Opinion
How we can improve reproducibility in science

Industrial strength research
Working with industry to improve our health and wealth
The UK’s first Dementia Research Institute to be led by the MRC

The UK’s first Dementia Research Institute (DRI) in the UK is to be led by the MRC.

The DRI, which will bring together world leading expertise in discovery science in the fight against dementia, is set to receive up to £150m in funding and be fully functional by 2020.

There are an estimated 850,000 people living with dementia in the UK and this figure is expected to double over the next 20 years. The devastating disease costs the NHS, local authorities and families around £20bn each year but there are currently no treatments available that can stop or reverse the disease. This is primarily because of our limited understanding of how dementia develops.

The DRI will place the UK at the centre of a global effort to tackle the disease, aiming to accelerate the pace of research and develop much needed new treatments. It will fill a gap by linking with the investment already made though the Dementias Platform UK and complement other translational activities funded through the NIHR, research charities and industry.

The DRI will have a central UK hub, which will be networked with the UK’s strongest partners in dementia research already operating across the UK. There is expected to be a strong industry component.

It is great news that the science budget was maintained in real terms in the Chancellor’s Spending Review in November. This is positive in the context of deep cuts across other government departments, and a welcome recognition of the value of investment in research. However, we await details as to how the £1.5 billion Global Challenges research fund, which delivers real terms protection, will be distributed.

The Chancellor also announced that the recommendations of Sir Paul Nurse’s review of the research councils, Ensuring a successful research endeavour: review of the UK research councils by Paul Nurse, would be implemented, including bringing the research councils together under the umbrella organisation Research UK. In a later evidence session to the House of Commons Science and Technology Committee, Sir Paul reiterated his view that this should not be a merger, and that each council must retain its distinct identity, including the right to employ researchers and own research facilities. We now need to understand this new environment and ensure that it can function effectively.

These proposals also align in many respects with our existing Research Councils Together plan to improve administrative efficiency by operating and acting as a single, collective organisation.

This is a time of opportunity, and the profile of research and development is likely to increase. We will continue to work, in partnership with the research councils, to ensure the best possible outcome for the medical research community and for research as a whole.

The MRC will open a competitive process in 2016 asking universities to come forward to host the DRI. Alongside this, the MRC will lead the search for a director.

Professor Sir John Savill, Chief Executive of the MRC said: “Dementias research is an extremely high priority for the Medical Research Council. We will work with our partners, and in particular with patients and their families, to build a vision for the UK Dementia Research Institute based on excellence in discovery science.

We want to attract world-class researchers with new and different perspectives so that we can make real progress in the race to discover the next wave of treatments for dementia.”

UKRMP Annual Report 2015

The UK Regenerative Medicine Platform (UKRMP) has published its second annual report, which details the progress made to date in the £25m initiative since its establishment in 2013 by the MRC, BBSRC and EPSRC. The UKRMP tackles the challenges of translating excellent discovery science in regenerative medicine – which aims to repair, replace and/or regenerate damaged cells, tissues and organs – into treatments that can benefit patients across a wide range of chronic and debilitating diseases. The report shows how the Platform has grown from its establishment phase to being fully operational, with the first fruits now beginning to emerge.

Visit www.ukrmp.org.uk to read the report.
Max Perutz Prize winners and runners up

MRC PhD student Emily Eisner from the University of Manchester won the 2015 Max Perutz Science Writing Award for her outstanding article ‘Premonitions of Psychosis’. Emily, who beat 13 other shortlisted entrants to the top spot, is investigating how smartphone technology may help identify when people are at risk of an episode of psychosis. Her winning article poses the important question: ‘Could monitoring basic symptoms help predict and prevent relapses of schizophrenia?’

MRC Chairman, and competition head judge, Donald Brydon, made the announcement at an awards ceremony at the Royal Institution on 22 October. On presenting Emily’s award, Mr Brydon said: “The quality of entries for the Max Perutz award continues to delight, even if it means that choosing a winner never gets any easier! This year’s winner, Emily, easily surpassed the competition criteria and I hope will continue to devote time to writing as well as to her scientific research.”

In addition to the £1,500 cash prize, Emily’s article has been published on the BBC News website where it has been read more than 80,000 times. The runner-up prize of £750 was awarded to Alex Birks from the University of Glasgow for his article, ‘Espionage, Martinis and Explosions: How Reprogramming Viruses can Help us Fight Cancer’. Commendation prizes of £400 went to Clara Humphston from Cardiff University, Stephanie Shoop from the University of Manchester, and Barry Bentley from the MRC Laboratory of Molecular Biology.

Now in its 18th year, this year’s award attracted an unprecedented number of entries and was run in association with BBC News.

To read the winning article, turn to page 16.

Read more about the Max Perutz Science Writing Award at: mrc.io/max-perutz-award

MRC Festival of Medical Research

Inspired by the MRC’s Centenary Open Week in 2013, the first annual MRC Festival of Medical Research will take place from 18 to 26 June 2016, focused around the locations of our participating MRC-funded units, centres and institutes.

Our MRC Festival objectives are:
- To engage the MRC community to increase understanding of the MRC’s strategic aims and their own contribution to these
- To build trust in medical research by sharing MRC-funded research with audiences
- To increase awareness and understanding of the benefits of medical research to society.

MRC Festival events will include open days, public lectures/debates, workshops, interactive seminars and art exhibitions.

More information can be found at: mrc.io/mrc-festival-of-medical-research

Ground broken by Science Minister on new £16m imaging centre

Clinical research in the UK is being given a helping hand thanks to the construction of a new University of Glasgow-led clinical imaging centre, with completion expected by the end of 2016.

Universities and Science Minister the Rt Hon Jo Johnson MP marked the construction of the Imaging Centre of Excellence (ICE) in October, which will be based at the Queen Elizabeth University Hospital and is supported by £16 million of UK Government funding through the MRC as part of the Glasgow & Clyde Valley City Deal.

The ICE will provide state-of-the-art clinical research facilities, including imaging technologies, such as a £7m 7 Tesla MRI scanner which will enable the development of advanced diagnostic methodologies for use in stroke, cardiovascular disease and brain imaging – and create more than 200 local jobs.

The centre has been built to encourage collaborations between academics, industry and the NHS, with a building layout specifically designed to facilitate the bringing together of these groups.

Mr Johnson said during the traditional breaking-ground ceremony: “As a one nation government we’re investing in this flagship centre and supporting collaboration that will help cement Scotland’s position as a world-leader in research and help save millions of lives in the UK and around the world. Glasgow’s Imaging Centre of Excellence will create jobs, attract global investment and boost the Scottish economy.”

Home office figures on animal research

The Home Office published its annual statistics on the use of animals in scientific procedures in the UK on 22 October, 2015. A ‘procedure’ is a whole programme of work with a specific scientific endpoint and a controlled number of protocols. An EU directive means animals are now counted when studies conclude rather than at the beginning, and figures are gathered on the severity of procedures every animal has experienced. This method should produce a more accurate picture of animal research in the UK.

Home Office chief statistician David Blunt said: “This means that any comparisons made between 2014 and earlier should be made with caution.”

Read more at: mrc.io/animal-research-figures-categorising-severity
Industrial strength research

It was once rare for industry and academic scientists to mix – but developing new treatments requires a much closer relationship between the two sectors than ever before. Sarah Harrop explores some of the ways in which the MRC is working with industry to improve our health and wealth.

Professor Dave Jones of Newcastle University is quite clear on why academic and industry researchers need to work together: “If you’re going to move your science forward to benefit patients, you have to work with industry at some point – because ultimately, drug companies make drugs.”

This is something of which he has first-hand experience. Two years ago, the MRC awarded £3m to a consortium of industry and academic researchers led by Dave. This money, part of a wider MRC investment of £60m in similar commercial pressures. But only to explore such questions without industry” because “that’s what they need, says Richard: “It allowed us to bring people together and say ‘we are supported by the MRC to do this’ – it made us look official and impressive and it got people to believe that we could deliver what we were saying we could.”

Old drugs, new uses
The MRC has led the way in finding new approaches to link up academic and industry researchers. Three years ago, in a pioneering deal with AstraZeneca (AZ), 15 projects were funded in which groups of academic researchers are investigating alternative uses for compounds that are no longer being developed by the company.

Dr Richard Mead’s group at the University of Sheffield was among the first to get involved in the project when it was launched in 2012. They are using a drug originally developed for Alzheimer’s disease by AZ – but subsequently abandoned – for a new purpose, to investigate a cell-signalling process which they suspect is involved in motor neuron disease (MND). Richard says he’s “hopeful” about what they have discovered so far from studies in mice.

Gaining access to AZ’s resources, expertise and toxicity data for the compound has given the group a great head start, and he is confident that it will allow them to get definitive answers to questions they’ve been chasing for many years.

And of course, the MRC has a long history of supporting nascent ideas before they are sufficiently well-established for industry to risk investment. For example, pioneering MRC-funded work on the development of monoclonal antibodies in the 1970s has since spawned a multi-billion dollar global drugs market.

The UK ecosystem offers trial expertise to global pharma companies that can’t be found anywhere else, says Richard: “It is a great way for us to do precisely this.”

Dr Richard Mead is investigating an alternative use for a drug originally developed by AstraZeneca

Six other ways we work with industry

The MRC/Industry Asset Sharing Initiative was launched in 2014 with AstraZeneca, GSK, Johnson & Johnson, Lilly, Pfizer, Takeda and UCB. This gave UK academic researchers access to 68 deprivileged compounds to examine the pathways involved in human disease and find new treatments.

The MRC and Innovative UK Biomedical Catalyst supports bench to bedside research where projects are planned to achieve specific milestones, allowing over 50 new drugs to be tested in people for the first time.

Dementias Platform UK brings together world experts and cutting-edge technology to speed up progress in dementia research and involves six industry partners.

The MRC/UCB Pharma Technology Platform Access programme grants university scientists access to leading technologies to discover new monoclonal antibodies for research and developing new treatments.

The MRC/AstraZeneca Centre for Lead Discovery is a unique partnership giving UK academic researchers free access to AstraZeneca’s 1.9m chemical compound library and associated high-throughput robotic equipment.

The MRC/GSK asthma alliance with Imperial College London is investigating the interplay between allergy and viral infection in acute asthma attacks.
Neurodegenerative disease research receives a boost

Neurodegenerative diseases are one of the toughest medical and economic challenges faced by our society. More than 7m people in Europe are affected by dementia, with care costs of an estimated €130bn each year, and these numbers will continue to grow as our population ages.

The EU Joint Programme – Neurodegenerative Disease Research (JPND) has awarded €35m (£25.7m) for 21 research projects across Europe, Canada and Australia, that will help researchers to better understand, treat and eventually prevent a wide range of neurodegenerative diseases. Nine of these projects involve UK research teams who will receive £2.5m in MRC funds through the JPND initiative.

The JPND was established by European funding agencies, including the MRC, to address the growing societal challenge presented by age-related neurodegeneration, and currently has 30 participating countries.

Director of Science Programmes at the MRC, Dr Rob Buckle said: “These exciting new projects will allow world leading scientists to work together to accelerate research progress and ultimately improve the lives of the millions of people with neurodegenerative disease. We’re proud to help spearhead collaborations across Europe and beyond.”

Read more at: mrc.io/dementias-research-boost

Imanova, a world leader in molecular imaging technologies, announced two successes this autumn. Established in 2011, Imanova is a joint venture between the MRC and three world-class universities: Imperial College London, King’s College London and University College London, benefiting from a state-of-the-art imaging facility developed by GlaxoSmithKline in 2007.

Imanova will collaborate with Imperial College as part of Dementias Platform UK’s (DPUK’s) new imaging network, creating the first nationally coordinated PET-MRI network in the world. DPUK will purchase five PET-MRI scanners, one of which will be installed at Imanova in West London. The combined PET and MRI scans will provide researchers and drug developers with a unique tool to better understand disease progression and to monitor the effectiveness of novel therapies.

Imanova is already involved in DPUK through the pilot phase of the MRC-NiHR Deep and Frequent Phenotyping study.

For more information see: mrc.io/imaging-for-dementia-drug-research

Imanova is also collaborating with Teva Pharmaceuticals and University College London (UCL) on a study aimed at building a better understanding of the role of inflammation – and the central role played by immune cells called microglia – in neurodegenerative disease. Defining reliable biomarkers of microglial activation, and their changes over time, will provide crucial information for developing treatment trials.

Imanova will provide structural and molecular brain imaging with key biomarkers in a study at the Dementia Research Centre and UCL, led by former MRC Clinical Fellow Dr Catherine Mummery.

For more information see: mrc.io/brain-imaging-study

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FUNDING

An international effort to tackle antimicrobial resistance

Antimicrobial resistance (AMR) is a huge and complex problem for healthcare and agriculture. The overuse and misuse of antibiotics has led to a growing number of bacteria that are resistant to them, and it is now estimated that drug-resistant infections will kill an extra 10m people a year worldwide by 2050.

A new international partnership between the UK and China is establishing a £10m joint fund for research into antimicrobial resistance. A workshop led by the funding agencies took place from 24 to 26 November 2015 in China to better understand the landscape for antibiotic resistance research in the UK and China and to explore four core themes that will form the backdrop of the fund.

The fund is supported by the MRC, BBSRC and ESRC, together with the National Natural Science Foundation of China (NSFC). The UK contribution of £4.5m will be channelled through the Newton Fund.

Read more at: mrc.io/uk-china-superbug-research

New health research projects for the UK and India

The MRC has announced the recipients of two major health research partnerships between the UK and India to address substance misuse and its relationship with mental health, and women’s and children’s health.

The Indian Council for Medical Research-MRC joint initiative: Astrology and life-course of substance misuse and relationship with mental illness, will provide £2.5m to fund collaborative research projects on substance misuse and its consequences. The second £5m partnership – the Joint Global Research Programme: Women’s and children’s health – will bring together the MRC and the Department of Biotechnology in India in collaboration with the UK Department for International Development, India Office, to address major health needs of women and children in low resource settings.

MRC Director of International Strategy Dr Mark Palmer said: “Bringing together researchers from the UK, India and low income countries gives an exciting opportunity to use the research strengths of each to address some of the biggest health challenges. Over the coming years we hope the outcomes of this work will make a real difference to some of the world’s most vulnerable people.”

Read more at: mrc.io/uk-india-health-research

PEOPLE

Professor Sheila Bird retires after 35 years

Professor Sheila Bird OBE FRSE, Programme Leader in Biostatistics Research at the MRC Biostatistics Unit (BSU), retired in November 2015. She tells Alison Quenault about her career.

It has been an enormous privilege, and a strong motive, to use statistical science to make a difference to public health. Public and press understanding of statistical science are also very important to me. As statisticians, we are privileged to analyse data about patients, and I believe that people who provide data for research should benefit.

That’s how I’d like to be remembered, as a statistician-scientist who tried to make a difference to public health, by making waves, if necessary.

It’s very difficult to pick out highlights from such a varied career. My PhD research looked at survival in breast cancer, and I developed an approach that was then applied to UK kidney graft survival and guided how kidney donors and recipients were matched in the UK for about a decade.

In 1996, using data from these studies, we showed that random mandatory drug testing of prisoners would severely underestimate the inside-use of heroin.

Drug-related deaths (DRDs) have been a neglected epidemic. My research group at BSU was the first to quantify the high risk of DRDs in the first fortnight after prison release. More recently, we discovered that, for Scotland’s ever-injectors, the four weeks after hospital discharge are also a period of high DRD risk, roughly half the risk that applies in the four weeks after prison release. The MRC-funded prison-based N-ALIVE pilot trial in England, and Scotland’s science-led before/after evaluation of its National Naloxone Policy, have investigated contemporaneously whether take-home naloxone (issued by prisons or in the community) is effective at reducing opioid-related deaths in the four weeks after prison-release.

Days as a biostatistician can be very enjoyable days completely absorbed in conferences. I’ve spent some of my most enjoyable days completely absorbed in designing studies, but it is also quite wonderful when analysis leads to new insights with important implications for the public health.

I’m immensely proud to have received four medals from the Royal Statistical Society. As Sir Austin Bradford Hill was a past director of MRC BSU, I am particularly pleased to have received the ABH medal in 2000 for contributions to medical statistics. Receiving the Howard Medal in 2015, which commemorates the 18th century prison-reformer John Howard, for my research work in prisons is especially dear to me because it was with Graham in 1991 that I began that work.

My advice for future biostatisticians is inspired by two pieces of my father’s advice which have stood me in good stead: “It’s not the wind but the set of your sail that determines the way you go.” (His father was a trawler skipper… but good advice also for study-design!). “Principle is the only thing worth fighting for.” (Scientific method matters hugely; and good scientists are intrinsically principled).

Career in brief

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Inflammation in the brain linked to risk of schizophrenia

Researchers at the MRC Clinical Sciences Centre have found that immune cells are more active in the brains of people at risk of schizophrenia as well as those already diagnosed with the disease.

The team used positron emission tomography (PET) scans to measure levels of activity of immune cells, known as microglia, in the brain. They tested a group of 56 people including those already diagnosed with schizophrenia, those at risk of the disease and those with no symptoms or risk of the disorder.

The results showed that activity levels of microglia in the brain increased according to the severity of symptoms in people with schizophrenia, and that people with diagnosed schizophrenia had high levels of activity of these immune cells in their brain.

The finding could completely change our current understanding of schizophrenia and raise the possibility that testing people most at risk of developing the disorder could allow them to be treated early enough to avoid its most severe symptoms.

Study author Dr Peter Bloomfield commented: “Our findings are particularly exciting because it was previously unknown whether these cells become active before or after onset of the disease. Now we have shown this early involvement, mechanisms of the disease and new medications can hopefully be uncovered.”

3D tumour model replicates oxygen starvation in cancers

Scientists from the MRC Cancer Unit at the University of Cambridge have created a three-dimensional tumour model to study how cancers can survive with low levels of oxygen.

As cancers rapidly grow, the creation of new blood vessels to supply oxygen can’t keep up. This creates an environment where the innermost parts of the tumour have to adapt to survive in these hostile conditions.

Until now there has been no accurate way to replicate this in the lab. Dr Christian Frezza and colleagues at the MRC Cancer Unit and the University of Toronto created their model by coating a thin surface with cancer cells, which is tightly rolled up to create an environment where the innermost cells are deprived of oxygen.

This creates an oxygen gradient that mimics that found within a tumour, providing a glimpse into the implications on cell growth and treatment response.

Commenting on the study, Dr Frezza said: “Our new model allows us to look at cellular metabolism in 3D and to see how a tumour response to low oxygen is tightly controlled and that without this control, cells are unable to adapt and survive. Armed with this knowledge it could lead to the development of new treatments that target these oxygen deprived cancer cells, which can be the hardest to target and destroy.”

New test to diagnose ‘face blindness’

The inability to recognise faces is estimated to affect around 2 per cent of people but there are no conclusive tests to diagnose the condition.

Now, researchers at the MRC Social, Genetic and Developmental Psychiatry Centre at King’s College London have developed a questionnaire that they hope will improve diagnosis of the condition. The questionnaire features 20 items that ask respondents to indicate the extent to which they agree or disagree with certain phrases about their facial recognition experiences.

Explaining the need for the test, lead researcher Punit Shah said: “In its most extreme form, people with face blindness cannot even recognise their family or friends. This can have a disabling impact on their life, including on their career prospects.”

Shah added: “Combining our test – termed the 20-item Prosopagnosia Index – with others will help improve diagnosis of face blindness, helping to remove much of the uncertainty around many existing tests.”

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To verify the questionnaire’s effectiveness it was tested in several validation studies. These showed its ability to detect face blindness and – by comparing questionnaire scores with computerised face recognition tasks – confirmed that people had the necessary insight into their face blindness for a self-reporting test such as this to be effective.

Shah added: “Combining our test – termed the 20-item Prosopagnosia Index – with others will help improve diagnosis of face blindness, helping to remove much of the uncertainty around many existing tests.”
Some people thought I was throwing my career away when I went to Africa. I was a bright student and was on track to become an eminent doctor via the standard pathway when I applied for a registrar position at University College Hospital in Ibadan in newly independent Nigeria. This was 1965 and the hospital was incredibly well equipped then – it was as if Hammersmith Hospital where I’d been working had been transplanted into Africa.

I spent about three years in Ibadan. The Biafran war started during this time and I went from being a junior doctor on a ward with eight doctors to having to help out in paediatrics and the emergency room as many doctors left the hospital during the war. It was a very steep learning curve.

I realised I needed some more research training and came back to the UK. I considered applying to both the MRC and the Wellcome Trust for a fellowship but the MRC wanted lots of forms filling in, whereas I was invited in for a cup of tea with the Wellcome Trust, which then had only a small office in Queen Anne St! I ended up doing a three-year Wellcome Trust fellowship in clinical immunology at the MRC Rheumatology Research Unit at Taplow and at the Middlesex Hospital.

I went back to Nigeria in 1970 to help set up a medical school at Ahmadu Bello University in Zaria. It was very different to Ibadan – the war was over but the hospital was just being established and everything was very run down. I enjoyed it immensely – you had to be a Jack of all trades. We ended up setting up a lab in the kitchen of a colleague. It was in there that we developed the latex test for meningitis, which is still in use today.

It was the seasons in Zaria that dictated the diseases I ended up focusing on. The three-month rainy season brought malaria, but we had to work on something in the dry season too. We had meningitis and cholera epidemics within about a year of arriving in Zaria. These were incredibly challenging but exciting too – I won’t forget making up intravenous fluid in our kitchen lab and testing it on ourselves.

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A ‘smart’ way to spot schizophrenia signs

The 2015 MRC Max Perutz Science Writing Award was won by MRC PhD student Emily Eisner from the University of Manchester. In her winning article she explains her research investigating how smartphone technology might help identify when people are at risk of a psychotic episode.

I am lying on my office floor. Swirling vision and shimmering lights have just begun. These are warnings. I know that if I take painkillers and rest I can avoid the intense pain of a migraine headache. The trick is to intervene early.

My research is not about migraines, but the rationale is the same – you’ve got to spot the signs.

Most people with a diagnosis of schizophrenia recognise warning signs that they are getting unwell – for example poor sleep or increased anxiety. Intervening early can prevent a full-blown psychotic episode. Rather than just sidestepping an afternoon of discomfort, like my migraine, prompt assistance could avoid months of distress.

Each new episode of psychotic illness brings its own fears, costs and risks. Aside from the distress of the psychotic symptoms themselves, the disruption to an individual’s work and social life can be huge.

When you’ve been ill for three months, revealing to your boss that you spent the time tormented by voices from the TV that commented on your every move and commanded you to kill yourself is tricky. What if we could prevent new episodes before they started, using a device that’s always with you?

What if we could prevent new episodes before they started, using a device that’s within reach right now: your mobile phone?

Mind ‘playing tricks’

In the next two years I’ll be trialling a smartphone app called ExPRESS. The aim is to help people track their own warning signs of relapse. It asks them a series of personalised questions every week and sends this information securely to their care team.

If warning signs increase above a critical level, the patient and their team take action to prevent relapse. The mathematics of misery is economic as well as personal, so using an app like ExPRESS could potentially save the NHS millions of pounds.

Three months of relapse is four times more costly than three months of remission. With the average hospital stay costing £12,198, most of the NHS’s £4bn schizophrenia outlay this year will be spent managing relapses.

This is life-saving work – studies have suggested that people with a diagnosis of schizophrenia are 16 times more likely to die by suicide than the general population.

Other researchers have used warning signs to predict relapse, but only one other research group has done this using a smartphone app. I have extended the range of warning signs that people can monitor by adding a group of experiences known as “basic symptoms” to the more commonly recognised warning signs such as anxiety and insomnia.

If you’ve ever had déjà vu – that odd experience where something feels very familiar but you know that it can’t be – you’ll have some idea of what the basic symptoms are like.

One woman I interviewed remembered that before her last psychotic episode the clock on the wall had looked a bit bent for a while. She was experiencing a basic symptom. Another noticed that colours seemed to be a bit brighter than usual. Both recognised that these odd experiences were just their mind playing tricks on them and, importantly, that they might mean they were getting unwell.

“A ‘smart’ way to spot schizophrenia signs”

“Half a picture”

Basic symptoms have already been used to accurately predict the first episode of psychosis. Until now, no one has looked in detail at whether they predict relapse. I interviewed 23 people who had recently had a relapse and asked them about their experiences beforehand.

Strikingly, three-quarters described basic symptoms. Some experienced as many basic symptoms as they did traditional warning signs such as insomnia.

If we don’t ask about basic symptoms, we are only getting half the picture. It’s like monitoring the cholesterol of someone with heart disease but ignoring their blood pressure. The next step is to ask people about basic symptoms as they happen. Memories are imperfect – that’s why some people keep a diary.

Patients will be invited to use the ExPRESS app to keep track of their basic symptoms for six months, so it will be possible to see if those who report increased basic symptoms tend to have a psychotic episode soon afterwards. This is more scientifically robust than simply asking people about what happened last time they got unwell.

It should help me to answer an important question – could monitoring basic symptoms help predict and prevent relapses of schizophrenia?

Of my 421 Facebook friends, the statistics suggest at least four will have an episode of psychosis in their lifetime. They might be your friends or relatives too. Three of those four will have a relapse within five years, with most relapsing a second and third time. That’s five years of disrupted work, interrupted friendships and unwanted hospital admissions.

With early detection and prompt action they could rewrite that story. That is why my research matters – even if it sometimes gives me a migraine.
How we can improve reproducibility in science

Late last year the MRC and a group of partner organisations published a report about the reproducibility and reliability of research, and what could be done to improve them. MRC Deputy Chief Executive and Director of Strategy Jim Smith discusses how the debate on reproducibility offers us the opportunity to improve the way science is done.

From basic discovery science to clinical studies, medical research works. When a new drug saves or extends lives, a new screen permits early detection of disease, or we find a new use for an old treatment, we can be confident in the research journey that got us there.

But things aren’t perfect. For some years there have been rumblings in the scientific community and beyond that all is not well. In 2005, John Ioannidis published a paper in PLoS Medicine provocatively titled ‘Why most published research findings are false’. In it he argued that most study designs will lead to conclusions that are more likely to be false than true.

And sure enough, a report by the Open Science Foundation, published in Science in 2015, described the replication of 100 papers in psychological research journals: 97 of the original studies reported significant results, compared with only 36 of the replications. Some might argue that science is self-correcting, and that the truth will eventually out. But wouldn’t we prefer the truth to come out a little sooner?

A global problem with global solutions

In April 2015 the MRC got together with the Academy of Medical Sciences, the Biotechnology and Biological Sciences Research Council and the Wellcome Trust to organise a symposium on reproducibility.

The report of that meeting concluded that there is no simple cause of irreproducibility. There does not seem to be, for example, an epidemic of fraudulent behaviour. Rather, problems arise from cumulative effects at different stages of the scientific process, from experimental design to the vicissitudes of publication.

There are general areas in which progress can be made. The importance of laboratory standards and quality control cannot be overstated. For example, cell line authentication by short tandem repeat profiling is a simple task and will prevent the use of misidentified or contaminated cell lines.

We should also address bias in experimental design, data analysis and data presentation. Taking a more ‘open science’ approach, in which protocols are pre-registered in advance and journals committed to publishing the results regardless of outcome, could be one way.

This would help to remove practices such as ‘p-hacking’ (choosing when to stop recording data, selecting which variables to use, or publishing whichever statistically significant result you find), or ‘HARKing’ (hypothesising after results are known).

We do not want such efforts to lead to huge increases in bureaucracy, and nor should they stifle creativity or inhibit the pursuit of new ideas – we certainly don’t want biomedical research to become a giant results-verifying machine. But we do want an environment in which conclusions can be trusted and taken forward, and in which negative results of well-designed and conducted experiments are valued in and of themselves.

The role of the MRC

While everyone must accept their responsibilities in the issues of reproducibility, the MRC, as a major funder of medical research, has an important role to play.

We have already made some changes. For example, applications for funding that do not provide enough detail to judge the significance of animal experiments are sent straight back, and our boards and panels are all instructed to look at the content of a paper, not where it was published.

In the future we might consider increased analysis and dissemination of the outcomes of completed grants, to record negative as well as positive results. This is an additional burden on researchers, but it could be a way to promulgate results that otherwise would not be published and to give credit where it’s due. Of course, this would not be allowed to jeopardise the publication of important positive results.

We might also establish additional training, to ensure that cadres of young researchers have a good understanding of the scientific method and statistical analysis, together with guidance in the skills needed to ensure scientific integrity. We are already exploring this with partners including the Wellcome Trust.

Finally, we could also consider supporting research into the scientific method itself.

Further information

Report of the joint symposium mrc.io/1Ty5Qp7
Why most published research findings are false mrc.io/1M9g16
Estimating the reproducibility of psychological science mrc.io/1Ms2TV
Reproducibility: changing the policies and culture of cell line authentication mrc.io/1QDboz
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3D computer illustration of the monoclonal antibody cancer drug cetuximab attacking cancer cells. Cetuximab is a chemotherapy drug, used to treat metastatic colon cancer.