chance of working."

"This science has not been done before so it's potentially game changing," added Balasubramanian. "Together, these approaches hold the potential to dramatically improve the effectiveness of future disease therapies on a patient-by-patient basis."

"We've come such a long way from thinking that we understand the genome – and it appeared that this structure could tell us something new."



From left: Dr Raphaël Rodriguez, Professor Steve Jackson and Professor Shankar Balasubramanian

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This work was funded by Cancer Research UK and the Biotechnology and Biological Sciences Research Council.

Life is for sharing

The first ever comprehensive study of egg-sharing between women undergoing fertility treatment reveals a striking level of empathy and reciprocity on the part of both donors and recipients – and will help to dispel concerns among policy makers about the potential downside of programmes that offer ‘benefits-in-kind’ in return for donated eggs.

Imagine the following scenario. Joelle and Lucia are two women using the same fertility clinic. They do not know each other but they have one important thing in common: both have been unable to conceive. Joelle has healthy ovaries; her partner has low-quality sperm. In vitro fertilisation (IVF) offers them the best chance of pregnancy but it costs around £4,500. The clinic tells Joelle that she can ‘share’ some of her eggs in exchange for a significant reduction of her treatment costs. Joelle undergoes hormone treatment and the eggs that develop are shared equally between Joelle and Lucia, who is unable to produce her own eggs. Both women’s treatments are successful and each is delighted to be pregnant with the child she so longed for.

Now imagine a slightly different scenario. This time, Joelle’s eggs develop well and two are implanted but they do not develop into a pregnancy. Lucia, however, does become pregnant using Joelle’s eggs and has a child. How does Joelle feel in the knowledge that she may well never have a child while another woman has carried her egg to term and has fulfilled her dream of becoming a mother? And how will Joelle feel in ensuing years as the child conceived as a result of her donation approaches his or her 18th birthday, at which point Joelle may have a phone call from the child she has never known?

Controversy has surrounded the practice of egg donation ever since it began in 1984. Sharing eggs by women within clinics, first introduced in 1998, has been particularly contentious. While egg-sharing schemes initially supplied a small proportion of the total number of donated eggs in the UK, today these schemes supply 60% of the total. However, the demand for donor eggs still considerably outstrips supplies. This shortage has become more acute as a result of legislation passed in 2005 that removes donor anonymity and gives donor-conceived children the right to discover the identity of their biological parents at the age of 18.

The greatest gift

A series of articles published recently in the journals *Human Reproduction*, *Ethics*, *Bioscience and Life* and *BioNews* sets out the findings of the first ever comprehensive research into the experiences of women who have taken part in egg-sharing programmes, either as donors or recipients.

The research, carried out by Zeynep Gürtin and Professor Susan Golombok at the University of Cambridge’s Centre for Family Research, in collaboration with the London Women’s Clinic, reveals a high level of empathy and reciprocity between women seeking assistance to achieve their ambition of becoming parents – and shines a light on the ways in which women navigate the emotionally fraught process of undergoing fertility treatments. Some of its findings confound expectations about women’s emotions, especially in cases with mixed or negative outcomes.

The two-year study examined the attitudes, feelings and opinions of 86 women (48 egg donors and 38 egg recipients) undergoing treatment at the London Women’s Clinic – a private clinic that treats 1,500 women per year. Gürtin used detailed questionnaires with a variety of both multiple-choice and open-ended questions to encourage women to describe their innermost feelings on aspects of egg-sharing – which ranged from their motivations in signing up to programmes to their retrospective reflections on their experiences.

Opponents of egg-sharing have been concerned that these programmes may harm the long-term welfare of the women opting to donate their eggs – for example that this group of donors, fertility patients themselves, might be financially motivated, that their consent will be compromised if they are otherwise unable to access much-wanted treatments, or that they might suffer psychological damage, especially if their own treatment ends unsuccessfully.



Quiet, an artistic interpretation of a cell; egg-sharing schemes enable a woman going through fertility treatment to share her eggs with an anonymous recipient in exchange for a reduction in her treatment costs



OBJECT BY KIND PERMISSION OF STEFANIE REICHEL (WWW.STEFANIEREICHEL-PHOTOGRAPHYANDPRINTS.COM)

“When we compared donors and recipients we did not find any significant differences in ethnicity, religion, educational levels and occupations. The one striking difference was that recipients tended to be older than donors – on average 11 years older – a factor that is directly related to the fertility characteristics of the two groups.”

Increasing demand for eggs

Infertility affects growing numbers of women and is the second most common reason (after pregnancy) for women aged 20–45 to consult their GP. Treatments for infertility have seen huge advances in the past 30 years and clinics offering IVF have proliferated. The shortage of donated eggs, the expense of treatments and long waiting lists have led to a big rise in the numbers of British women seeking treatments overseas. It is thought that many would prefer to receive treatments in their own country.

In April this year, the Human Fertilisation and Embryology Authority introduced a flat-rate compensation of £750 in order to encourage more women to donate eggs. Gürtin said: “This move was clearly targeted at non-patient donors, and there was no discussion of whether or how egg-sharing within clinics should be increased. However, we think that with more information provision and more focus, egg-sharing schemes have the potential to meet an even greater proportion of the demand for donor eggs in the UK, in a way that is beneficial to both donors and recipients.”

“Contrary to expectations, donors whose own treatments were unsuccessful were not resentful of recipients who became pregnant... some were comforted by the thought that their efforts may have benefited someone else wishing to have a child.”



JACQUELINE GARGET

Zeynep Gürtin

For more information, please contact Zeynep Gürtin (zbg20@cam.ac.uk) at the Centre for Family Research (www.cfr.cam.ac.uk/).

“It felt right to share”

Clinics operating egg-sharing schemes offer substantially lower IVF costs to those willing to donate their eggs to other women receiving treatments – and sometimes waive donors’ fees altogether. However, the Cambridge University research suggests that much of the criticism levelled at egg-sharing, including concern about financial inducements, is ill-founded.

What emerged from the study was that women made nuanced decisions, taking account of a range of emotional, financial and practical factors. One recipient wrote: “Taking part in the egg-sharing programme made me feel most comfortable because the donor went through the whole procedure mainly for herself and not just for me.” A donor reported simply: “It felt right to share.”

“The women’s motivations to share their eggs were multiple: their own desire to have a baby, the opportunity of accessing cheaper treatment and the chance to help someone else all played an important role. We also found very low levels of regret among egg-share donors. Contrary to expectations,

donors whose own treatments were unsuccessful were not resentful of recipients who became pregnant. In fact, some were comforted by the thought that their efforts may have benefited someone else wishing to have a child,” said Gürtin.

“Many of the feelings and opinions expressed in the questionnaire were moving to read. Donors and recipients clearly empathised with one another, as fellow women experiencing fertility problems, and imagined themselves as part of a reciprocal relationship with this important stranger.”

The study enabled Gürtin and colleagues to build a picture of the demographics and background of egg sharers – both donors and recipients. “When people think about women going through fertility treatment they tend to picture heterosexual couples having problems with conceiving, however the landscape of assisted reproduction is changing. For example, 27% of donors were in lesbian relationships. These women had already embraced the idea of using donor sperm so the notion of giving eggs also made sense to them,” said Gürtin.

Call of the wired

For generations, we have dreamed of machines with artificial intelligence with which we can have real conversations but, despite amazing technological advances, such devices seem some way off. Now researchers at Cambridge are changing the picture, by remodelling the essence of spoken dialogue systems.

Following the death of Steve Jobs, one of many videos which started to circulate widely on the internet showed the Apple Co-founder at a watershed moment, launching the very first Macintosh in 1984. After demonstrating the machine's facility for word processing, design and even animation, the climax came when Macintosh literally announced itself to the world, talking to an amazed audience with synthetic speech before handing back to Jobs and announcing that it was going to "sit back and listen". A beaming Jobs received a five-minute ovation.

How far we seem to have travelled. Modern smartphones are pocket computers that talk to us using speech recognition software, and owners of an Apple iPhone 4S can ask their device about the weather, or tell it to text a friend. Unlike the early Macintosh, this is no slick gimmick using pre-programmed speech on a floppy disk. Machines can listen to us, interpret our words, and respond.

Yet in a sense we have also come less distance than we hoped. An historian of science might argue that the self-aware illusion of intelligent speech that Jobs created back in 1984 met with euphoria because of a vision that is more science fiction than fact. Computing pioneers in the mid-to-late 20th century imagined conversations with far more sophisticated artificial intelligence in the future. They dreamed less of the iPhone 4S, more of HAL from *2001: A Space Odyssey*.

This type of interface remains a distant prospect. Siri, the speech recognition software used in the iPhone, is a system we talk to, but not one with which we converse. Achieving that remains a complex

mathematical challenge and usually throws up new problems with every breakthrough achieved. In this demanding field, researchers at Cambridge have traditionally been leaders. Today, the University's Dialogue Systems Group, in the Department of Engineering, are making more advances than most.

"Siri is a sort of personal assistant," Professor Steve Young, who leads the group, said. "If you ask it a question, it comes back with an answer, but after that you more or less have to start again. We want to develop systems with which you can have a proper conversation."

Such devices are likely to become more necessary over time. The amount of information on the internet is rapidly growing and, before long, it will take more than question-answer interfaces to cut through it. We need systems that are attuned to our needs – in short, we need computers that discuss things.

Young's group, along with an international team of collaborators, are developing one such spoken dialogue system (or SDS), in a European Union (EU) project called PARLANCE. As with some of their earlier work, this is a project which involves statistically modelling a system that talks to humans and learns as it goes. Fundamentally, the idea is not dissimilar to teaching a child new vocabulary, and the shifting set of ideas the words may represent.

Made marketable, PARLANCE would be far more three-dimensional than current systems. Where an existing SDS can, for instance, help house-hunters find properties for sale in a given town, PARLANCE would be able to process a request for a three-

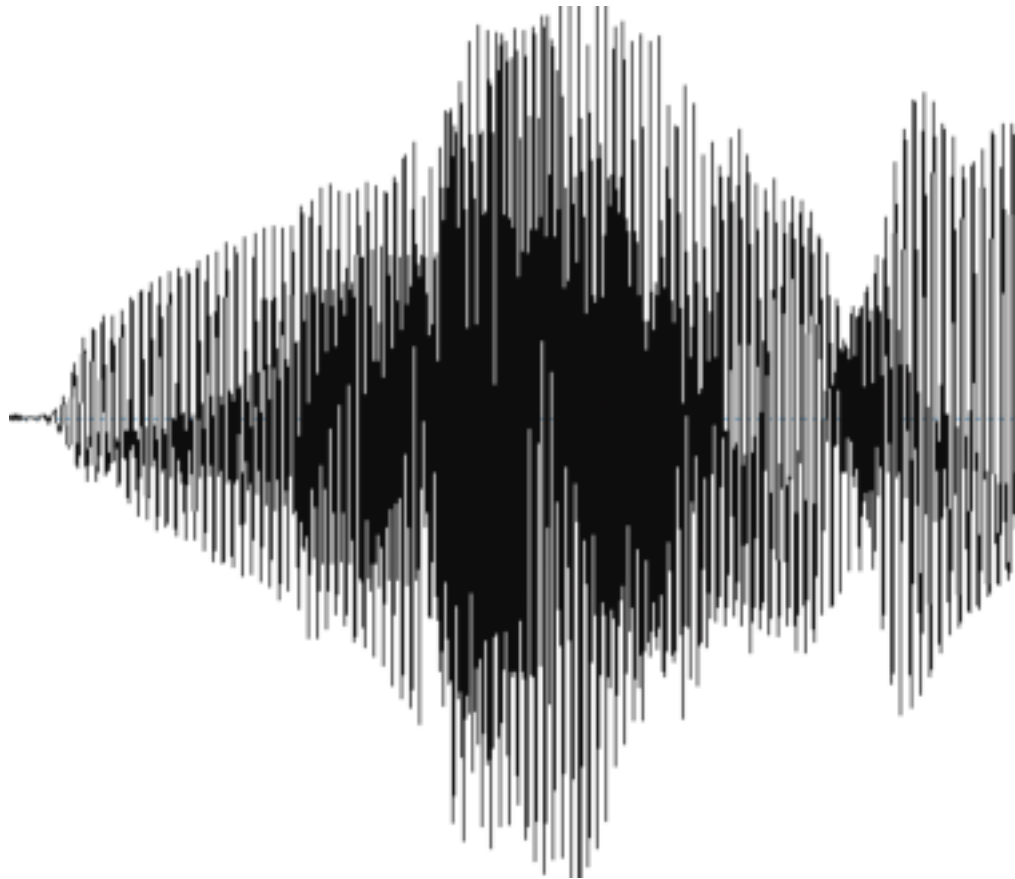
bedroomed house, with two bathrooms, near a good school and within walking distance of the local supermarket. Users would be able to ask it for one of these attributes, then add more to refine their results.

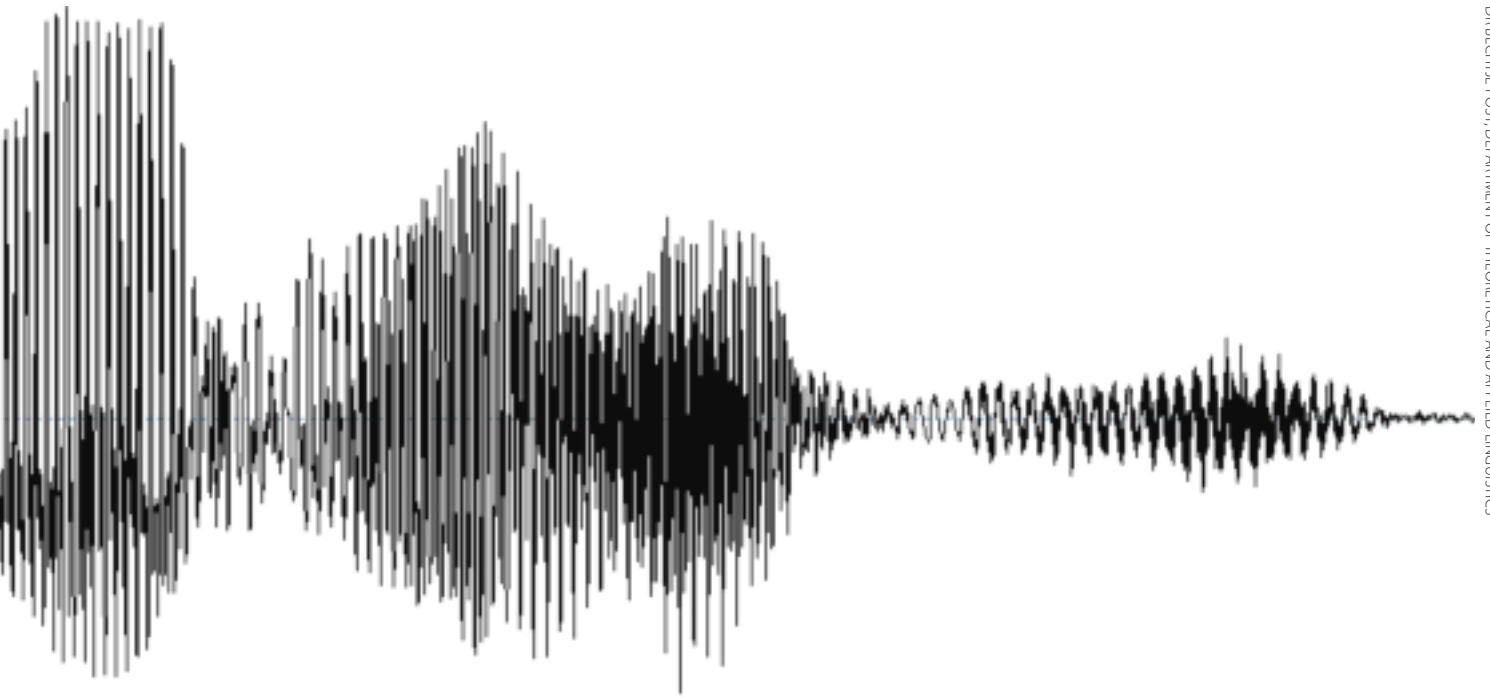
Creating this, however, requires a reconception of how such systems work. A 'cognitive' SDS like PARLANCE has to be able to model uncertainty, or cope with the fact that humans rarely mean exactly what they say. No current SDS is able to handle this, because their modelling is too simple. In existing systems, speech is converted into data, then given to a 'dialogue manager', which tests the data's assorted attributes against an internal database of pre-programmed information, looking for what it thinks is an appropriate response.

"All the systems out there do this on the basis of pre-written programmes," Young explained. "Essentially, the developer programmes the system with a flow chart of possible conversation routes. This is very labour-intensive, and also very fragile. The user can very easily end up in the wrong bit of the flow chart altogether."

PARLANCE is different because, unlike a typical SDS, it refines its responses with experience. Critically, it takes into account not just the last thing its user said, but its overall assumptions about their intentions, their earlier questions, and its experiences from previous conversations. This combined knowledge is merged into a 'belief state' – the system's overall, shifting grasp of what is going on.

Underlying this is an approach called reinforcement learning. The system's decision processes are continually refined depending





on whether it receives positive or negative feedback from users. A high score, for a correct response that gives the user exactly what they need, or a negative score, for useless information, allows it to refine its future behaviour.

In 2008, Young's team launched CamInfo, an SDS that people could telephone to ask about local restaurants, and which was developed in an EU project named CLASSIC. A 2009 demo on YouTube shows the system responding to a caller asking for a Chinese restaurant in a town's main square. There is no Chinese locally, but when the caller then says "What about an Italian restaurant?", the system retains details from earlier in the conversation, and finds an Italian in the same place.

Now PARLANCE aims to progress this by helping users with multiple goals. As with the house-hunting example, it will try to cut through swathes of information online and cope with multiple types of requests in one conversation, rather than a single enquiry about a restaurant.

Young and his team are also developing various new features. These include 'hyperlocal search', which allows the system to focus the conversation on the amenities in the local neighbourhood. The system is also being developed to use and respond to back-channel signals. These are the murmurs and grunts of agreement or disagreement such as 'hu-huh' and 'hmmm' that humans use unconsciously in natural dialogue to orchestrate the turn-taking and flow of information.

Do we really need this stuff, however? After all, it often seems that nothing can

replace real human interaction. Young agrees, but points out that the increasing investment in speech technology by major corporations such as Apple, Google and Microsoft clearly shows that we are heading towards a world of speech interaction with our computers.

Nor is this simply a story about the unstoppable rise of the machines. In fact, it may become one about the empowerment of the Luddites. "Speech is one of the most inclusive media we have," Young observed. "Potentially, speech-controlled systems will enable us to bridge the generation gap in computing. We need to get away from crude systems that require users to constantly learn to push different combinations of buttons, which presents real barriers to some sections of the population such as the elderly. Speech will make complex systems accessible to virtually everybody."

Fluent dialogue systems that can cope with the most subtle aspects of human expression remain some way off – and perhaps we will never be able to chat with computers like our science fiction alter egos. Yet projects such as CLASSIC and PARLANCE are not only incrementally taking us closer to the goal of truly cognitive systems, but they are also changing the playing field by altering the basis on which it will be done. The SDS in your phone requires the pre-existing calculation of a programmer, but future systems will adapt on the basis of the conversations they have with you. Socrates once said that the only true wisdom is in knowing you know nothing. Perhaps the same is now becoming true for machines.

PARLANCE is a spoken dialogue system that not only converts speech (such as recorded in the oscillogram above) into data but refines its response with experience

"We want to develop systems with which you can have a proper conversation."



Professor Steve Young

For more information, please contact Professor Young (sjy@eng.cam.ac.uk) at the Department of Engineering. Information on how to access the Cambridge Dialogue Systems Group demonstration systems can be found at <http://mi.eng.cam.ac.uk/research/dialogue/demo>

CLASSIC and PARLANCE are funded through the European Commission 7th Framework Programme.



Still from the film *The Beaches of Agnès* (2008), directed by Agnès Varda

Death and the image: an introduction to palliative filmmaking

A new book by Professor Emma Wilson from the Faculty of Modern and Medieval Languages looks at how death is addressed through modern artworks based in visual media.

You don't see her slip away, even though you are watching. A woman lies motionless in bed for 13 minutes, attended at intervals by nurses and her daughter – the artist Sophie Calle. Without these intrusions you might think you were looking at a still photograph. By the end of the film clip the woman has moved from life to death, but the point at which she dies remains invisible.

The clip is part of an art installation by Calle called *You Couldn't Capture Death*, which is one of the contemporary artworks explored by Professor Emma Wilson from the Department of French in her new book *Love, Mortality and the Moving Image*. In the book, Wilson's research involves moving image artists who are working with the space between life and death in a variety of ways – from home movies to photographic collages.

Wilson, who is also Course Director of the University's MPhil in Screen Media and

Cultures, examines the way different artists use both moving and still images to generate works as a coping mechanism for the emotional wrench that comes with the death of loved ones – and how we use visual media to see the dead as living, helping to manage the pain of loss.

"I'm interested in artists who are using their own intimate experiences to test how far a moving image artwork can offer recall of the deceased as still responsive," said Wilson. "Art and its creation can be used to organise experience, the editing process allowing a sense of control in the face of brute, annihilating emotions."

"I wanted to investigate moves from family acts of mourning to more public acts – the instigation of dialogue around death through moving image displays. In the case of Calle, the installation was a space that could be entered, opening the private experience up to other views and opinions."



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images of herself and her husband Jacques Demy with moving film footage she took of him during the last months of his life. They knew Demy was dying, and Varda wanted to build a collage of her husband by overlaying different forms of visual tribute.

Varda created a photographic inventory of Demy as he existed – close-ups of his hair, skin, eyes and so on – and blended it with reconstructions of Demy's childhood and extracts from his films to create a sensory impression of the person, the idea of the palliative seen in the attention of the camera to the body and the subjectivity of the person facing death – the same type of respect and tenderness.

The use of photography for direct commemoration that addresses death without flinching dates back to the 19th century, when common memorial practices included mortuary photography, the creation of daguerreotypes depicting the bodies of loved ones as if they are sleeping. For many people, the only pictorial record of their existence came when they had ceased to exist.

Hidden memory

Some argue that photography innately carries the reminder of death by 'stilling' a person – capturing a moment that will never be again. "There is a range of theory around this subject. The theorist Roland Barthes tells us that mortality is inherent in all photography, it creates a 'temporal slip' that draws attention to the emotion frozen in time," said Wilson. "The moving image as a medium however can present the subject as living by depicting action – so that boundaries between living and dead are, if only in illusory form, disturbed."

Bringing the dead 'to life' as it were through moving images is also addressed in the book's analysis of Alina Marazzi's film *For One More Hour With You*, in which the filmmaker reconstructs a vision of her mother through home movies and family photos. Marazzi's mother committed suicide when the filmmaker was a young child, and Wilson explores how Marazzi creates a version of her mother, and develops a relationship with a woman she barely knew through the imagery.

"Home movies have been used in acts of mourning since the earliest available cameras," explained Wilson. "In this work, Marazzi both creates and seeks the kick of hidden memory. As this was recovered footage it gives the illusion of a fresh glance of the dead still living, allowing her to address a part of her past previously uncharted."

"I use Marazzi's film to examine representations of childhood memory in moving images, and how it can be a conduit for emotion, as the filmmaker is introduced through film to her mother as a child, and how this relates to memories of her mother from her own childhood."

The camera can be seen to allow access to the dead as living, or to the trauma of a loved one dying – Calle has said that having the camera in her mother's room as she died was her way of being there in every respect that she could. But the camera can also create distance, reflecting and acknowledging the fact that death is ungraspable.

Alternative narratives

In palliative health care, thought is given to pathways and the stages that one faces. For Wilson, artists exploring this area can offer opportunities to imagine a variety of journeys through the extreme emotions involved in losing people to death.

"It's not about finding a programmatic way of coping through art, but looking at how this kind of work can offer alternative narratives of death – by inviting people to share an example of how one person managed the loss of a loved one."

Visually invoking and describing the dead will continue to be reinterpreted as technologies progress. Today, the images of those we've lost linger in the photo indexes of our smartphones and Facebook pages – testament to the power of the image, moving or otherwise, to prolong the illusion of a living presence, at the same time as it embodies the fleeting nature of all life, by trapping forever a moment never to be recaptured.

"Art and its creation can be used to organise experience, the editing process allowing a sense of control in the face of brute, annihilating emotions."



JACQUELINE GARGET

Professor Emma Wilson

For more information, please contact Professor Wilson (efw1000@cam.ac.uk) at the Department of French (www.mml.cam.ac.uk/french/) in the Faculty of Modern and Medieval Languages.

Love, Mortality and the Moving Image by Emma Wilson is available from Palgrave Macmillan.

Wrapping, soothing, holding

Calle's controversial installation contained details of the last book her mother read, her last trip to the coast and the inscription she wanted on her gravestone. A sense of the active planning for death that mother and daughter went through becomes part of the artwork. In this way, aspects of these artworks could be seen as 'palliative', providing a framework to assist with preparation for eternal separation.

In health care terms, palliative refers to 'end of life' care in which treatment protocols are established and the emphasis is on well-being and dignity as an individual prepares to conclude their life. Artworks like Calle's can be seen to feed into this ethos, regarding death as a natural process that to an extent may be planned for.

Palliative derives from the Latin word 'palliare', meaning 'to cloak'. Moving image art can contribute to this 'cloaking' in a number of ways. Cloaking can be allied with covering, enclosing, wrapping, soothing and holding. One of the works that Wilson gives a close reading of in the book strives for this embracing of a dying loved one through moving and still images – both commemorating and 'cloaking' them with the camera.

In her work *Jacquot de Nantes*, the filmmaker Agnès Varda interposes still

Into eternity: the nuclear waste challenge

How can we make nuclear waste safe for millennia? Fundamental research led by the University of Cambridge will help find the answers.

The timescale for keeping hazardous nuclear waste isolated from living organisms is unimaginably long, with times specified by nuclear regulators in Europe and the USA ranging from 10,000 to 1,000,000 years. Who knows what the human race, or indeed the planet, will be like 40,000 human generations from now.

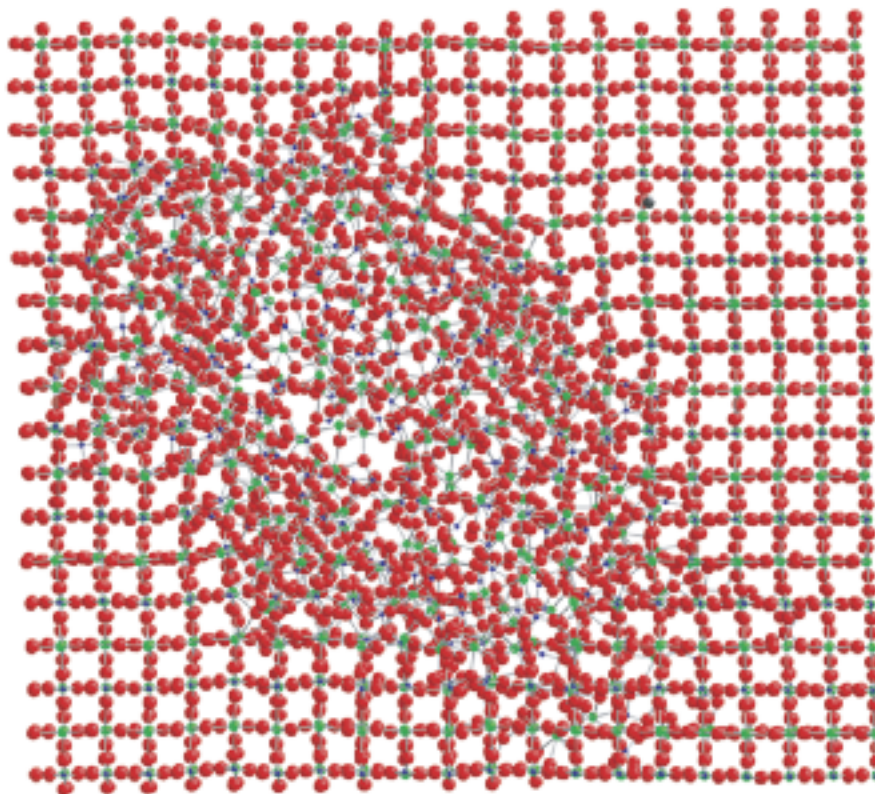
Already, the world's nuclear power plants, which generate around a fifth of global electricity, have yielded in excess of 300,000 tons of high-level nuclear waste, a figure that will dramatically increase in the context of a world nuclear renaissance. Most of the waste is currently stored above ground in spent fuel pools or dry storage. But, as the Fukushima accident in 2011 showed, above-ground nuclear waste storage is vulnerable and there is broad agreement among nuclear-generating countries that the best option is to bury it deep and inaccessibly in the Earth.

Understanding how to keep nuclear waste safe is clearly a considerable challenge, one that new research led by the University of Cambridge aims to help solve through fundamental studies of how nuclear materials behave, and are likely to behave, over massive timescales.

Led by Dr Ian Farnan from the Department of Earth Sciences, the study involves overcoming radiological protection issues to apply state-of-the-art analytical techniques to nuclear materials. These techniques are being used to quantify the atomic-scale interactions producing radiation damage and driving alteration processes.

The project is based on over a decade of pioneering research in which the researchers developed the first system to use nuclear magnetic resonance (NMR) under strict radiological safety constraints to look deep within radioactive material in its crystalline and amorphous forms – a transition that occurs during radiation damage. The new experiments, which are funded by the European Commission, are being conducted at a secure nuclear facility in Germany and will spread this research capacity throughout European nuclear organisations and universities.

Moreover, this new approach will critically test existing models of nuclear waste behaviour and allow regulators to implement sustainable solutions to the nuclear waste challenge through the



When an α -particle is emitted, the daughter nucleus of the emitting atom recoils, causing significant damage, which greatly effects the physical and chemical properties of nuclear waste and spent fuel

development of scientifically robust safety cases.

"We already know that when you look at radiation damage with local atomic-scale techniques such as NMR then you see a lot more damage than was predicted by computer models or conventional measurement techniques," said Farnan. "Swelling of the material is often taken as the first sign of radiation damage. We've found that pockets of damage are produced before swelling occurs and that swelling only really starts when these damaged areas join together. What this means is that the behaviour of the material is not linear – it can change dramatically over the small dose interval when this coalescence occurs."

One particular type of nuclear waste is specific to the UK. Unlike in European countries and the USA, which elected to build a fleet of pressurised water reactors (PWR) or boiling water reactors (BWR), the main reactor type operating currently in the UK is the advanced gas-cooled reactor (AGR). "Traditionally, the UK has reprocessed its nuclear fuel rods to extract and reuse the uranium and plutonium," explained Farnan. "However, due to problems with reprocessing facilities, the government is having to move away from reprocessing of AGR fuel towards disposal in a suitable geological repository. The difficulty for the UK is that much less is known about AGR than PWR/BWR spent fuel."

Now, with funding from the Nuclear Decommissioning Authority and the

Engineering and Physical Sciences Research Council, Farnan hopes to reverse this. "Our aim is to predict the chemical alteration of the fuel for ages between 1,000 and 100,000 years, which spans the lifetime of the disposal canisters," he explained. "By the time a UK geological disposal facility is ready to accept waste, projected to be in about 30 years, we should be able to answer most questions about the long-term durability."

Results of these two research projects will not only enable the researchers to underpin the safety cases for nuclear waste storage with fundamental science but will also have implications for predicting the integrity of radioactive material over millennia.



Dr Ian Farnan

For more information, please contact Dr Farnan (if203@cam.ac.uk) at the Department of Earth Sciences (www.esc.cam.ac.uk/).

Egg Cetera: Nature's paradoxical packaging

The remarkable structural properties of the avian egg can help us to design novel materials, as the scientists involved in a new study explain.



ROBERTO VERZO ON FLICKR

The avian eggshell is curiously paradoxical: it protects the developing chick against physical damage and microbial attack, yet it is sufficiently porous to allow the chick within to breathe. It is constructed to withstand a surprising amount of physical force but is sufficiently fragile to allow the chick to emerge.

How is all of this accomplished? Finding the answer, we discovered, is as important to zoologists wanting to understand how birds break free of the egg as it is to engineers interested in developing new materials inspired by nature.

We have embarked on a collaboration that uses state-of-the-art materials characterisation techniques to determine the fine structure of the eggshell and to relate this to the shell's extraordinary mechanical properties. In doing so, we're spending a great deal of time and effort working to understand a material that is inexpensive and so ubiquitous that many of us encounter it daily.

Our first step was to devise a set-up in the mechanical testing lab to simulate a variety of mechanical challenges an egg might face in a real nest: everything from a poke from a predator's claw to the force applied by an incubating parent. The egg's ultimate task is to remain intact until the chick hatches, and what we're discovering is that it achieves this through a number of finely tuned adaptations that make the avian egg remarkably strong in the face of diverse structural challenges.

One special characteristic of the eggshell is that its physical properties are affected by the arrangement of crystals in the shell's microstructure, a phenomenon we're exploring using mechanical tests and scanning electron microscopy. Another is the shape of the egg, which contributes to its strength. The ends of an egg are similar in shape to a three-dimensional dome – one of

the strongest architectural structures – and our research is exploring how an egg, like a dome, distributes the load evenly to minimise strain.

Another key advantage to studying the avian egg is that it is similar in composition to other natural materials, like tooth enamel and seashell, which are made up mostly of hard and brittle mineral reinforced with just a few percent of protein. The key to the fracture resistance of these materials is in the mechanism by which these two dissimilar materials, protein and mineral, are organised at the smallest of length-scales. Eggshell is unique in that it represents one of the fastest biomineralisation rates known in nature: in a chicken, the eggshell forms completely in under 24 hours.

We want to know how eggshells can form so rapidly yet still possess such impressive physical properties. If we can understand this process, and mimic natural processes such as eggshell biomineralisation, we would be a step closer to being able to provide new models for the creation of robust materials for the engineering industry while leaving a minimal carbon footprint. Natural materials are composites formed in near-ambient conditions, which is quite different from the mechanism by which engineers usually make materials – using high temperatures and pressures. We are also making an eggshell-like material from scratch in the laboratory, tweaking parameters such as the precise temperature of formation of the protein–mineral composite.

A remarkable 150 million years of natural selection on the avian eggshell have engineered a strong, lightweight material that is energetically cheap to manufacture and adaptively fragile when necessary. Discovering exactly how this is accomplished will be of immense interest to biologists and engineers alike.

Egg Cetera: the series

Eggs feature in a surprisingly diverse collection of studies across the University, from cell biology to literature, engineering to earth sciences and archaeology to art history. Find our recent series of articles on egg-related research at www.cam.ac.uk/research/tag/Egg-Cetera/



From left: Oliver Armitage, Dr Michelle Oyen, Dr Rebecca Kilner and Mary Caswell Stoddard (Sarah Greasley not shown) Dr Oyen, Oliver Armitage and Sarah Greasley are at the Department of Engineering (www.eng.cam.ac.uk/); Dr Kilner and Mary Caswell Stoddard are at the Department of Zoology (www.zoo.cam.ac.uk/).

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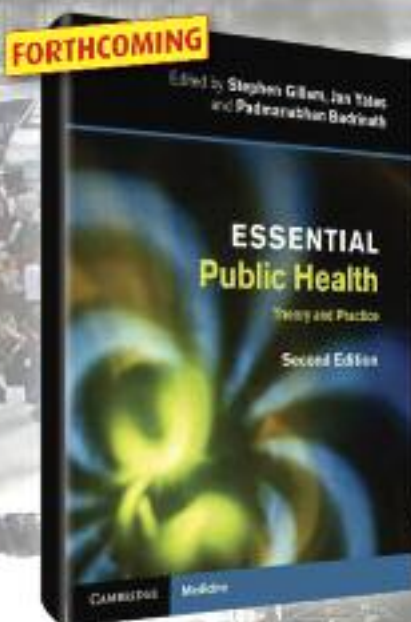
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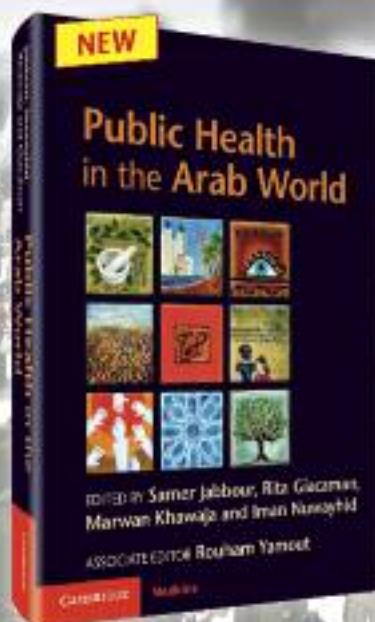
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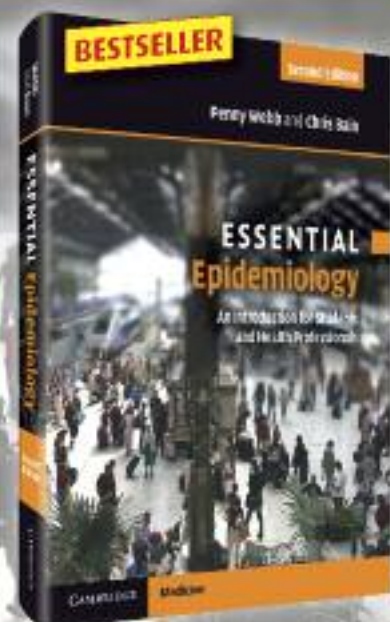
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