



Delivery Plan 2019

105 years of life-changing discoveries

1913



MRC set up to tackle tuberculosis.

1936



Sir Harold Himsworth discovered two types of **diabetes**, now known as Type 1 and Type 2 diabetes.

1948



MRC scientists developed what is today the **gold standard** for clinical trial design worldwide while testing streptomycin to treat pulmonary tuberculosis.

1953



By noticing that bus drivers were more likely to have a heart attack than bus conductors, Professor Jerry Morris linked physical inactivity to **heart disease**.

1995



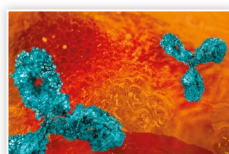
Neurosurgeon Professor Tipu Aziz invented deep brain stimulation as a treatment for **Parkinson's disease**. The therapy is now used worldwide.

1983



Researchers discovered that exposure to **asbestos** increases lung cancer risk, leading to the introduction of new safety standards.

1975-1990s



Researchers at the MRC LMB developed humanised monoclonal antibodies. A third of new drugs in development today are **antibody based** and many diagnostic tests are based on this technology.

1973



Magnetic resonance imaging (MRI) was invented after Sir Peter Mansfield produced images using the natural magnetic properties of cells.

2000



The first draft of the full **human genome sequence** was published, under the direction of Sir John Sulston.

2006



MRC scientists showed that low vitamin D levels during pregnancy increase the risk of **bone fractures** during a child's life. Pregnant women are now advised to take vitamin D supplements.

2015



Research showed that playing a visually demanding computer game after reliving a **traumatic memory** reduces negative memories.

2018



MRC researchers are using **ribosome engineering** to re-write the genetic code.

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1. Foreword

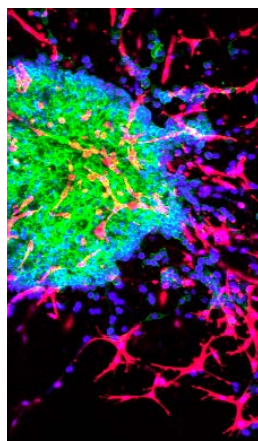
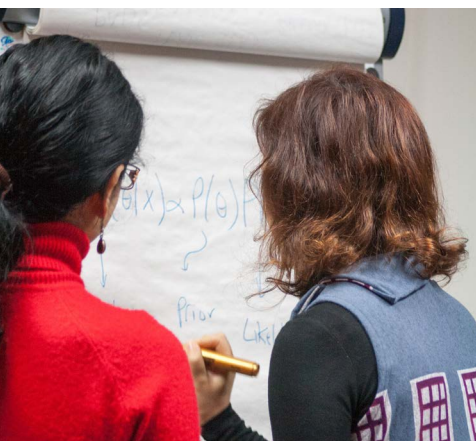


Professor Fiona Watt
Executive Chair, MRC

MRC's mission is to improve human health through world-class medical research, from fundamental science to early clinical trials and preventive medicine. For the good of society, we strive to find better ways to treat and prevent disease and to advance people's health worldwide. Working in partnership with other UKRI councils, the National Institute for Health Research (NIHR) and devolved administrations, the NHS, charities and industry, we are a dynamic organisation continually evolving and embracing new opportunities to achieve a mission first framed over a century ago.

Over the past five years, we have had much to celebrate. Researchers at the MRC Laboratory for Molecular Biology won the Nobel Prize in Chemistry two years in a row. In 2017, Richard Henderson secured the award for developing cryo-electron microscopy, which has produced unprecedented insights into protein structure and function. A year later, Greg Winter won the prize for pioneering work on the directed evolution of antibodies, which has underpinned development of new pharmaceuticals. In 2016, the MRC-funded National Institute for Medical Research became part of the Francis Crick Institute, which houses 1,500 staff and students and, with a budget exceeding £100 million per year, is Europe's biggest single biomedical laboratory.

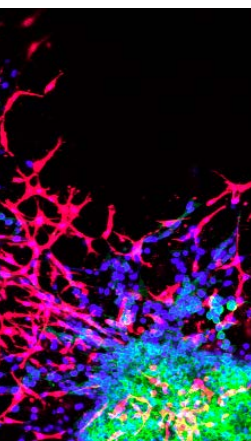
Other collaborative projects have also got off to a great start. These include the Dementia Research Institute and Health Data Research UK, pioneering new institutes with sites across UK universities. It is also a delight to see that 15 years of ground-breaking work and partnership funding are now paying off with global recognition of UK Biobank. This unique resource will improve prevention, diagnosis and treatment of chronic and life-threatening illnesses by monitoring half a million volunteers and providing anonymised health information to approved researchers from academia and industry around the world. Another important development has seen the rebranding and relaunch of MRC Technology as the charity LifeArc, which can now fund more projects and collaborations directly, thanks to income raised through antibody humanisation services for businesses that began two decades ago.



While celebrating these and all our other successes, we must also look ahead. Since joining MRC last year, I have helped launch three initiatives that will drive our activities forward over the next five years: firstly, the Clinical Academic Research Partnership (CARP) scheme provides a flexible, alternative route for skilled clinicians interested in research to partner with non-clinical researchers; secondly, we have consulted our black and minority ethnic PhD students to discover how best to increase diversity in the medical research community; thirdly, backed by UK Research and Innovation's (UKRI's) Strategic Priorities Fund, we have launched a call for proposals in the Human Cell Atlas, a global effort to create a comprehensive reference map of all cells in the body and an initiative that I expect to stimulate more investigator-led research at many levels as the basis for understanding healthy and diseased tissue.

In preparing this delivery plan, we have had valuable input from individual MRC research boards, panels, our Strategy Board and Council. We have held meetings with postdoctoral fellows and scientists from institutes, universities, industry and the health sector. We have shared our plans with colleagues in a broad range of organisations, including the NIHR, Wellcome, Cancer Research UK, the British Heart Foundation, learned academies, overseas funders and a spectrum of industries, including life sciences, diagnostics, and digital companies. Moreover, based on the important input of our PhD students, we are confident that the future of medical research is in capable hands.

I wish to express my sincere thanks to my predecessor, John Savill, to Donald Brydon, previous chair of our Council, to all MRC staff who work so hard for our organisation and to all our researchers for creating a culture that is stimulating, productive and demonstrably successful.



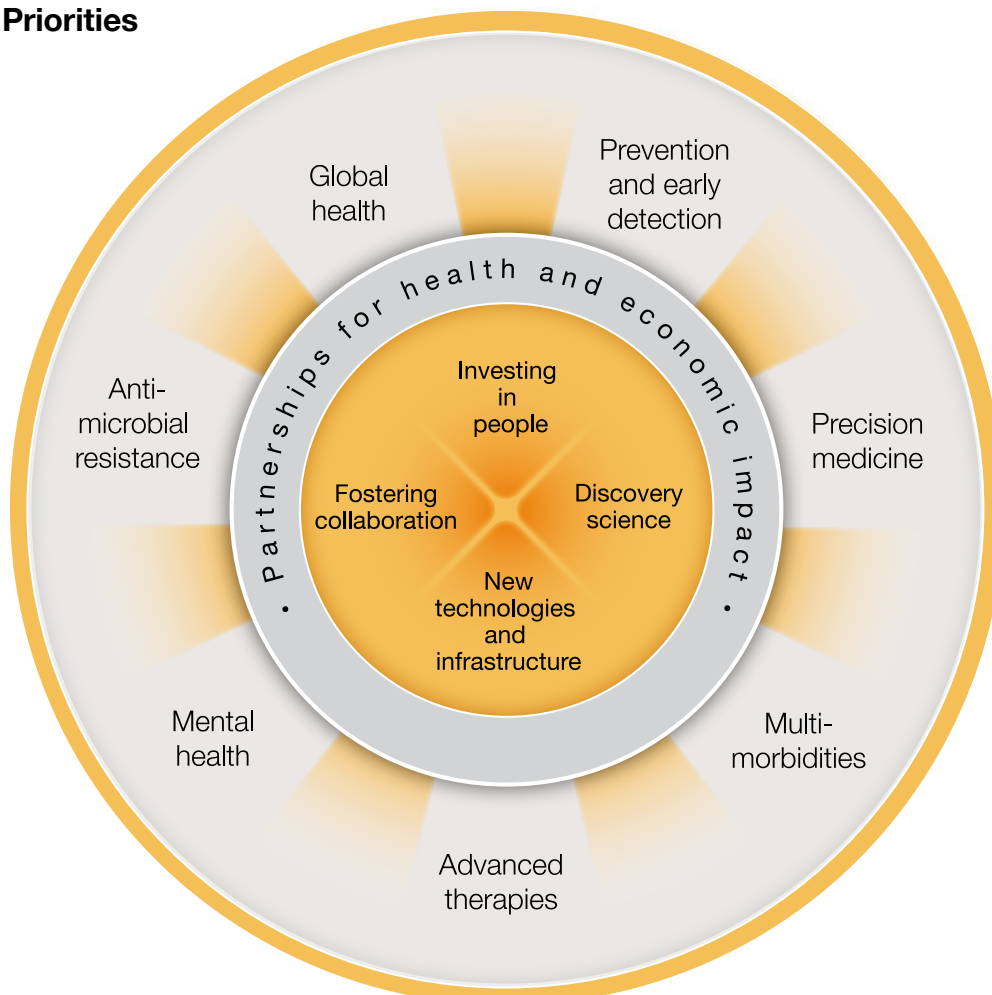
2. Vision and objectives

Health research epitomises the ‘fourth industrial revolution’. It is based on a fusion of technologies across sectors, is data-rich and relies on advances in an astonishing range of fields, from molecular and structural biology to population health. It also requires expertise and discoveries in social science, physics, maths, engineering and humanities. The formation of UKRI therefore creates a special opportunity to accelerate progress and MRC will play a central role in linking across disciplines and developing new partnerships to improve health, building on longstanding UK research strengths. This will be vital for delivering the ambitions of the UK Industrial Strategy to become the most innovative economy by 2030. It will also ensure that we deliver the grand challenges set on meeting the

needs of an ageing society and harnessing the potential of artificial intelligence and data.

Faster progress in medical research and its application depends on good connections between the research base, industry, healthcare and the public. We will continue to make the most of our synergistic and complementary relationship with the NIHR and the Office for Strategic Coordination of Health Research (OSCHR). Other important partnerships are exemplified by Health Data Research UK, NHS Digital and the UK Collaborative on Development Research (UKCDR). Life sciences are a key facet of the government’s Industrial Strategy and we will help ensure the UK stays at the forefront of business research investment worldwide.

MRC Priorities





Our vision is to support excellent discovery science and strengthen partnerships to accelerate impact on health and wealth. Central to this is the translation of MRC-funded research to patient benefit and commercialisation. Looking to the next five years, four foundations for excellence will help us achieve our vision: discovery science, investing in people, fostering collaboration and enhancing access to new technologies and infrastructure. These underpin the health focus themes that constitute our seven strategic priorities, ranging from disease prevention and early detection to advanced therapies. We cannot make progress in any of these without investing in the foundations for excellence, but equally our strategic priorities greatly enrich and inform those foundations.

There are many examples of discovery science leading to major improvements in human health and we highlighted some of them in our 70th-birthday tribute to the NHS¹. Nevertheless, it can be hard to predict how a particular line of investigation will ultimately open up a new therapeutic approach. For example, CRISPR/Cas genes are part of the bacterial immune system, yet they are now being applied to correct genes in devastating human diseases such as muscular

dystrophy. We will continue to invest in the very best investigator-led research in our units and institutes and open-funding calls, aiming to accelerate findings more often and more quickly to impact on health.

We know that outstanding research is made possible by investing in people: outstanding individuals and outstanding teams. We will ensure that research training and careers, in and across academia, industry and the health services, continue to attract and support the best people, fully reflecting the diversity of researchers in the UK and internationally. We will support wider PhD and postdoctoral-level training and more mobility across disciplines and sectors, and aim to accelerate development of advanced analytical and informatics skills in medical research. We will refresh our fellowship schemes to ensure they are optimised for the current research environment and we will strengthen support for team scientists and expert technologists. We are committed to supporting the staff in our offices in Swindon and London, providing more satisfying careers and more opportunities to interact with the research and researchers we fund. We will also pilot new ways to increase diversity in our community and work across UKRI to stamp out bullying and harassment.

¹ <https://mrc.ukri.org/news/browse/celebrating-the-nhs-at-70/>



Getting to know medical research – a public engagement event for the MRC Festival of Medical Research 2018 at the University of Sheffield

We are also committed to ensuring that, no matter where they work, MRC-funded researchers can access the best technologies and infrastructure. Developments in technologies such as imaging have accelerated in recent years and depend on investment in powerful data processing and data storage solutions that will be driven in part by support for the Industrial Strategy Grand Challenge on Artificial Intelligence & Data. But we must also ensure the everyday equipment that scientists rely on is replaced as it ages or breaks. In a recent survey of our institutes and university units, we found that over half of scientific equipment needs replacing. Uncertainty over availability of capital funding hampers proactive management of our investments and poses a risk to research continuity and progress. We will plan for improved capital funding to ensure research facilities remain state-of-the-art and will encourage increased sharing of high-value equipment.

Collaboration, meanwhile, is more important than ever. In the past 10 years, some of our most successful investments have been in MRC centres and precision medicine consortia. Each is a time-limited activity giving us ongoing opportunities to pump-prime strategic new areas and maintain flexibility to re-invest funds in new research areas. We intend to expand these initiatives and

to encourage our core-funded institutes and university units to benefit the wider community. For example, the MRC Protein Phosphorylation and Ubiquitylation Unit runs a highly successful kinase-profiling service that provides reagents to researchers in academia and industry and enables the Unit's PhD students to gain experience of working in the commercial sector.

Our health focus themes are at different stages: some are at the pilot stage, others are well-established but still evolving to fully address complex challenges. For example, for the prevention and early detection of illness, we need to understand the role of many factors such as genetics, lifestyle, diet, environment and socioeconomic status, as well as the underlying pathophysiology. In 2016, we launched the UK Prevention Research Partnership, providing a template for action for major areas of unmet health need, including obesity and its complications, life-long mental health and dementia.

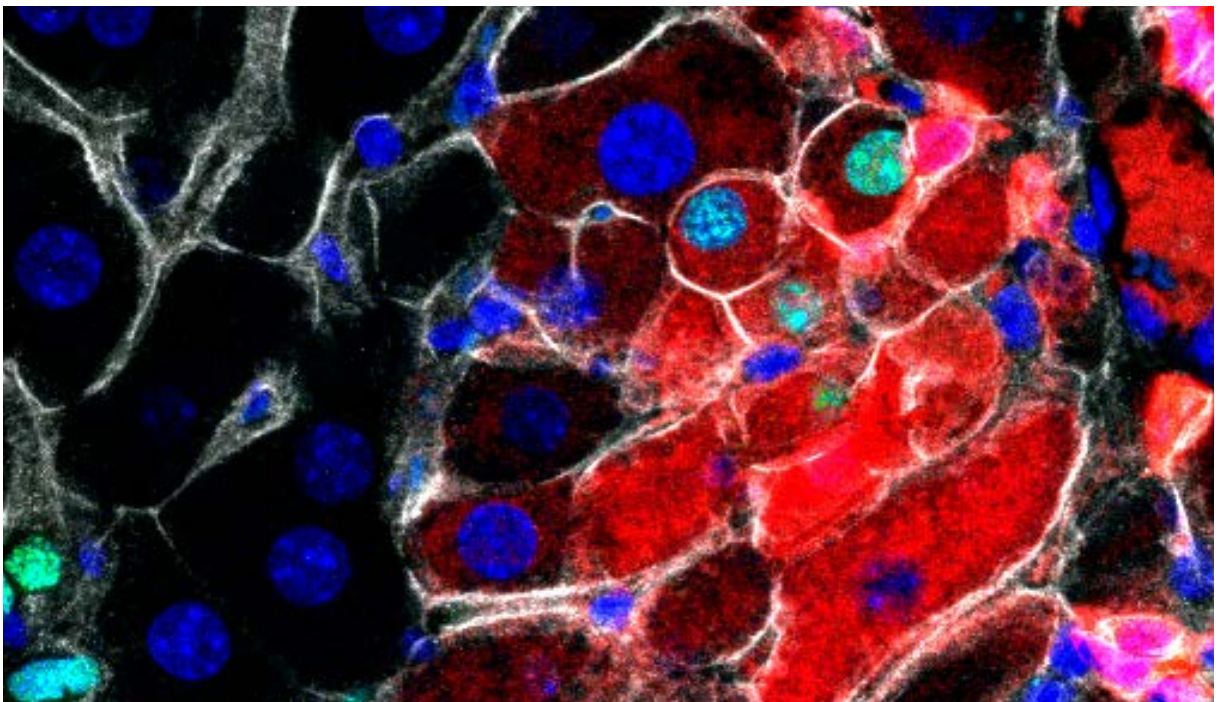
Whole-system research is also the key to managing antimicrobial resistance, an area where we have been active for a number of years, and multimorbidity (the presence of two or more chronic conditions in one person), where we recently launched our first call for pilot funds.

While we have invested substantially in dementia research, we now feel it is important to boost our overall mental health portfolio. Another of our priorities, advanced therapies, builds on many years of supporting fundamental and applied research into gene and cell therapies, and it is now important to explore how best to make and deliver promising new treatments such as gene silencing. Across these areas we will promote research in the human context: in experimental medicine studies, population research and better use of human tissue, advanced cell models and data.

Over one-sixth of our research is oriented to global health. Historically, the emphasis has been on infectious diseases but we now recognise the need to invest more in noncommunicable diseases. We will develop new approaches and programmes that reflect the current and future health needs of rapidly changing populations and economies, supporting more work on prevention, metabolic disease and mental health, and ensuring our work helps build research capability and leadership in developing countries. We will work to ensure countries are equipped with the know-how, data, treatments and technologies to improve their populations' health so that, in partnership, we help develop sustainable health improvement worldwide.

In setting out our vision, we are mindful of several important, welcome, changes in the research landscape. The renewed focus on demonstrable research impact rather than journal impact factor, the rise of preprint servers and ongoing efforts to ensure research and data are made fully open-access are positive developments. We will go further to strengthen the usefulness and reproducibility of our research and accessibility of data. Here a multi-pronged approach is necessary and one of our contributions will be to ensure researchers have access to the training they need in order to properly design and interpret their studies, and have simple, direct access to guidance on methods and protocols.

Finally, a key strength of the UK is strong public support for and participation in medical research. For example, one in 30 people participate in cohort studies, which provide valuable resources for research. We will work to maximise opportunities for patients and other members of the public to engage with new discovery research and help shape our research agenda, with an emphasis on connecting with 'hard to reach' groups from diverse backgrounds across the UK.



Bile ducts differentiate into hepatocytes (red) and proliferate (green) to regenerate the liver. MRC Centre for Regenerative Medicine.

3. Research and Innovation priorities

3.1 FOUNDATIONS FOR EXCELLENCE

3.1.1 Discovery Science

Context

Basic discovery science of the highest quality underpins our impact on health. We see all forms of excellent research as valuable and complementary, whether carried out by an individual in an academic institution or NHS hospital, within our core institutes and university units, or as part of a team. The most fundamental discoveries, often at the interface between disciplines, have the potential for the most wide-reaching impact in the longer term. For example, the isolation of monoclonal antibodies as a research tool to study the immune system in the 1970s is now the basis of a third of all new drugs in development.

What is the appropriate success rate for grant applications? Of course, it depends on the applications' quality. When funding rates dip below 15%, however, there is a risk that arbitrary decisions will be made or that 'safe' topics will be viewed more favourably than 'risky' ones. Our goal is therefore to protect investigator-led funding. At present, budgets are devolved to individual boards and this has worked well for a number of years. But in future we will review the number and composition of the boards and explore the possibility of more flexibly moving funds between them according to quality and public need.

We also want to ensure scientists are not lost at pinch-points in their careers. We already have a highly flexible means of funding where applicants can apply for larger or smaller amounts of support, and we pay particular attention to supporting new investigators. We intend to do more to explain and promote these opportunities and to provide better support during the application process, while encouraging universities to ensure robust mentoring across all career stages.

New and emerging analytical technologies and methodologies offer an exciting opportunity for the biomedical sciences to develop a more integrative and dynamic understanding of biological processes. Our aim is to capitalise on these tools and bring together functional readouts from across different scales (molecular, cellular, tissue, organ and whole-body physiology) and across time to obtain a systems level understanding of biomedicine in health and disease. This will drive a more comprehensive understanding of the causes and progression of disease, identify new biomarkers for early diagnosis and improve target discovery and validation to help combat high failure rates in drug development. Example areas in which we aim to push the frontiers of knowledge are listed below.

Long-term ambitions

- Close the gap between molecular, structural and cell biology to understand the dynamic and functional interplay between molecules and complexes, their interaction with signalling pathways, their spatial organisation and their role in cellular metabolic states
- Develop improved experimental models (3D tissues, organoids and animals) to dissect and manipulate biological systems and provide transformational insights into disease mechanisms. Harness these models to develop new treatments in areas of unmet clinical need such as immunotherapy and regenerative medicine
- Capitalise on the rich molecular and phenotypic data sets from human and experimental systems to promote integration and interrogation of complex multidimensional data, harnessing machine learning and computational models that can be evaluated experimentally in the lab
- Improve our understanding of how the immune system interacts with tissues during homeostasis and ageing, and in diseases ranging from infections to cancer, degenerative and chronic inflammatory disorders

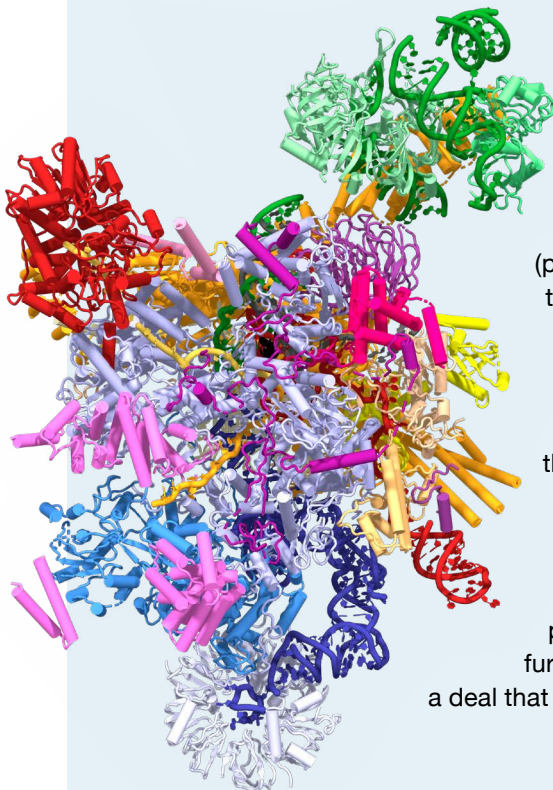
- Strengthen our knowledge of the human brain, including neural and glia cell biology, neuronal circuits and brain function, bridging the knowledge gap between the ‘micro’ (molecules and cells) and the ‘macro’ (behaviour in society)
- Strengthen the development and use of novel analytical, sensing and imaging technologies to improve understanding of biological mechanisms and facilitate in-depth human phenotyping at scale and over time.

Near-term actions

- Consider the balance of funding across our portfolio to ensure appropriate support for high-quality investigator-led discovery science
- Support the UK’s contribution to the Human Cell Atlas programme (£6.9m), delivered with the British Heart Foundation, and help redefine

human cell types in terms of their distinctive patterns of gene expression, physiological states, developmental trajectories and location

- As part of the UKRI Physics of Life partnership (£30m), support new interdisciplinary research programmes that bring together physical and life sciences to further our understanding of living systems and disease
- Step up support through open competition for more ambitious proposals addressing data integration across scales and linking human genotypes and phenotypes using in vitro models, clinical research and population studies
- Work with BBSRC to pump-prime the next generation of cutting-edge research technologies to transform impact on life sciences research (£500k).



Pushing boundaries in structural biology

Now adopted worldwide to advance basic science and drug development, an innovative technique to study the molecular machinery of living things at near-atomic dimensions earned Dr Richard Henderson the 2017 Nobel Prize in Chemistry. Cryo-Electron Microscopy (popularly known as Cryo-EM), which he developed over two decades at the MRC Laboratory of Molecular Biology with other academic and industry researchers, allows us to discover the atomic structure of many important biological molecules in more natural conditions than can be achieved using crystallography. In 2007, Dr Henderson co-founded the company Heptares Therapeutics to commercialise a new technique for studying human disease drug targets that had been too unstable to work on with other methods. Since then, the R&D programme at Heptares has advanced four drug candidates into the clinic and partnered with many pharma and biotech companies to further drug discovery. In 2015, Sosei acquired Heptares in a deal that valued the company at US\$400 million.

P complex spliceosome as modelled by researchers at the MRC Laboratory of Molecular Biology. Spliceosomes are large complexes that cut out sections of an RNA sequence and splice together the remaining sequence. Figures reproduced, with author permission, from Postcatalytic spliceosome structure reveals mechanism of 3'-splice site selection – Wilkinson et al., 2017 Science 358(6368)

3.1.2 Investing in people

Context

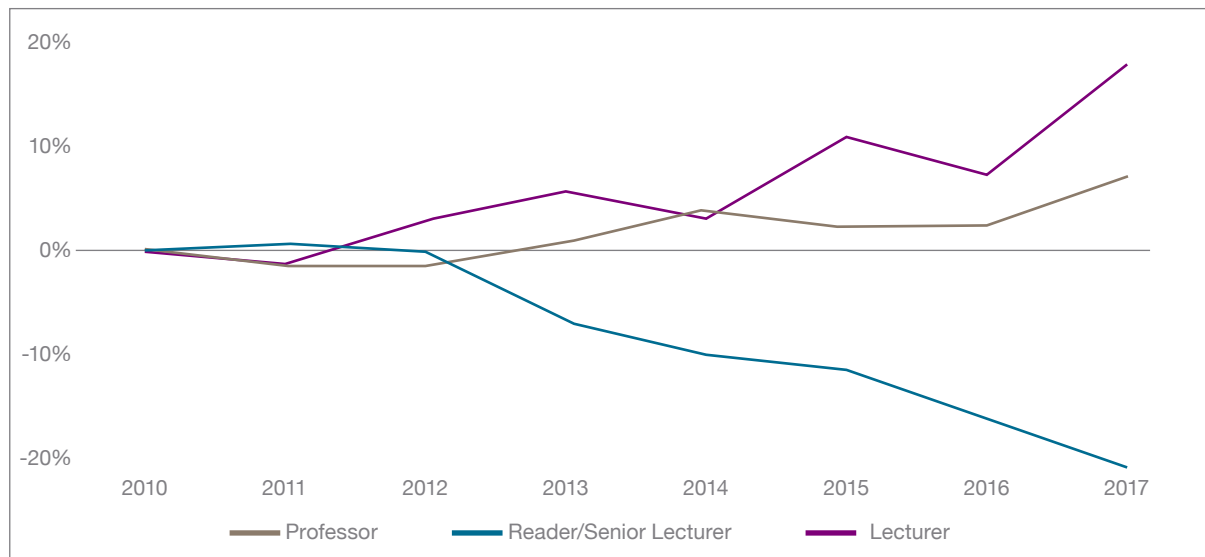
Scientific advances critically depend on diverse perspectives and original, curiosity-driven creative thinking. Training, motivating and developing people in their research careers has long been central to our mission. A highly skilled research base and mobility between academia, clinical practice and industry are essential to the UK's continued leadership in medical research. We are committed to funding outstanding individuals to perform ground-breaking research, regardless of where they work.

Supporting the breadth of research careers, while attracting a diverse range of people into medical research, requires a flexible career structure, porosity between academia and other sectors, and scope for training and development at all career stages. Beyond MRC and UKRI funding, the successful development of talent in the health sector will need alignment of policies across funders and employers, in research and the NHS, and expansion of the number of R&D-based jobs in industry. Our strategy will be to work as a funder and influencer to develop a well-coordinated set of attractive and competitive career paths in universities, hospitals and industry. We will actively promote opportunities and mobility between disciplines and sectors, with an emphasis on promoting the talent in under-represented groups.

Reports indicate that numbers of clinical academic staff employed by medical schools have fallen across the UK since 2010, particularly at reader/senior lecturer level. The number of emerging and established independent researchers holding fellowships has also fallen, with application rates static, despite increased investments at earlier career stages and more NIHR funding for applied research. We believe our new Clinical Academic Research Partnership (CARP) programme provides a novel approach to increase numbers of research-active clinicians while supporting and strengthening clinical engagement of basic researchers. But we anticipate a need for additional interventions and will develop these in close dialogue with the NIHR, the Academy of Medical Sciences (AMS) and others, including novel shared-funding models with universities and industry.

We also want to invest in technologists, building on the findings of the AMS 'team science' review and implementation of a technologist career pathway at some universities. Technologists can be broadly defined as experts in specific fields such as informatics, next-generation microscopy and advanced cell and gene therapies. Providing them with a stable, transparent career structure, with appropriate salary support at different career stages, will enable them to gain independent recognition, promote stability in our world-leading technological expertise and encourage mobility in and out of the public sector.

Summary of change in staffing levels by academic grade from 2010-2017 (FTE). Data taken from the Medical Schools Council report, Survey of Medical Clinical Academic Staffing Levels 2018



Long-term ambitions

- Build high-quality capacity in existing and emerging priority areas, including precision medicine, experimental medicine, diagnostic and data analytics, to drive future industry investment and equip the breadth of the UK research workforce with the required skills
- Grow the number of active clinical researchers in partnership with key stakeholders
- Attract and develop interdisciplinary scientists, particularly those with quantitative and data science expertise, to apply their skills to medical research questions
- Support people flexibly at key stages through research career funding, grants and other means, identifying and addressing bottlenecks and barriers to attraction, retention and progression, and encouraging transition to longer-term positions
- Build capacity and support the development of clear career paths for technologists and team scientists in a range of areas, from advanced analytics, artificial intelligence (AI) and data science through to wet-lab skills such as mass spectrometry and cell culture
- Increase the diversity of individuals pursuing research careers by understanding ambitions and barriers and piloting interventions to promote and facilitate diversity
- Enable researcher mobility between sectors, supporting talented people to move between different parts of the research and innovation ecosystem.
- In the context of UKRI's equality, diversity and inclusion (EDI) strategy, pilot a new initiative with the overarching goal of increasing diversity in the medical research community
- Refresh our existing fellowships and other funding schemes to target key career transition points and support careers in the most effective way
- Set out clear expectations for stronger support of priority skills areas, such as the development of quantitative skills for application to health data, interdisciplinary skills and whole organism physiology in the next rounds of funding for our Doctoral Training Partnerships
- Through Health Data Research UK, support technology specialists, including the development of apprenticeships for NHS data analytic roles. Initiate a review of best practice in 2019, thereby driving creation of transparent, sustainable career pathways for bioinformaticians.



Digital health services informed by public attitudes in social media

Health systems worldwide are looking to online delivery of services and better health data analytics to improve efficiency and effectiveness. Public support and acceptability are essential. Using the National Productivity Investment Fund to build new data-science expertise across all disciplines, we have awarded Dr Lamiece Hassan of the University of Manchester a fellowship with Health Data Research UK to apply new techniques in natural language processing to social media data. This will answer questions about the trustworthy use of health data and investigate how social media data can be used to rapidly and ethically distill insights about changing public opinions on health and care.

Near-term actions

- Pilot the new CARP scheme to provide a flexible, alternative route for research-skilled clinicians to partner with established academic groups (£12m MRC and NIHR). Up to 50 awards will be made in two funding rounds by August 2019
- Launch the UKRI Innovation Scholarship scheme to provide courses and training to meet industry demand, and to fund individual secondments between sectors, to increase porosity and facilitate exchange of ideas and skills

3.1.3 New technologies and infrastructure

Context

We see three challenges in ensuring that when we commit to fund excellent individuals to perform ground-breaking research inadequate infrastructure will not hamper them. Firstly, biomedical research increasingly relies on tools that cannot be made available in every host institution because of their expense, complexity and rapid obsolescence. A good example is proteomics, where mass spectrometers with new functionality and sophistication come to market every 1-2 years. Furthermore, funding for new equipment must go hand-in-hand with funding for highly skilled technologists who can provide training and expertise to support users while keeping at the cutting edge of developments. We are also seeing crossover in areas that were once separate, such as metallomic analysis of tissue sections, spatial transcriptomics and combined mass spectrometry and flow cytometry.

The second challenge is to ensure replacement, when it becomes outdated, of the day-to-day equipment that research depends on. Uncertainty over availability of capital funding poses a risk to research continuity and progress. We will therefore tie capital funding to expenditure. Within UKRI we are developing a long-term roadmap for national-level infrastructure and working to ensure we provide well-coordinated, efficient, sustainable support.

The third challenge, articulated many times, is to support access to and analysis of health data². Here, there must be an emphasis on infrastructure, governance and training. Investment in infrastructures for data science, data management, cloud-enabled platforms, archiving, software and curation services, and computing will need to increase. To achieve this, we will build on our Medical Bioinformatics awards and the formation of Health Data Research UK, whilst continuing to promote data security and good governance and maintaining dialogue with the public about the benefits and challenges of health data research. We will also support access to high-quality human tissue resources, ensuring these are interoperable.

Long-term ambitions

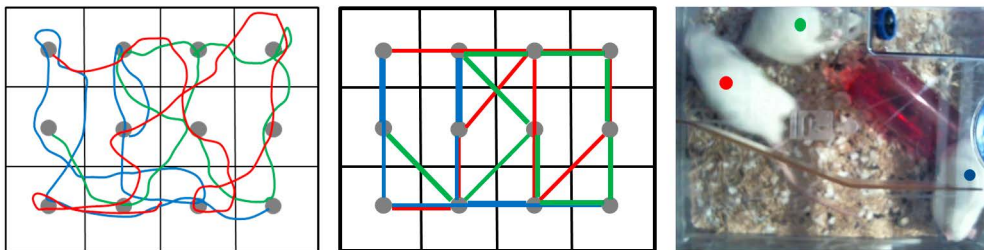
- Support new technology development in discovery science to deliver our vision to understand the dynamic interplay between biological processes across multiple scales
- Ensure that all our researchers, regardless of geography, can access the appropriate tools and technology to support their work
- Ensure outdated equipment does not hamper discovery research
- Continue to strengthen capabilities for informatics and data science
- Work with health departments and research charities to strengthen UK clinical and population research infrastructure. We will place particular emphasis on the growing need for multi-site networks with aligned capabilities in advanced imaging, genotype/phenotype analysis and data science
- Accelerate translation by developing, or co-developing with industry, centres of excellence in emerging health technologies, with robust governance, regulatory and quality management for experimental medicine and early-phase clinical trials
- Continue to provide support services for researchers in areas such as research governance, data or software standards, human tissue banks, best practice in animal research, via the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs), regulatory support and methodological advice.

Near-term actions

- Complete a survey of capacity and needs to inform the development of well-networked, technology-focused centres for biomedical research (for example in proteomics or single-cell analytics) for investment from 2020/21
- Refresh our mechanisms for funding equipment in open-response mode with a target investment of 10-15% relative to resource, along with support for technologists

² <https://acmedsci.ac.uk/policy/policy-projects/use-of-patient-data-in-healthcare-and-research>

- Complete an evaluation of initial outcomes of the 2015 Clinical Research Infrastructure Initiative to inform needs for future investment in partnership with the NIHR, health departments and other funders
- Work via Health Data Research UK with health departments and research charities to strengthen UK capacity in secure data management and analytics, linked to a public dialogue about the challenges and benefits of health data research
- Work with STFC and BBSRC to complete planning for the sustainability of funding for the Electron Bio-imaging Centre (eBIC) at Diamond Light Source beyond 2020.



An automated home cage monitoring system for rats was developed through the NC3Rs CRACK IT open innovation platform. The system allows the recording and analysis of the behaviour of individual rats whilst socially housed in their familiar home cage. The illustration shows the actual movement of the rats/automated tracking of RFID transponder.

UK Biobank reveals drug targets

UK Biobank has provided researchers with anonymised data from half a million people in the UK to help understand the causes and variation of disease. Initially funded by MRC and Wellcome, with contributions from the Department of Health and devolved administrations, this flagship initiative has, since its launch in 2006, set the standard for large-scale population studies, running a decade ahead of the USA's All of Us study, which aims to recruit a million participants. The next step is analysis and release of full genome sequences with funds provided by industry consortia, but already basic anonymised genetic data on links with disease in all participants is being mined for new target genes for drug development. Two 2018 studies underline UK Biobank's importance: one study found relationships of genetic risk for major depression with educational attainment, body mass, and schizophrenia; the second study identified around 500 genes that are linked to high blood pressure, with nearly 200 of these being potential targets for developing new blood pressure medication.



MRC promotes coordination and innovation across a network of biobanks, such as this collection of brain tissue at the South West Brain Bank. Image Credit: Martin Phelps

3.1.4 Fostering collaboration

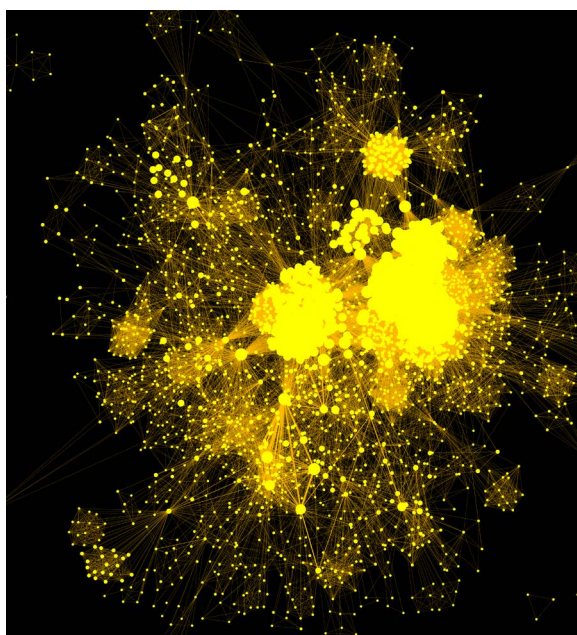
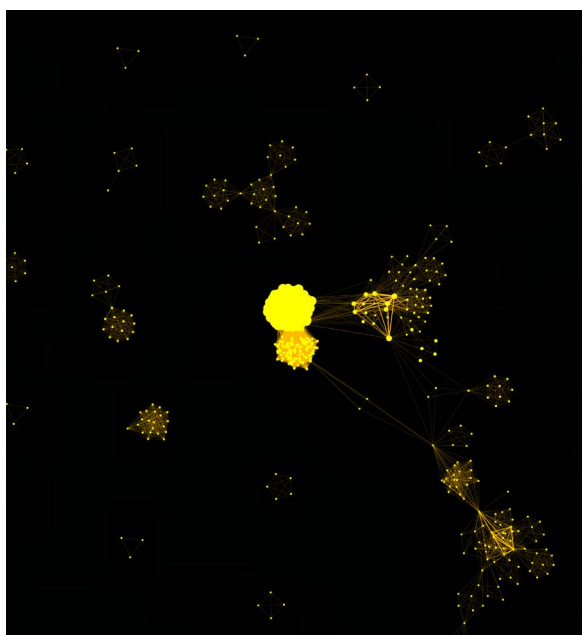
Context

To accelerate research, we need to connect individual researchers with one another, bringing together the right knowledge and skills to address a given question. This applies regardless of whether researchers are laboratory or data scientists, technology specialists or clinicians. Across UKRI, there are now more opportunities to support interdisciplinary research than ever before.

Our portfolio of institutes and units constantly evolves. While these long-term investments have been outstandingly successful, we also need agile ways of responding to new research requirements, increasingly in partnership. We therefore plan new centres and consortia, focused on high-risk but high-gain scientific challenges and on clinical and industry partnerships. Our centres are currently funded for five years, renewable for a further five, and support excellent researchers with a mixed portfolio of funding who come together and are co-located to tackle an important challenge. We will develop this format further, with increased support for team science and technologists.

Our new, multi-funder institutes (Health Data Research UK and the Dementia Research Institute) are based at sites across the UK, with strong networking to link to and support other research groups. These institutes will support the Industrial Strategy aim of developing prosperous communities throughout the UK by developing local skills and expertise and utilising the strengths of other research groups. We will also encourage each of our existing units and institutes to identify ways of adding value to the local community and to researchers who are not within their core funding, such as by providing access to equipment, reagents, training or techniques.

Precision medicine consortia are geographically distributed and have a budget comprising MRC and industry funding with, typically, NIHR, charity and patient involvement. Our investment is of the order of five years and is non-renewable. Increasing this funding route will enable us to build on pilot activity in areas such as multimorbidity and mental health. Precision medicine consortia also facilitate development of innovative public-private partnerships at scale across academia, the NHS and industry in areas of societal need, building on previous successful interventions.



Change in co-author publication networks between the first and final 30-months of the Farr Institute of Health Informatics Research. Each dot represents a unique author and lines connect authors publishing together. Reproduced with permission from the Farr Institute of Health Informatics Research

Long-term ambitions

- Increase investment in centres of excellence with transparent guidance on opportunities for renewal
- Ensure our units and institutes provide added value to external researchers
- Increase funding for precision medicine consortia.

Near-term actions

- Initiate a review of our portfolio of centres, institutes and units to provide expert advice on its evolution during the next decade and to establish key areas of opportunity for new investment in the next spending review period
- Strengthen support for our researchers to facilitate best practice in experimental design, analysis, reproducibility and ethical conduct in research, including an improved portal on our website.

Helping children affected by rare diseases

A healthy child is every parent's top priority. Sometimes when a child is unwell the diagnosis is straightforward, but sometimes the symptoms do not provide enough clues. Through Genomics England, families of children with rare genetic disorders are finally obtaining a correct diagnosis and appropriate support and treatment. Supported through the Department of Health and Social Care (DHSC), Genomics England is the main pillar of the government's strategy to deliver genomic medicine to the NHS. We have provided substantial funding to Genomics England and facilitated collaborative links across the UK. In 2018, Genomics England announced successful completion of its flagship project, which sequenced 100,000 whole genomes from NHS patients with rare diseases and their families, opening up the potential for highly tailored treatments.



Daniel Sone © 2016 National Cancer Institute

3.2 HEALTH FOCUS THEMES

3.2.1 Prevention and early detection

Context

Like many developed countries, the UK is facing a sharply rising burden of avoidable illnesses. Levels of morbidity and mortality arising from obesity and metabolic diseases, mental ill health, cardiopulmonary diseases and cancer are increasing, in some areas alarmingly.

The increasing burden of ill health is not equally distributed across the population. There is a gap of over 18 years in healthy life expectancy between the least and most affluent people in England, rising to 26 years for men and 22 years for women living in Scotland. If we are to continue to meet the UK population's healthcare needs, the traditional model of provision is no longer an option. There is an urgent need to drive forward an ambitious research agenda that shifts the focus from treatment and palliation to prevention of ill health and early detection of disease. This has been recognised for some time and in 2017 an AMS report highlighted the pressing need to address it³.

New insights from biological research into genetic risk and disease mechanisms and new monitoring and diagnostic technologies play an important role in targeting preventive work and enabling earlier diagnosis and action, critical to meeting the Industrial Strategy's Artificial Intelligence & Data Grand Challenge. In cancer and many other conditions, early detection gives a much higher chance of disease-free survival and less invasive treatment with less suffering and disability. Building further on increased capability for vaccine development will also help address global needs for the prevention of infectious and other diseases.

Long-term ambitions

- Continue cross-funder work to develop whole-systems approaches targeting population health and the 'upstream' causes of ill health, building on the UK Prevention Research Partnership (UKPRP). This requires interdisciplinary working and close engagement with users, including local authorities, public health professionals, industry and the public. In the UKPRP, we work with EPSRC, ESRC, NERC, government health departments, Wellcome Trust, the Health Foundation, the British Heart Foundation and Cancer Research UK
- Improve our understanding of food systems, working across UKRI, by investigating the factors that shape diets at the population level and the key levers for change within food systems. The aim is to develop a toolkit of interventions that delivers beneficial dietary change
- Strengthen our agenda in precision prevention, capitalising on the UK's infrastructure of population cohorts, and cohorts in our overseas units, which are increasingly being genetically and biochemically characterised. Augment these measures by building digital phenotypes encapsulating lifestyle factors and environmental exposures. Working across UKRI, this will help develop more precise and informative health-risk profiles beyond genetics, to guide the targeting of preventive interventions
- Shift healthcare from treating illness to pre-empting illness by testing and validating new diagnostic tools at scale, discovering entirely new indicators of disease and disease susceptibility in individuals not yet showing symptoms. Work with partners to explore creation of a large early-diagnosis cohort of highly phenotyped people of sufficient size to detect small changes in pre-symptomatic populations, and in parallel promote public engagement with the opportunities and issues in early prevention.

³ <https://acmedsci.ac.uk/file-download/41399-5807581429f81.pdf>

Near-term actions

- Complete our first UKPRP call for consortia (two or three awards of £4-7m each) and networks (up to six awards) and launch a second call informed by gaps in the first funding round
- Work with UKRI councils and government departments to facilitate a joined-up approach for addressing food systems and future challenges in clean air
- Strengthen prevention research through partnerships developed as part of the UKRI Industrial Strategy Challenge Fund and grand challenges by facilitating whole-genome sequencing of UK Biobank volunteers and driving the accelerated detection of disease
- Through the UK Nutrition Research Partnership, invest up to £2m in fostering new interdisciplinary research, and support early-career researchers to lead on innovative thinking in areas of greatest need.

Football helps overweight fans to slim

A healthy, active lifestyle greatly reduces the risk of illness or premature death, but it is hard to achieve and sustain change across large populations. Football Fans in Training is the world's first randomised controlled trial of a public health programme to be conducted in professional sports club stadiums, in this case to help fans' commitment to lose weight. Men who have taken part lost 5.6kg compared with 0.6kg among those who did not participate in this trial, organised by the MRC Social and Public Health Science Unit at the University of Glasgow and the Scottish Professional Football League Trust. There were also reductions in their blood pressure. First developed with 12 football clubs in Scotland, the programme has been extended to more Scottish and English clubs and the Scottish Government has funded a spin-off for women.



Interactive display to explain the Football Fans in Training programme at the MRC Millennium Medal 2017 event at the House of Commons. Image Credit: James Green.

3.2.2 Precision Medicine

Context

Precision medicine is designed to optimise therapeutic benefit for particular groups of patients based on genetic or other data. It remains an area of rapid growth with great diagnostic, predictive, prognostic and therapeutic potential across many diseases. Given its impact on targeted drug development and the widespread use of genetic testing for clinical decision-making at point-of-care, it is an increasingly important priority both for industry and clinical medicine. At its heart, precision medicine aims to move away from a one-size-fits-all approach to better target interventions to individuals, pre-empting illness in early, possibly pre-symptomatic, stages and avoiding unnecessary treatment and side-effects.

Our partnership programmes in this area coordinate multidisciplinary approaches across clinical research sites nationally, with an agenda co-developed with industry and in collaboration with charities and patient groups. There is also potential to capitalise on the UK's strengths in detailed experimental investigations in well-phenotyped clinical groups and in large-scale clinical studies and cohorts. Advances in computational tools and measurement technologies offer unique, timely opportunities to extract significant new insights on an unprecedented scale to tackle long-term complex diseases and their interplay in multimorbidities in UK and global contexts.



Long-term ambitions

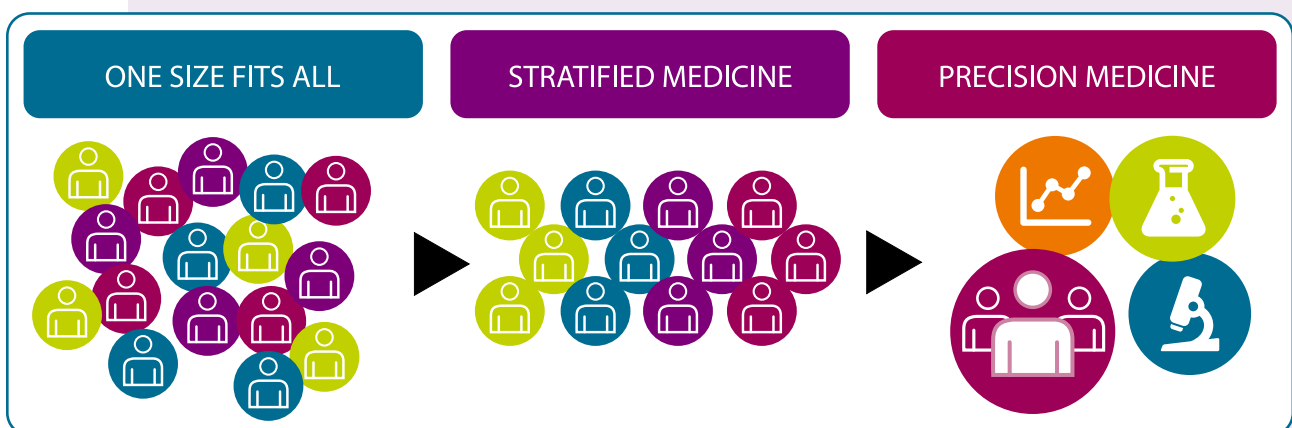
- Identify subtypes of diseases and subgroups of patients where there is potential to gain significant new insight into disease mechanisms, to tackle the most pressing and hardest-to-understand diseases such as mental health and immune-mediated inflammatory disorders, including rheumatoid arthritis and inflammatory bowel disease. Beyond the more straightforward genetic drivers of disease, explore environmental and lifestyle factors and their interplay, such as in cancer where precision medicine is already saving lives
- Identify and understand common mechanisms that drive multiple diseases and disease subtypes, cutting across historic disease classifications that are often based on clinical symptoms rather than underlying pathology. Detailed molecular phenotyping is likely to reveal common mechanisms across diseases and therefore common targets that open up opportunities for new treatments and repurposing of existing drugs
- Detect and understand earlier disease states in order to diagnose and intervene earlier in disease progression or prevent more aggressive disease. Stratification of patient cohorts by risk, progression and prognosis, as well as by response to treatment, will identify when, how and with whom an intervention would be most effective
- Generate new opportunities and facilitate R&D collaborations suitable for a wide spectrum of health industries including pharma, med/biotechnology, digital technologies and medical devices. Better disease definition and understanding, and the ability to target earlier disease stages with good evidence of disease progression and interim outcome measures, will provide strong reasons for industry to invest in UK R&D
- Build clinical and non-clinical capability and capacity in the wide range of expertise needed in precision medicine, experimental medicine, data analytics and diagnostic research.

Near-term actions

- Work with stakeholders to support research aimed at understanding the complexity of pain
- With Innovate UK, implement major strands of the Industrial Strategy Challenge Fund Wave 2 ‘data to early diagnosis and precision treatments’ challenge, establishing up to five digital innovation hubs, and plan investment in collaborative R&D to advance tools for early diagnosis
- Launch a call for proposals with a view to investing £10-15m in new disease-focused precision medicine clinical/industry/academic consortia, targeting more challenging and complex diseases and earlier manifestation of disease
- Invest further in precision and experimental medicine research in dementia through:
 - developing the next phase of the Dementia Platform UK, working with a consortium of 10 companies
 - contributing to a European Joint Programming Initiative with the aim of establishing 10-15 multinational, interdisciplinary collaborative awards in precision medicine.

Precise disease data accelerate new drug for rare illness

A unique collaboration between patients, doctors, scientists and industry has informed the approval and adoption of the first new drug in 20 years for treatment of the rare liver disease primary biliary cholangitis (PBC). The collaboration, led by Professor David Jones at Newcastle University and Professor Gideon Hirschfield at the University of Birmingham, was established in 2013 to better understand why some patients with the disease do not respond to existing treatments, to identify targets for new drugs and to evaluate novel treatments, working with seven companies. Work with industry partner Intercept Pharmaceuticals helped secure US approval in 2016 and UK approval in 2017 for obeticholic acid, making it one of the fastest approvals to date for an ‘orphan medication’ aimed at a rare disease.



Precision approaches will deliver the right treatment to the right patient at the right time, with fewer side effects and reduced costs.

3.2.3 Multimorbidities

Context

Multimorbidity represents a significant and rapidly increasing health, economic and societal burden⁴. Treatments associated with long-term conditions already account for 70% of NHS expenditure and multimorbidity is becoming the norm in the ageing population. With associated and often ineffective use of multiple medicines, the pressure on the healthcare sector is increasing. Moreover, the prevalence of multimorbidity is rising not only in the elderly but also increasingly among those of middle age and younger⁵. Currently, one in four adults is estimated to have two or more health conditions, equating to over 14 million people in England alone, with socioeconomic deprivation contributing to the burden. Historically, clinical trials have focused on single conditions and usually exclude people with multimorbidities.

The ability to exploit large-scale longitudinal, imaging, whole-genome and multi-omic data, coupled with advanced statistical, informatics and machine learning capabilities, provides a unique opportunity for multimorbidity research in the UK and globally. Equally, advances in clinical-trial designs and opportunities to use real-world data can be harnessed to develop more effective interventions.



MRC is working with other Funders to develop a strategy to tackle the global challenge of multimorbidity

Long-term ambitions

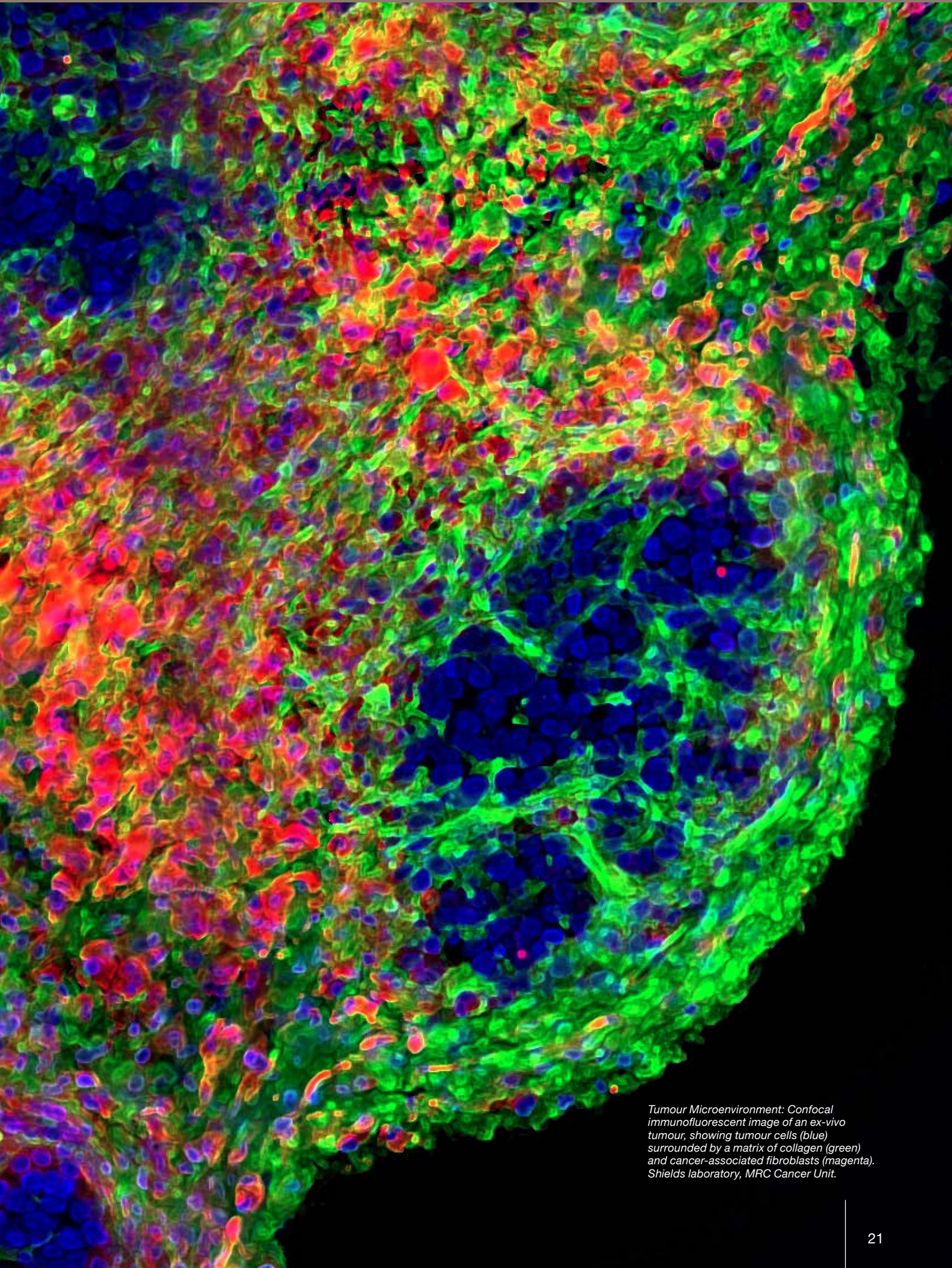
- Identify patterns and trends in disease clusters, building on well-powered, extensively phenotyped epidemiological data
- Move away from a one-disease, one-mechanism approach and understand the common root causes of multimorbidities, the timing and direction of causal relationships and the interactions and variations in biological disease mechanisms
- Take a whole-systems approach to better understand the dynamic relationship within and between biological and social factors linked to multimorbidity. Enhancing classical epidemiological methods with new approaches to complex data collection, and analysis of data sets originating from multiple sources, may point to previously unknown risk factors and/or socio-biological 'tipping points' contributing to multimorbidity
- Build on well-powered, highly phenotyped longitudinal population and patient cohorts, as well as technological advances, to discover entirely new indicators of co-morbid diseases and disease modification in pre-symptomatic individuals. New biological or technological ways of measuring and predicting individual risk, as well as addressing known lifestyle or environmental factors in illness, will allow early intervention and could transform prevention.

Near-term actions

- Build on our joint first-phase call with the NIHR to understand disease clustering in the context of multimorbidity in the UK population, and work with the NIHR and other funders to support further research in this field.

⁴ <https://acmedsci.ac.uk/policy/policy-projects/multimorbidity>

⁵ <https://www.ncbi.nlm.nih.gov/pubmed/29370339>



Tumour Microenvironment: Confocal immunofluorescent image of an ex-vivo tumour, showing tumour cells (blue) surrounded by a matrix of collagen (green) and cancer-associated fibroblasts (magenta). Shields laboratory, MRC Cancer Unit.

3.2.4 Advanced Therapies

Context

Innovations in stem cell engineering and gene editing have led to the generation of a group of therapeutic technologies collectively termed advanced therapies. Some are already transforming patients' lives, such as Chimeric Antibody Receptor (CAR)-T cell therapy in cancer and gene therapy for severe combined immunodeficiency. We expect the scope and effectiveness of such therapies to steadily improve for decades to come as the basic technologies develop and the science of targeting, control and delivery progresses. Advanced therapies have the potential to offer treatments for currently unmet clinical needs, such as muscular dystrophy, and provide new approaches to conditions with a heavy treatment burden, such as haemophilia.

Advanced cell therapies range from stem cell transplantation and promoting tissue regeneration to cell-based immunotherapy to treat cancer. For these to succeed we need to understand the molecular mechanisms that govern behaviour of cells in vivo, such as the tissue microenvironment. Generation of effective cell transplantation protocols requires manipulation, expansion, purification and preservation of the cells to establish robust, standardised cell-product preparations for use in clinical studies and treatment.

Nucleic-acid therapies directly target disease through modifying gene expression (single-stranded oligonucleotides), silencing deleterious genes (double-stranded siRNA/exon skipping), switching-on advantageous genes (mRNA) or directly editing genes (CRISPR). Nucleic-acid therapies (or gene medicines) have significant potential to improve health but also present substantial challenges, particularly in their delivery and the need for specialist manufacturing.

The UK is ideally placed to lead on advanced cell and nucleic-acid therapies due to our strong underpinning research capabilities in academia and industry. Progress has already been made in ensuring that facilities and infrastructure are

in place, for example through the Cell and Gene Therapy Catapult and the UK Regenerative Medicine Platform (UKRMP). Many parts of the research base can contribute to progress, including BBSRC-supported synthetic biology and EPSRC-funded materials science and neurotechnologies. There is also strong support for first in-human studies through MRC, the NIHR and medical research charities. UKRI offers new opportunities to strengthen these links and progress more quickly to commercialisation and clinical use.

Long-term ambitions

- Continue to identify and de-risk the development of new advanced therapies and their underpinning enabling technologies, and develop capabilities in conducting early-phase clinical studies
- Promote research into alternative nucleic-acid targeted delivery methods with enhanced tissue penetrance for currently inaccessible organs such as the brain, and into therapies with decreased immunoreactivity and toxicity
- Nurture emerging technologies and develop critical mass to ensure the UK stays at the forefront of this area
- Build on our collaborative work with the NIHR, charities and UKRI partners to ensure support for promising treatments throughout the development pipeline towards commercialisation and patient benefit
- Encourage scientific engagement with medicine regulators, so that regulations keep pace with innovation while protecting patient safety.

Near-term actions

- Further develop the UKRMP, with investment of £3m with charities, including forming new disease-specific partnerships ranging from diabetes to multiple sclerosis
- Stimulate research into the development of new technologies for nucleic acids, working with academic and commercial stakeholders.

Gene therapy for children lacking an immune system

A UCL team has successfully used gene therapy to treat severe combined immunodeficiency (SCID), where children are born with a defective immune system. During the early development of gene therapy in the 1990s, there were concerns about safety and efficacy. While commercial investment dipped at that time, continued MRC support for the underpinning science maintained critical capability and UK research groups are now at the leading edge of gene therapy. MRC, Wellcome and NIHR-funded work at UCL has made significant progress to date in treating rare childhood immune diseases including SCID. Led by Professors Bobby Gaspar, Adrian Thrasher and Waseem Qasim, the team has successfully treated over 50 SCID patients using gene therapy, permanently freeing them from weekly injections and saving the NHS millions of pounds. Orchard Therapeutics, a spin-out based on this MRC-funded work, has raised over £200 million as of 2018 and has four therapies at various stages of clinical development.



Professor Gaspar and Teigan, who received treatment for severe combined immunodeficiency (SCID) at Great Ormond Street Hospital (GOSH). Image credit: GOSH



This image of a retina shows areas of increased pigmentation following the transplantation of stem cell-derived retinal cells. Image Credit: The NIHR Biomedical Research Centre at Moorfields and UCL.

Reversing blindness with cell and gene therapies

Patients with the most common age-related cause of blindness, wet age-related macular degeneration, had their vision partly restored using implants derived from human embryonic stem cells in an initial trial led by Professor Pete Coffey at UCL, reported in March 2018. Professor Coffey has received funding from MRC since 2004, when he first discovered that embryonic stem cells could be converted into retinal cells. Patients with inherited forms of blindness receiving another pioneering treatment, this time using gene therapy, have also benefitted after sustained MRC funding for research by Professor Robin Ali at UCL. Spin-out MeiraGTx already has clinical trials under way for four different forms of inherited blindness.

3.2.5 Mental health

Context

Mental health problems pose a major societal challenge, with depression the leading cause of disability worldwide. In the UK, poor mental health costs the economy £70-100 billion per year. Three-quarters of mental disorders first emerge during childhood and adolescence and an estimated one in six adults is affected by mental illness each year. People with serious mental illness have significantly lower life expectancy. Furthermore, addiction and substance abuse have devastating effects on lives and communities, with young people particularly vulnerable. Despite the burden of disease and unmet clinical need, drug development in neuroscience and mental health has declined in the last decade and there have been no new effective types of treatment for over 30 years.

Mental health and illness stem from a complex interplay of biological, psychological, social and environmental factors that influence risk and resilience to illness and response to treatment. A multidisciplinary approach to mental health research is therefore needed.

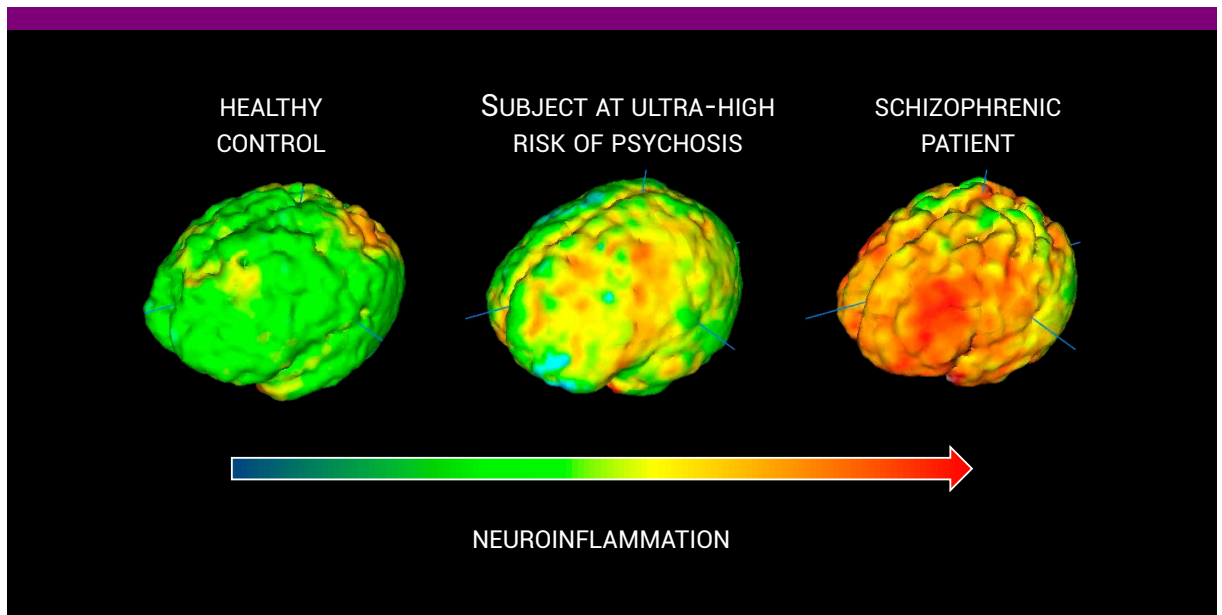
Long-term ambitions

- Gain a comprehensive understanding of the major biological, social and environmental risk factors for mental health disorders, placing a particular emphasis on neurodevelopment and the transition from childhood through adolescence into adult life. Employ a holistic approach across the brain-mind-body interface, characterising interrelationships between the immune system, metabolism and physical conditions co-morbid with mental health disorders
- Develop new ways to detect and measure mental health disorders, incorporating novel technologies to enable evaluation in a home environment
- Develop effective early interventions for child and adolescent mental health disorders

- Strengthen the prevention of mental health disorders that start in childhood and adolescence by incorporating whole-system approaches
- Establish a national infrastructure for mental health research, consolidating existing investment into a comprehensive data platform embedded within existing informatics infrastructure. This will foster multidisciplinary across psychiatry, psychology, neurology, cognitive and developmental neuroscience, bioinformatics, genetics, immunology, social sciences and population health sciences
- Advance mechanistic understanding by exploiting recent developments in psychiatric genetics, immunopsychiatry and cognitive neuroscience. This will identify new drug targets that we will de-risk through new industry partnerships involving experimental medicine and early-phase clinical studies delivered by a precision mental health platform
- Support research and partnerships that will develop digital technology solutions for mental health, such as low-cost wearables, smartphones and virtual and augmented reality, to diagnose, monitor and treat mental health problems
- Scope a major new UK flagship investment in mental health research that will build on current investment to provide international leadership.

Near-term actions

- Building on Mental Health Data Pathfinder awards and working across mental health and health data-science research communities, work towards establishment of a mental health research platform in partnership with other funders, the NHS and industry partners
- Work with ESRC, AHRC and government departments to strengthen multidisciplinary research into adolescent mental health.



PET imaging shows increased activity of microglia, which act as immune cells in the brain, with increased severity of schizophrenia symptoms. Figure adapted from work by researchers at the MRC London Institute of Medical Sciences: Microglial activity in people at ultra high risk of psychosis and in schizophrenia: an [11C] PBR28 PET brain imaging study – Bloomfield et al., 2016 American Journal of Psychiatry 173(1).

Collaborative science pursues new leads in schizophrenia

The MRC Centre for Neuropsychiatric Genetics and Genomics at Cardiff University, working with a global consortium, has identified 50 new gene regions and confirmed 145 in total that increase the risk of developing schizophrenia. The largest of its kind, this study examined genetic data in 100,000 people including 40,000 with a diagnosis of schizophrenia.

It also found that some of the genes identified as increasing risk of schizophrenia have previously been associated with other conditions such as intellectual disability and autism spectrum disorders. The study has provided evidence of the complex genetics of schizophrenia and common genetic factors across mental illnesses. Ongoing research into the mechanisms of action will pave the way for new treatments.

3.2.6 Antimicrobial Resistance

Context

Antimicrobial Resistance (AMR) poses a global challenge to human health, animal health and the environment. It is estimated to cause 700,000 deaths each year worldwide, a figure predicted to rise to 10 million by 2050 if no action is taken. The Organisation for Economic Cooperation and Development (OECD) has estimated that 2,120 people die each year in the UK due to infections with drug-resistant bacteria; without intervention this will rise to 90,000 by 2050, with associated healthcare costs of US\$3.8 billion.

Overuse and misuse of antibiotics has led to a growing number of bacteria in humans, animals and the environment that are resistant to life-saving antibacterial therapies. AMR is driven by a complex interplay of biological, economic, cultural, environmental and technical factors that can allow resistant organisms to emerge and spread rapidly from one country to the next. Tackling AMR therefore requires a coordinated interdisciplinary and international approach, working with policymakers, practitioners and industry, to develop and implement effective actions.

Working with 20 other funders as part of the UK AMR Funders Forum, the cross-UKRI programme has created a network of research projects in the UK and internationally. We will develop this programme further, with more complete analysis and modelling of spread and control options. Together, these projects will support development of new therapies and diagnostics, provide insights and interventions to prevent infections and the spread of AMR, and protect existing antibiotics.

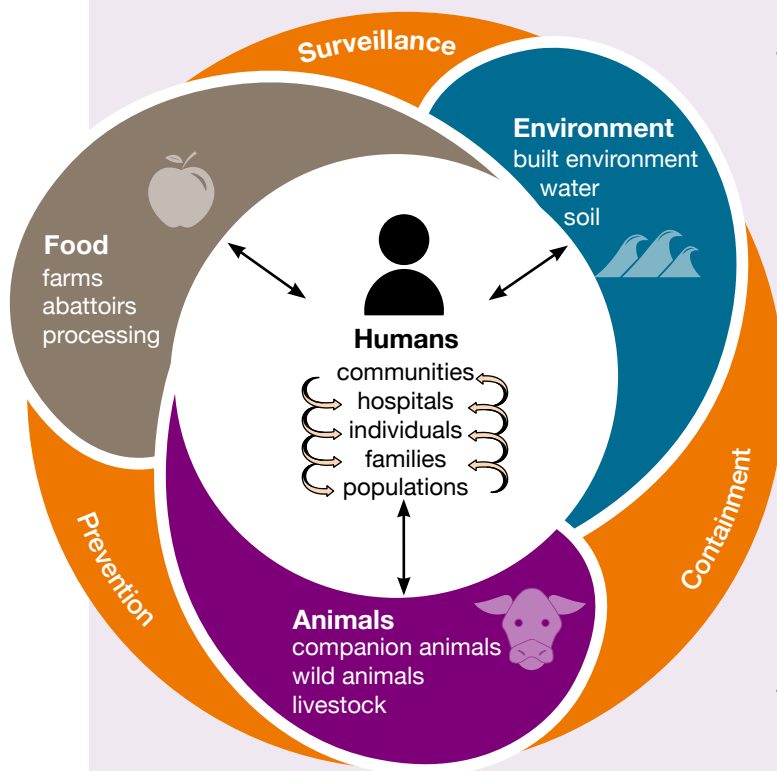
Long-term ambitions

- Contain and control the threat posed by AMR by:
 - closing gaps in our understanding of the emergence, amplification, spread and impact of AMR within and between environmental, animal, food and human domains
 - integrating studies across disciplines and domains to develop robust predictive models of the threat, allowing identification and prioritisation of tractable, cost-effective points for sustainable intervention and action. These include models of health and food systems that are less reliant on antibiotics and that provide improved health and food-security outcomes
 - developing and evaluating innovative targeted interventions and actions, establishing coordinated programmes and capabilities that bring together intervention developers, policymakers, industry and users
 - working with UK, regional and global efforts to minimise duplication and capture benefits of scale and scope, and with international research and policy partners to develop context-dependent solutions for mutual benefit
 - building capacity and capability in interdisciplinary AMR research in the UK and overseas
 - expanding efforts beyond the current focus on antibacterial resistance to include anti-fungal, anti-viral and anti-parasitic resistance
 - continuing support for fundamental research as a critical source of insight and potential avenues for intervention.



Near-term actions

- Working with UK partners, review the strength and completeness of evidence on emergence and spread of resistance across humans, animals and the environment, and define the next steps needed in research and knowledge transfer for predictive modelling of prevention and interventions
- As part of collective UKRI strategy work, review international progress in discovery science, industry partnerships and translation underpinning new diagnostics, vaccines, antimicrobials and alternative interventions, to shape funding for discovery and innovation research and training from 2020 onwards
- Support development of the implementation roadmap of the Strategic Research and Innovation Agenda of the Joint Programme Initiative in AMR (JPIAMR)
- With Newton Fund support, £2m matched by South Africa, establish a joint UK-South Africa antibiotic accelerator, linking and supporting UK and South African research and drug-discovery strengths to target resistant bacterial priorities of low and middle-income countries.



Helping lower-income countries to combat superbugs

In partnership with DHSC, we have launched an initiative to find the primary drivers of resistance to antibiotics in low to middle-income countries by backing four interdisciplinary consortia that foster engagement between national research and policy partners. For example, one consortium, led by the University of Glasgow's Professor Ruth Zadoks, will support the National Action Plan for AMR in Tanzania, harnessing anthropology, economics, genome sequencing and human and veterinary medicine to understand the social, cultural and economic drivers of antibacterial use and the main sources of resistance in different communities. Working with Tanzanian research and policy partners, the consortium seeks to deepen understanding of opportunities for, and barriers to, responsible use of medicines in human and veterinary healthcare. This will help guide policy and practice to achieve sustainable use of antibiotics both in people and in the livestock on which communities depend.

Inappropriate use of antibiotics has led to an increase in bacteria that are resistant to life-saving antibiotics. This illustration depicts the complex interplay between different sectors, the potential sources and routes of transmission of resistance, and activities required to protect human health.

3.2.7 Global health

Context

Global health research is a well-established part of our work. It has delivered major impacts in effective and affordable responses to HIV, malaria and other infections. Increased government support for research to improve the health of people in low and middle-income countries has enabled us to double our global health expenditure to more than one-sixth of our annual total spend, including contributions from the UK Department for International Development (DFID) and the government's Newton Fund and Global Challenges Research Fund (GCRF).

Our aim is to address the most important health challenges, providing evidence for how to improve health and how best to translate research evidence into practice. We develop and implement our global health strategy within an extensive network of partnerships, including multinational initiatives, such as the Global Alliance for Chronic Diseases and the European Developing Countries Clinical Trials Partnership, and UK partnerships including programmes with DFID, ESRC, DHSC and Wellcome. Our units in The Gambia and Uganda also represent long-term MRC investment in global health. These activities deliver on the UK's commitment to international development whilst exploring research questions that are relevant worldwide.

Long-term ambitions

- Continue our approach of funding the spectrum from fundamental science through to applied health systems research. This includes basic research, for example where diseases are particularly endemic in low-income countries, pragmatic effectiveness trials in real-world settings and research into the improved and systematic implementation of interventions
- Increase our investment in global health research capacity-building. We will work in partnership with research institutions and funders globally to establish skills and capacity that are sustainable and driven by the needs of the local research and health context

- Diversify and integrate health topics. While global infections have been a longstanding priority and remain a key part of our portfolio, we will invest in a broader range of health topics, reflecting shifting burdens of disease globally. These include work on mental health, cancer, nutrition, chronic noncommunicable diseases and the complex interactions between diseases during life. Having developed new areas through calls since 2015, we will ensure ongoing response-mode funding is available across all these areas
- Form new multidisciplinary and cross-sector links. To achieve an impact on public health outcomes it is important to consider wider determinants of people's health status and the context in which they live. We will work with colleagues across UKRI on programmes addressing the interrelations between health and socioeconomic factors, food and agriculture, environmental change and culture, and we will encourage wider NGO, charity and private-sector participation.

Near-term actions

- Continue diversification of our global health research portfolio with strategic investments in:
 - global maternal and neonatal health with the NIHR (£10m in three calls)
 - nutrition and noncommunicable diseases in low and middle-income countries (£7.5m)
 - global mental health (£15m)
- Engage with global partners to gather evidence to develop our programme for research capacity-building in low and middle-income countries for implementation in 2020-21
- Work with 14 other global research funders in the Global Alliance for Chronic Diseases to develop a clear business plan for strategic investment in research to tackle chronic noncommunicable diseases, leading to the launch of a new joint call within the next 12 months supported with £3m MRC investment
- Lead work on behalf of other UK research councils to tackle intractable and multifaceted global health challenges. This includes leading the £20m UKRI GCRF health and context call with grants starting in March 2020.

New vaccine helps children to survive pneumococcal disease

A study of 14,650 children by the MRC Unit The Gambia at LSHTM has demonstrated the benefits of introducing pneumococcal vaccination in a low-income country. Use of the new vaccine PCV13 in The Gambian Expanded Programme on Immunisation more than halved serious health problems that arise from pneumococcal infection, notably pneumonia, sepsis and meningitis. Children in The Gambia who develop serious pneumococcal disease have a one-in-seven chance of dying, so the vaccine will save lives as well as reduce the economic burden on the health system and families. The project was carried out in collaboration with the World Health Organization, The Gambian government, Pfizer and Gavi, the Vaccine Alliance.

Physician administering vaccine to a child at a clinic at the MRC Unit The Gambia at LSHTM.



3.3 PARTNERSHIPS FOR HEALTH AND ECONOMIC IMPACT

Our partnerships with R&D activities in industry are vital to achieving a major impact on health. Many important changes need three-way alignment across industry, the health systems and the research base. We also achieve our objectives via strong international partnerships.

National partnerships with the health sector and industry

We will continue to work closely with health departments and charities to explore future research needs, develop strategy and assess the impacts of our research. We will work together to support clinical research infrastructure, health-data resources and effective clinical research career paths. Over the next five years we will continue working in concert with the NIHR, devolved health administrations and charities to:

- increase the numbers of research-active health professionals and the time and support available for their research
- ensure the UK can achieve its full potential in combining health data from routine services and research for discovery and implementation
- cooperate to develop research capacity in new priority areas such as mental health and emerging therapeutic technologies.

We also aim to form new or closer links to reflect new research directions by:

- strengthening public and patient involvement, especially in rapidly changing areas such as predictive genomic medicine, prevention and digital healthcare, and also where new technologies allow the public to engage in gathering research data
- continuing to narrow the gaps between research and practice. Innovation in NHS provision, such as in genomics, will drive opportunities in more basic science, and research capabilities in informatics can be used immediately to inform health service decisions. Both call for close two-way links
- connecting our research better with the wider set of government departments and public services in areas such as education, housing communities, local government, and the environment.



NiCoLa-B is an advanced drug discovery robot that can test up to 300,000 compounds a day, working three times more quickly than previous drug discovery robots. The MRC has provided funding for academic researchers to run high throughput drug screening projects within the AstraZeneca UK Centre for Lead Discovery. Image courtesy of AstraZeneca©



Translation and industry partnerships are now firmly embedded in our research portfolio and, following 10 years of targeted funding, a major evaluation of impacts and changing needs is under way to shape future funding. Ensuring the UK stays at the forefront of health R&D investment worldwide, supporting multidisciplinary collaboration and maximising the impact of discovery research for the health and wealth of the nation are key priorities for us that align fully with the government's Life Sciences Industrial Strategy. Building on the MRC/ Innovate UK Biomedical Catalyst, we will support a strong pipeline of new academic translation across the full range of health sciences, enabling industry innovation in diagnosis, treatment and prevention, and ensuring universities are well-positioned to swiftly de-risk and advance innovative projects and products towards the clinic and/or commercialisation.

Long-term ambitions

- Strengthen support for collaborations to enhance two-way knowledge transfer, training and people exchange while recognising differing skills, facilities and interests in different sectors
- Through support for translation and collaboration, broaden our contribution to UK industry, enabling opportunities in areas such as diagnostics, data analytics, machine learning, medical devices and technologies

- Facilitate development of innovative public-private partnerships across academia, the NHS and industry in areas of societal need, building on previous successful activities in, for example, precision medicine
- Work with business and the research community to identify emerging areas not currently attractive to industry that have the potential to support long-term innovation.

Near-term actions

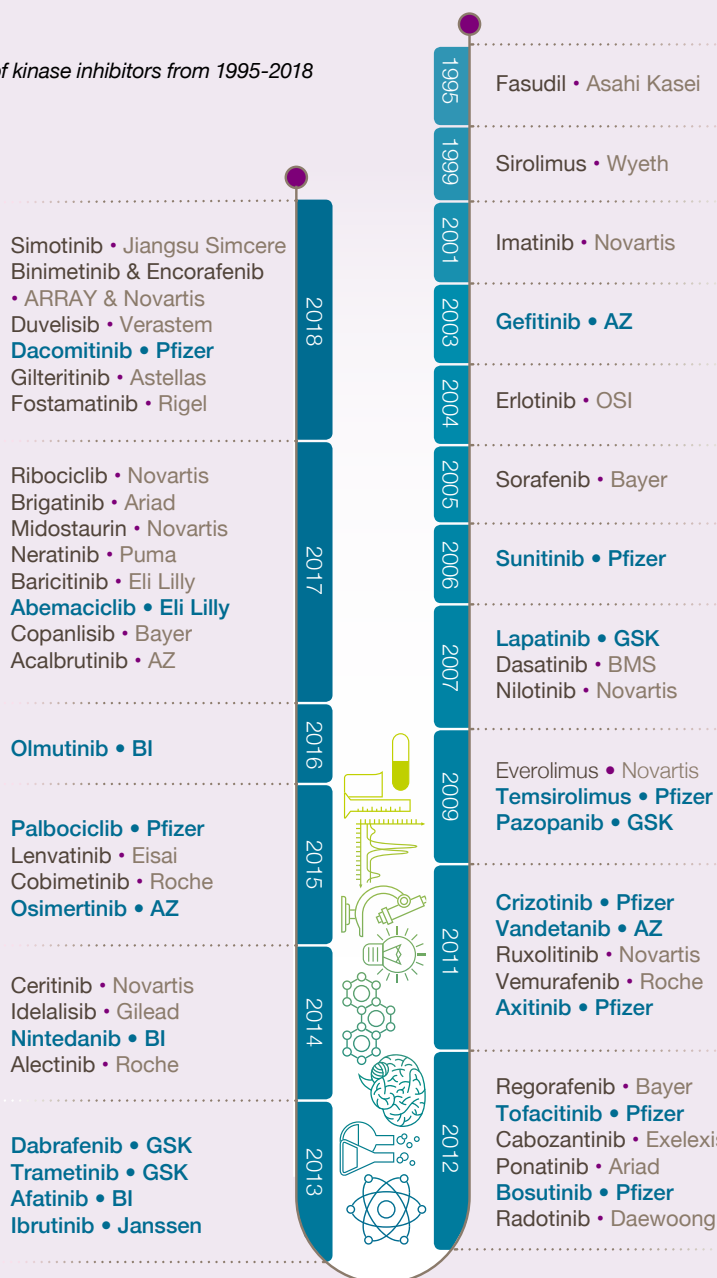
- Refresh our translational strategy, informed by findings from our 10-year evaluation
- Extend UK sector engagement, including wider business sectors, fostering new connections that reflect the growth of novel technologies applicable to medical research
- Identify opportunities for novel collaborative approaches between industry and academia to support and accelerate co-discovery, technology development, commercialisation and longer-term translational research.

From discovery science in Dundee to global impact

Founded in 1998, the Division of Signal Transduction Therapy Dundee, with close links to the MRC Protein Phosphorylation and Ubiquitylation Unit, works with companies to identify new drug targets and develop enabling technologies. It is the world's longest-running collaboration between academic basic research laboratories and the pharma industry. When the collaboration was founded, most pharma companies were sceptical that kinases were

good drug targets and doubted that this novel collaboration would last. Not only is the collaboration still going strong over 20 years later, it has also attracted almost £60 million of investment, helped achieve clinical approval of dozens of drugs for use, such as Dabrafenib for skin cancer, won the prestigious Queen's Anniversary Award in 2018, and led to sales of drugs worth billions of pounds per year. Kinase-based drugs have accounted for up to 30% of worldwide drug R&D, in areas such as cancer, inflammation and neurodegeneration.

FDA approval of kinase inhibitors from 1995-2018



Key
Developed by collaborators in the University of Dundee's Division of Signal Transduction Therapy.

International partnerships

We aim to ensure UK scientists can engage with the best minds, ideas and resources wherever they are located and can take advantage of research opportunities and respond to global challenges both for developed and less developed nations. We will go on influencing the international research agenda and providing leadership in international partnerships that enhance the competitiveness of the UK knowledge and health base. By supporting international and intergovernmental partnerships, we can actively leverage overseas funding and bring additional inward investment to the UK science base. We will continue to support and develop the excellent work of intergovernmental programmes at the European Molecular Biology Laboratories (EMBL), European Molecular Biology Organisation (EMBO), International Agency for Research on Cancer (IARC), Global Alliance for Chronic Diseases (GACD) and Human Frontiers Science Programme (HFSP). We will play an important diplomatic role in promoting the UK as the research partner of choice globally.

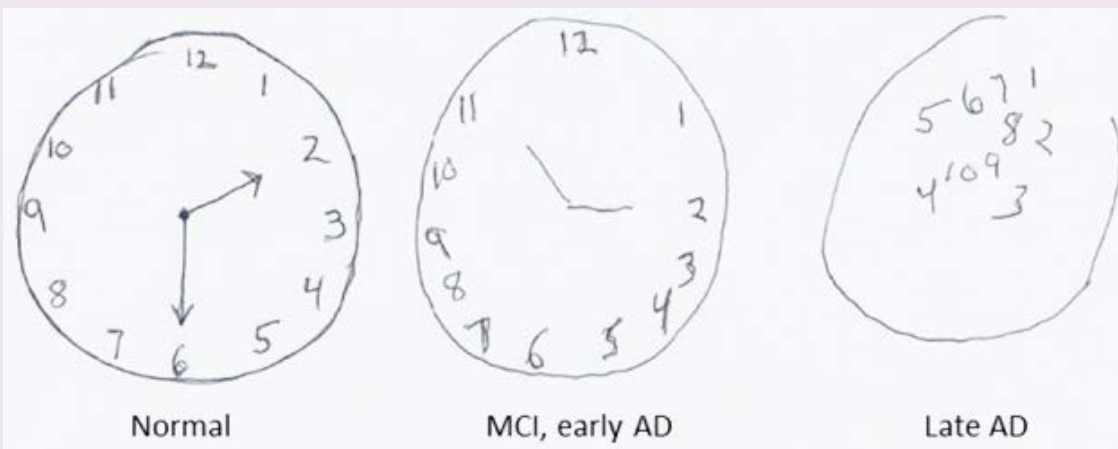
Long-term ambitions

- Deliver joint funding activities, for example through the Newton Fund and the Fund for International Collaboration, to support researcher collaboration with key science nations and leverage funds from partners to increase the scale of the challenges we can tackle
- Capitalise on our reputation for excellence, authority and independence to influence international research and provide leadership in research policy areas. Our lead in areas such as health-research classification, open access, research integrity and research evaluation, plus our expertise in clinical trials management, career development and support for research excellence, means we have a responsibility to work with international colleagues and others to share best practice and improve the global research environment

- Continue to engage with international leaders in biomedical research through meetings of the Heads of International (Biomedical) Research Organisations, a forum for informal exchange between leaders of the world's largest biomedical research funding agencies
- Facilitate UK researchers' access to international research infrastructures and funding opportunities such as ELIXIR, the European bioinformatics research infrastructure. We will support European initiatives such as joint-programme initiatives in neurodegeneration and AMR, and the European and Developing Countries Clinical Trials Partnership
- Maintain our commitments to working bilaterally through memorandums of understanding with countries such as Japan and Korea.

Near-term actions

- Launch new joint-funding partnerships with the Korean Ministry of Health and Welfare through the Korea Health Industry Development Institute (KHIDI), and with the Korean Ministry of Science and Technology through the National Research Foundation, backed by the UKRI Fund for International Collaboration
- Develop a partnership with the Japan Agency for Medical Research and Development in Regenerative Medicine supported through the UKRI Fund for International Collaboration (£5m matched by Japan)
- Support joint-funding activities in neurodegeneration and AMR through European joint-programming initiatives in partnership with European and global partners.



Global research programme advances research into Alzheimer's

Insights into the subtypes of Alzheimer's disease have emerged from the world's largest research initiative aimed at tackling neurodegenerative diseases. We play a pivotal role in the EU Joint Programme for Neurodegenerative Disease Research, which gathered data from 175 peer-validated cohorts from disease-focused and general population studies into an online portal. This provides an overview of activity among member countries to help coordinate research investment with the goal of developing earlier, more targeted treatments for neurodegenerative diseases. Investments made through the programme are already starting to pay off, as demonstrated by the REfrAME project. This collaboration between the UK and six other countries has shown that Alzheimer's has several different molecular subtypes, deepening our understanding of why patients respond differently to treatment.

In this clock drawing task the subject is asked to draw a clock with the hours and showing the time 2:30. When the person has mild cognitive impairment (MCI) or early Alzheimer's disease (AD) the numbers for the hours on the clock are drawn in proper order, but during the time it took to draw the clock the subject forgot that they had been asked to show the time 2:30. In the case of the patient with late-stage AD, the drawing bears little resemblance to a clock. Reproduced with permission from Superior pattern processing is the essence of the evolved human brain – Mattson 2017 Frontiers in Neuroscience 8(265)

4. Delivering and being accountable as an outstanding organisation

Efficient and effective operations

We will strengthen our scientific networks and advisory systems to ensure we are an agile and responsive organisation. Within UKRI we will fully explore multidisciplinary opportunities and provide a strong voice for biomedical research. We will invest more time in engaging with our research communities, horizon scanning and field reviews, and will continue to strengthen public engagement and dissemination support for key research issues.

We will refresh our Head Office structure. We will continue to develop a core of skilled scientific research managers and part-time leadership and delivery roles for top researchers as Board Chairs. We will introduce a new Clinical Director role, a Health Innovation Champion and shorter-term roles to bring academic and project expertise into areas such as mental health and cohort development and piloting.

Subject to funding, by 2020 we will offer opportunities to form new MRC centres in a revised format with greater support for team science and technologists, building on areas of excellence to develop critical mass, support multidisciplinary, core technologies and capabilities. New centres will also provide a focus for industry and translational collaborations.

We will strengthen evaluation of the impact of our funding and explore secondments and collaboration to bring in new analytical capabilities and approaches. We will work with UKRI on the transformation programme to deliver effectiveness and efficiency. This will build further on the reductions in our operational costs achieved between 2015 and 2018, which have decreased our administration budget by £6.8 million (27.7%) through closure of administration centres, IT improvements and reduction of senior-level staff costs, as well as the £17 million of procurement savings made by our institutes and units.

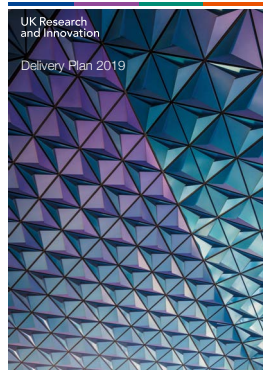


MRC Festival of Medical Research 2017 – MRC Laboratory of Molecular Biology open day. Image: Lesley McKeane.

5. Financial allocation

MRC		2019-20
Research and Innovation Budgets		562.4
Science Infrastructure Capital		65.7
ODA		66.3
o/w	GCRF	51.9
	Newton Fund	14.3
NPIF		50.6
o/w	Skills	14.5
	Future Leaders	32.4
	Funds For International Collaboration	0.8
	Strategic Priorities Fund	2.8
MRC Programme		745.1

UK Research and Innovation Delivery Plans



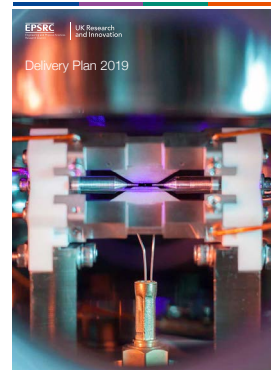
UKRI



AHRC



BBSRC



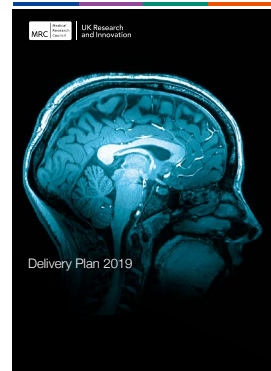
EPSRC



ESRC



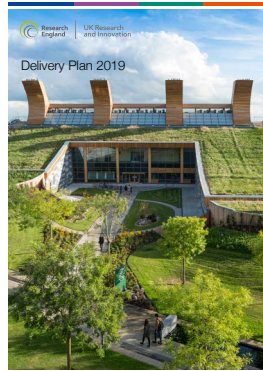
Innovate UK



MRC



NERC



Research England



STFC