

ISBN 978-0-903730-24-2

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When providing a citation for this document we recommend the following:

Medical Research Council (2017) MRC Economic Impact Report 2015/16. Publisher: Medical Research Council, Swindon, UK. ISBN: 978-0-903730-24-2

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This publication is available at http://www.mrc.ac.uk/successes/economic-impact-report/

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Introduction

Since 1913, the MRC's mission has been to support research and skilled researchers to improve human health, advance the dissemination of knowledge and technology for the benefit of society and the economy and engage with the public to promote medical research. From producing the first antibiotic and developing the first monoclonal antibodies to demonstrating the link between smoking and lung cancer, MRC-supported researchers have been at the forefront of medical advances that have had a profound impact on society¹. The MRC's approach is guided by its long-term **Strategic Plan 2014-19** *"Research Changes Lives"*.

The MRC regularly gathers feedback from its researchers about the progress of the research it supports², commissions high quality studies and internal analysis to assess delivery against its strategic objectives³, and works closely with other stakeholders globally to develop improved ways to support excellent research with the greatest opportunity for impact.

It is clear that medical research provides significant and positive impact on health, the wider society and the economy⁴. This report emphasises examples where MRC research is generating substantial health gains, generating new understanding in areas of significant public health concern, delivering economic returns, and realising societal benefits such as improved security against emerging diseases.

¹ Timeline of 100 years of MRC research impact https://www.mrc.ac.uk/successes/timeline-of-mrc-research-and-discoveries/

² Details of the MRC evaluation programme and approach to gathering research output

https://www.mrc.ac.uk/successes/evaluation-programme/

³ MRC economic impact research programme

https://www.mrc.ac.uk/funding/how-we-fund-research/highlight-notices/economic-impact-highlight-notice/

⁴ Many studies, worldwide, have highlighted these positive effects. We include details in this report of research supported in the UK by the MRC and other partners which demonstrate an estimated health gain of around 10%, and wider economic spill-over effects of 15-18% (see HERG, OHE, RAND Europe (2008) Medical Research: What's it worth? Estimating the economic benefits from medical research in the UK. London: UK Evaluation Forum, and Sussex et al. (2016) quantifying the economic impact of government and charity funding of medical research on private research and development funding in the United Kingdom. BMC Medicine 14(32):

DOI: 10.1186/s12916-016-0564-z.



Investing in research

Investing in research

Income and allocation

In 2015/16 the MRC's budgetary allocation from the Department for Business, Energy and Industrial Strategy (BEIS) was £798 million. Additional income, from other government departments, other bodies, and commercial activities was £206m. With net expenditure totalling £864m, leverage according to BEIS definition is £65m (see Annex 2). For more on MRC's research spending, see our Annual Report 2015/16.

The support for world-class medical research to improve human health and enhance the economic competitiveness of the UK in 2015/16 included:

E	EXPENDITURE		Value
	Research ncluding:	 £445m on research grants (Inc. programme, centre, trial and new investigator research grants) £173m on MRC institutes and units £84 on the Francis Crick Institute 	£846.3m
	Training Comprising:	£65.6m on studentships and fellowships in Universities, Medical Schools and research institutes £5.4m within MRC institutes and units	£70.9m
	Support ncluding:	£78m in technology transfer £47m in corporate expenditure £16m in international subscriptions	£152.9m
Total operating expenditure		ating expenditure	£1,070.2m
	Total Oper Comprising:	Exacting Income£96.0m from commercial activities£44.2m from other Government departments£39.6m from other bodies£16.6m from other research councils£9.5m from other income	£206.0m
Total net expenditure		xpenditure	£864.2m

Overall return on investment from medical research

The MRC has also supported a range of studies aimed at better understanding impact and refining estimates of the economic return from medical research. In 2008 the "**What's it worth?**" report⁵, commissioned by the MRC, Wellcome Trust and Academy of Medical Science, found that cardiovascular disease research generated a nine per cent return on investment in terms of the health gain from new interventions. This approach was subsequently used to estimate the average health gain from cancer research⁶ and is currently being applied to musculoskeletal disease research⁷. In 2016 MRC funded research provided the first UK-specific estimate of spillover benefits from medical research⁸. The analysis concluded that investment in medical research had stimulated the private sector to invest more in UK research and development, equivalent to a return on investment from public and charitable funding for medical research of 15-18 per cent. When added to the health gain from cardiovascular disease and cancer research, the total return on investment from medical research is estimated to be 24-28 per cent.

The best estimates of the return on investment from medical research are shown below:



⁸ Sussex et al. (2016) Quantifying the economic impact of government and charity funding of medical research on private research and development funding in the United Kingdom. BMC Medicine 14(32): DOI: <u>10.1186/s12916-016-0564-z</u>

⁵ HERG, OHE, RAND Europe (2008) Medical Research: What's it worth? Estimating the economic benefits from medical research in the UK. London: UK Evaluation Forum. Available via MRC website: https://www.mrc.ac.uk/publications/browse/medical-research-whats-it-worth/

⁶ Glover et al. (2014) Estimating the returns to UK publicly funded cancer-related research in terms of the net value of improved health outcomes. BMC Medicine 12:99 DOI: <u>10.1186/1741-7015-12-99</u>

⁷ Begun in 2015, with support from Arthritis Research UK, Wellcome Trust, MRC, Department of Health and Academy of Medical Sciences. http://bit.ly/2l6D4BK

Large scale Investments

The majority of MRC expenditure is via research grants, mainly awarded to Universities. However the MRC also provides dedicated support in the form of institutes, units and centres. These Director-led investments are established to address a series of inter-disciplinary research questions over the long-term, often in partnership with other research organisations and funders. For current information on MRC Institutes, Units, Centres and other large investments see the MRC website⁹.

Highlight:

The Francis Crick Institute

The Francis Crick Institute is a new UK biomedical discovery institute dedicated to understanding the fundamental biology underlying health and disease.

The MRC **National Institute for Medical Research** (NIMR) officially closed in April 2015 as researchers from NIMR and Cancer Research UK's London Research Institute transferred to the new **Francis Crick Institute**. The Crick represents a unique partnership between the MRC, Cancer Research UK, the Wellcome Trust, University College London, Imperial College London and King's College London, with the partners collectively raising £650 million to build and run the largest biomedical research institute under one roof in Europe. As of September 2016, **the first scientists moved into the new institute.** When it is fully occupied and operational, in early 2017, the Francis Crick Institute will employ 1500 staff, including 1250 scientists, and have an operating budget of approximately £130 million a year.

"One of the most significant developments in UK biomedical science for a generation" – Sir Paul Nurse, Chief Executive, Francis Crick Institute



Photo: Images of the Francis Crick Institute. Source: MRC

https://www.mrc.ac.uk/about/institutes-units-centres/list-of-institutes-units-centres/

Highlight:

The MRC Laboratory of Molecular Biology

The MRC <u>Laboratory of Molecular Biology</u> (LMB) has the goal of understanding biological processes at a molecular level with the ultimate aim of using this knowledge to tackle specific problems in human health and disease.

In 2015 the LMB <u>received a visit</u> from Universities and Science Minister Jo Johnson MP (below), providing an opportunity for researchers to explain some of the impact of their research and highlight how the world-leading reputation of the LMB has helped attract significant new industry investment. This includes AstraZeneca's new <u>global R&D centre</u> and the <u>Cambridge</u> <u>Pharmaceutical CryoEM Consortium</u>. The consortium brings five pharma companies together with researchers at the LMB and Cambridge Nanoscience Centre, and a leading developer of CryoEM machines, FEI.

In a world first, the five companies involved in the consortium share access to the cutting-edge electron microscope with colleagues from the LMB and the University of Cambridge in return for expert guidance on the use of cryo-EM technology. FEI's Titan Krios machine was installed at the Nanoscience Centre in May and, using software developed at LMB, will help create 3D models of viruses and proteins to allow rapid early-stage drug discovery and modelling.



Highlight:

UK Biobank

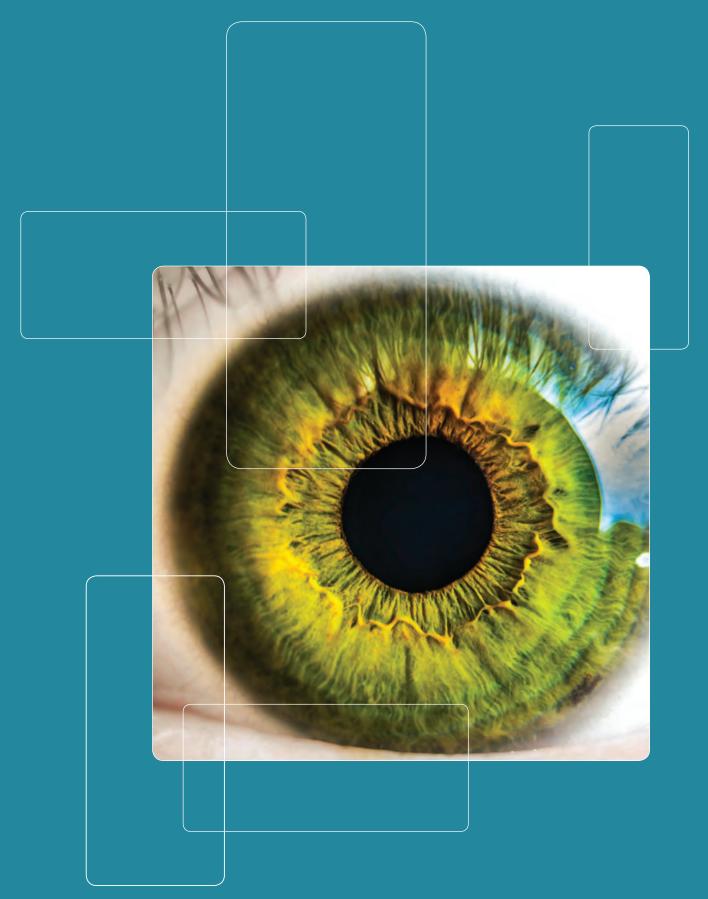
Established in 2006 by the Wellcome Trust, MRC¹⁰ and other UK funders, the <u>UK Biobank</u> has established a world-leading research resource of half a million people across the UK to improve health.

In 2013, an 18-month pilot study to carry out brain and body imaging of 8,000 participants began (MC PC 12027), alongside the genotyping of all 500,000 cohort members. In late 2015 the MRC built on this work by awarding a total of £43million, together with the Wellcome Trust and the British Heart Foundation, to support the **imaging of 100,000** participants over the next seven years.

Many research teams are interested in accessing the UK Biobank to examine specific associations between the genetic, physiological and lifestyle data accumulated by the programme, and long-term health and disease. For example, **Professor Ian Hall** at the **University of Nottingham** and **Professor Martin Tobin** at the **University of Leicester** are examining the relationship between lung health in a subset of 50,000 UK Biobank participants and information on 28 million genetic variants. The team were able to find parts of the human genome that have never before been associated with a person's lung health, as well as five sections of DNA shown for the first time to have a link to being a heavy smoker. Understanding how genes underpin susceptibility to both lung disease and smoking behaviours are key first steps in developing new treatments for these diseases and for helping smokers to quit.



Photo: The ALICE supercomputer which processes UK Biobank data. Source: University of Leicester.



Making people healthier

Making people healthier

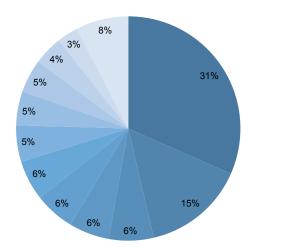
The MRC has a long history of successfully translating discovery science into new products and interventions that have widespread impact on medicine and healthcare.

In the last five years, MRC researchers have reported:



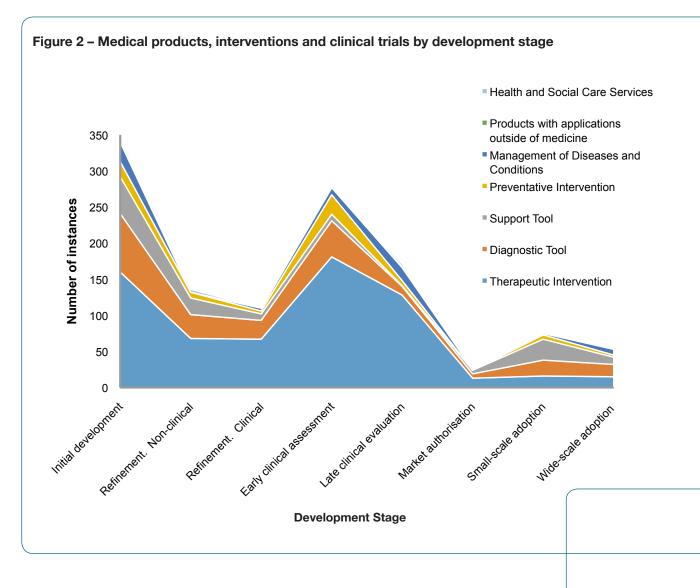
From the early development of the first antibiotic (penicillin) to vaccines, stem cells and monoclonal antibodies MRC discovery science has provided a rich pipeline of exploitable opportunities for the UK's strong pharmaceutical sector. However, the scope of MRC-funded research is not limited to the development of new therapeutic drugs. These account for just 32 per cent of medical products reported (see Figure 1 below). New surgical techniques, behavioural and physical therapies and approaches for disease prevention are all developed as a result of MRC research. Likewise technological advances for disease monitoring and diagnostics, ways to guide treatment decisions and predict patient outcomes, are also impacting positively on health care.

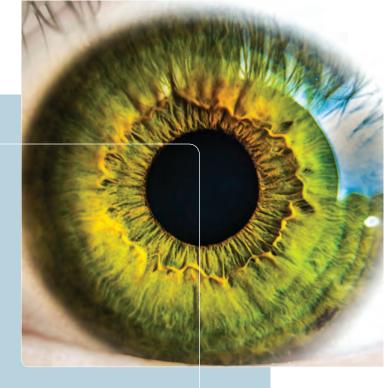
Figure 1 – Types of medical products and interventions in development as a result of MRC research (2006-2015)



- Therapeutic intervention drug
- Diagnostic Tool Non-imaging
- Support tool for fundamental research
- Diagnostic Tool imaging
- Therapeutic (psychological/behavioural)
- Management of diseases and conditions
- Therapeutic (cellular and gene therapies)
- Therapeutic intervention vaccines
- Support tool for medical intervention

As with other outputs, the MRC collects information on medical products, interventions and clinical trials resulting from MRC-funded research via **researchfish®**. More information on this process can be found in **Annex 1 – Reporting Requirements and Methodology.** The development of each product or intervention may involve a number of stages, from initial development to wide scale adoption. Over time we expect to have products reported at various development stages as translation progresses. Figure 2 (below) shows the most recently reported stage for all products linked to MRC research. The majority of products (32 per cent) are classified as 'in initial development'. In most cases this means that the potential for a particular project to develop a product has been identified, and further research is on-going or additional funding is being sought. Those in early clinical assessment (25 per cent) may be recruiting or at the earliest stages of formal clinical trials, ready to embark on 'first in man' studies.





Fighting blind – advanced therapeutics for eye disease

The first patient has been treated with a new stem-cell-derived treatment for 'wet' age-related macular degeneration (AMD) as part of a pioneering clinical trial in London.

In the <u>first clinical trial</u> of its kind in the UK, a woman with 'wet' AMD, the leading cause of blindness in over 50s, was successfully treated in September 2015. The technique involves inserting a patch seeded with lab-grown stem cells into the patient's retina to replace the cells lost as a result of wet AMD. Current AMD treatments only prevent or slow progression; by replacing the cells themselves, such techniques should restore sight for people with severe vision loss.

The MRC has funded the co-leader of this research, **Professor Peter Coffey, University College London Institute of Ophthalmology** since 2004 (<u>G0300288,</u> <u>G1000730</u>). Over this period, Professor Coffey and his team have been able to carry out the basic research behind the cell transplants for retinal repair, alongside developing imaging techniques to allow them to look at the survival and function of the cells after transplant. The MRC also funded **Professor Harry Moore** at the **University of Sheffield** to establish a bank of human embryonic stem cell lines, one of which has been used to develop this technique.

The MRC has recently made a further £1.5 million award as part of the **UK Regenerative Medicine Platform** to further support the Coffey team in developing this technology for use in the clinic (**MR/L022842/1**). Given their initial success, the trial will recruit another nine patients over 18 months, each of whom will be followed for a year to assess the safety and stability of the cells and whether there is an effect in restoring vision.

The clinical trial is part of the **London Project to Cure Blindness**, a partnership between Moorfields Eye Hospital, the UCL Institute of Ophthalmology, the National Institute for Health Research (NIHR) and Pfizer Inc. Its aim is to bring stem cell therapy for retinal diseases to the clinic as rapidly as possible. While AMD is a prime target, the use of stem cells can be applied to other conditions such as the inherited eye disease Stargardt's Macular Dystrophy.

The MRC also supports cell and gene therapies for Retinitis Pigmentosa, the leading cause of inherited blindness (e.g. <u>MC PC 13038</u>, <u>MR/N00101X/1</u>) and <u>ReNeuron</u>, a spin-out company from MRC research, is developing <u>stem cells for use in eye</u> <u>disease</u> as well as other diseases, such as the cardiovascular condition critical limb ischemia.

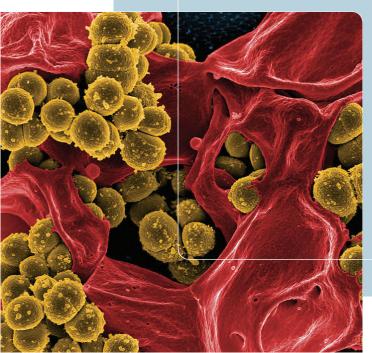
The digital weapons against anti-microbial resistance

Urgent action is needed to halt the development of anti-microbial resistance (AMR), and to accelerate new treatments for bacterial infection. The MRC <u>funds a wide range of research in AMR</u> from laboratory to bedside. As part of this interdisciplinary initiative a new open-access database of bacterial genome sequence data will be exploited by researchers for future surveillance and outbreak investigations and as a guide to prevention and treatment strategies.

Professor Sharon Peacock at the **University of Cambridge** is a clinical microbiologist who works on the translation of high throughput whole genome sequencing technologies into diagnostic and public health systems. Methicillin-resistant *Staphylococcus aureus* (MRSA), one of the best-known strains of antibiotic resistant bacteria, is often found in a hospital setting and can spread between vulnerable populations. Hospital infection control measures are designed to prevent the spread of these bacteria but these measures can sometimes fail. One way to reveal how bacteria spread and pinpoint where preventive strategies require strengthening is to perform bacterial genotyping to determine if MRSA affecting two patients are highly related (suggesting that it passed from one person to another) or different.

In 2013, Professor Peacock began a database of whole genome sequencing data for *S. aureus* isolates, including MRSA isolates. She has made these results available on the open access **European Nucleotide Archive** and assembled a team of expert users of genomic data and metadata. In 2016, the database user group **published their work**, and it has become a valuable resource for the future surveillance and outbreak investigation of MRSA in the UK and Ireland.

Professor Peacock's research project is part of the UKCRC Consortium (UK Clinical Research Collaboration). Six other organisations are involved in funding the UKCRC, including the BBSRC, MRC, NIHR, and the Wellcome Trust. Large-scale, multi-funder research projects such as this herald the multi-disciplinary future of AMR research.



Scanning electron micrograph of methicillin-resistant Staphylococcus aureus and a dead human neutrophil. Credit: National Institute of Allergy and Infectious Diseases (NIAID)

Stratified medicine

Therapeutic strategies are increasingly being customised at the molecular level to deliver personalised or stratified medicine. The MRC has provided <u>significant strategic support for stratified medicine</u> with the aim of developing treatments that have greater efficacy in target populations and fewer side-effects.

One of the defining characteristic of cancer is the uncontrolled growth of cells. Normal cells exist in a stable state of no division until they move into an active state of cell division, known as mitosis. Cellular processes that control cell division (known as "checkpoints") are commonly disrupted in cancer cells. The proteins involved in these checkpoints can be viewed as valuable targets for developing new drugs against cancer.

One such target is the WEE1 kinase, a protein influential in mitosis and DNA repair but also increased in some cancers. Drugs that can inhibit WEE1 kinase have been trialled in a number of different types of cancer. For example the FOCUS4 clinical trial being conducted via the **MRC Clinical Trials Unit** is aimed at improving treatment outcomes for colorectal cancer (**MC U122861325**). The MRC CTU researchers are working in collaboration with AstraZeneca, who are providing their WEE1 inhibitor AZD1775 as part of a 'molecularly-stratified' randomised control trial that has been designed to test multiple novel therapies in a quick and efficient manner¹¹.

Dr Tim Humphreys at the **MRC/CRUK Institute for Radiation Oncology** the University of Oxford has been working on the molecular mechanisms of DNA repair, supported by almost £2 million MRC funding since 2012 (MC PC 12003). A detailed understanding of the role of WEE1 kinase in the underlying process of DNA repair has led Dr Humphrey's team to investigate how another protein, Histone H3K36m3, may modify patient responses to WEE1 inhibitor treatment. Dr Humphrey's team have identified a biomarker for H3K36m3-deficient cancers that can be used to determine the right treatment for these patients. As the lack of H3K36m3 is common in kidney, bowel and ovarian cancers and its absence is associated with a poor prognosis¹², this approach may represent an important new avenue for treatment.

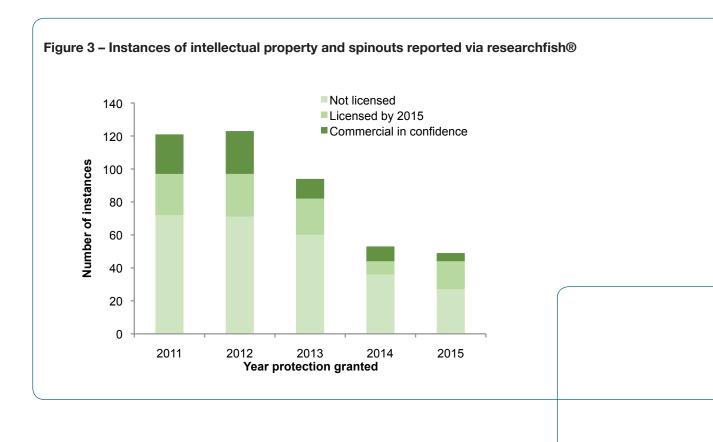
¹¹ Kaplan et al.(2013) Evaluating Many Treatments and Biomarkers in Oncology: A New Design J Clin Oncol 31: p4562-4568. DOI: **10.1200/JCO.2013.50.7905**

¹² Pfister et al. (2015) Inhibiting WEE1 Selectively Kills Histone H3K36me3-Deficient Cancers by dNTP Starvation. Cancer Cell 28(5): p557-568. DOI: <u>10.1016/j.ccell.2015.09.015</u>

Innovation to commercialisation - Intellectual property and spinouts

The MRC collects data on intellectual property via **researchfish®**. Since 2006 there have been 1,327 instances of intellectual property reported, 436 in the last five years (see Figure 3). Overall, 23 per cent of discoveries were reported as 'licensed' by 2015.

By ensuring protection of intellectual property, discoveries from MRC research can be commercially exploited and result in positive economic impacts such as employment, provision of new goods and services, and direct investment into the UK – as well as improving human health. In some cases, the development of IP can extend to the formation of a new company, where researchers, their parent organisation and investors can come together to benefit from commercialisation. Such 'spin-out' companies can develop independently and have the potential to generate further commercial benefits beyond the original IP. Since 2006, MRC funding has contributed to the set up or growth of 96 companies, 61 in the last five years, including eight in 2015 (see Figure 3). It is estimated that these 96 companies represent approximately 560 new highly-skilled jobs in the UK¹⁴.



¹⁴ At point of submission, researchers reporting spinouts are asked to provide an estimate of employee numbers within set ranges (1-4, 5-9, 10-19 etc.). The data submitted in 2016 gives a minimum of 353, Median of 562 and maximum of 796 employees based on the range criteria.

New targets for neurodegeneration

Studying the underpinning biological mechanisms of neurodegeneration allows the research community to develop a rational approach towards discovering new treatments.

One of the hallmarks of neurodegenerative disease is the accumulation of misfolded proteins, which lead to the formation of plaques. Our cells attempt to counteract this by activating a programme known as the unfolded protein response (UPR). Once activated, this programme halts the production of any new proteins, destroys misfolded proteins, and increases the production of 'molecular chaperones' that make sure proteins are folded correctly. But if this programme is active for too long, it can also lead to damage; our cells constantly need to replenish proteins, so persistently halting the production of any and all new proteins can lead to the death of these cells. When nerve cells die because of this, it results in neurodegeneration.

But what if there was a way to selectively keep this programme active without any detrimental effects? **Dr Anne Bertolotti** at the **MRC Laboratory of Molecular Biology** has identified a novel compound called Sephin1 that seems to be able to do just that. Early experiments with mice have shown that treatment with Sephin1 was able to mitigate the effects of these plaques for neurodegenerative diseases such as Amyotrophic Lateral Sclerosis (ALS) and the hereditary neuropathic condition Charcot-Marie-Tooth disease. It is possible that Sephin1 could have a similar effect on other neurodegenerative diseases as well.

Sephin1 has been patented and licensed to **InFlectis BioScience**, a start-up company based in France. InFlectis BioScience has since raised €6 million to perform a clinical trial in humans using this drug (now named IFB-088) and it has also been given Orphan Drug status¹⁵ by the US Food and Drug Administration for treating the Charcot-Marie-Tooth disease.

Case study:

Gene therapy in haemophilia

A new company is using advanced therapeutic approaches to provide improved treatments for an inherited blood clotting disorder.

In 2015, **Freeline Therapeutics** was established with the aim to deal in virus-based therapies, using the latest techniques to reprogramme a virus' ability to infect cells with its own DNA to repair or replace genes that cause disease. These gene therapies have been long been suggested as treatments, even cures, for otherwise difficult to treat diseases. The Chief Scientific Officer of Freeline Therapeutics is **Prof Amit Nathwani** from **University College London**, an expert in the field of gene therapy with £3.2 million in MRC funding since 2007 (**MR/L013185/1**). Professor Nathwani specialises in haematological disorders, and has a particular interest in haemophilia, an inherited blood disorder which prevents blood from clotting. The establishment of Freeline Therapeutics comes from £25 million series A financing from Syncona LLP and support from UCL Business PLC, UCL's technology transfer company. This follows successful phase I/II clinical trials of Prof Nathwani's gene therapy¹⁶ conducted at St. Jude Children's Research Hospital in Memphis.

¹⁵ The term 'orphan drug' refers to treatments for very rare diseases. Because the market for such a drug is small, legislative and financial benefits are used to encourage pharmaceutical companies to develop new treatments.

¹⁶ Nathwani et al. (2011) Adenovirus-Associated Virus Vector–Mediated Gene Transfer in Hemophilia B. The New England Journal of Medicine 365: p.2357-2365. DOI: <u>10.1056/NEJMoa1108046</u>

Influencing policy

Dissemination of research is about more than simple advocacy and visibility. To enact changes, research findings must reach policymakers, politicians and regulatory organisations with a duty to use the best possible evidence to benefit society's health and wellbeing. In the last five years, MRC researchers have reported several thousand instances where their research has had an evidenced part to play in policy development.

These policy influences include the development and revision of clinical guidelines; recommendations to clinicians on diagnosis, management and treatment in specific areas of healthcare based on systematic evidence. Examples of these include:

- Evidence to Parliamentary Select Committees¹⁷, including research findings that led the UK to become the first country in the world to allow **mitochondrial donation** to prevent serious genetic diseases.
- Changes to the World Health Organisation (WHO)'s **guidelines for treatment of HIV**, following results of two studies coordinated and co-funded by MRC.
- That better **adherence to guidelines** for treatment of heart attacks could improve patient survival rates.
- How work from an MRC PhD student on alcohol consumption in pregnancy has led to the Royal College of Obstetricians and Gynaecologists (RCOG) <u>changing its guidance</u>, now recommending women avoid all alcohol during the first trimester.
- Influence on 50 guideline documents issued by the National Institute for Health and Clinical Effectiveness (NICE) and the Scottish Intercollegiate Guideline Network (SIGN) over the last five years. These guidelines set quality standards and metrics for commissioning public health and social care services in the UK.

Case study:

Prevalence and costs for dementia in the UK

Tackling neurodegeneration and dementia at a societal level requires approaches that can identify the factors likely to modify the risks of developing these conditions and provide an accurate estimate of prevalence in the UK.

Led by **Professor Carol Brayne** at the **University of Cambridge**, the MRC Cognitive Function and Ageing Study (CFAS) is a landmark study funded by the MRC and the Department of Health, starting in the 1980s. The earliest figures from 1989 to 1994 demonstrated that dementia is much more common than previously thought (6.6 per cent in over 65s, increasing to 25 per cent in over 85s), while more recent data¹⁸ surprisingly showed that dementia prevalence in over 65s had decreased slightly. Effective planning of health social care needs good quality data on prevalence, and identifying changes in prevalence may provide clues as to the factors that modify the risks of developing dementia.

The CFAS study has also provided data on costs of informal care to support people with dementia. This proved to be much greater than previously estimated. The group was also able to predict future demand for long term care and likely associated costs. Modelling long term care needs and forecasting costs have been invaluable tools for policy makers, and Professor Brayne made significant contributions to the <u>NICE</u> <u>Dementia Guidelines in 2015</u>.

¹⁷ Particularly the Science and Technology Select Committees for the **<u>Commons</u>** and the <u>**Lords**</u>. Other connections to parliamentarians include RCUK internships in the **<u>Parliamentary Office of Science and Technology</u>**,

¹⁸ Matthews et al. (2013) A two-decade comparison of prevalence of dementia in individuals aged 65 years and older from three geographical areas of England: results of the Cognitive Function and Ageing Study I and II. The Lancet 382(9902): p1405-1412. DOI: **10.1016/S0140-6736(13)61570-6**

Identifying new antibiotic resistance gene leads to unprecedented policy change in China

MRC-funded scientists identified a new form of an antibiotic resistance gene in China, a discovery that resulted in the Chinese Government rapidly moving to ban colistin supplements for animal feed.

Antibiotic resistance is genetically transmitted and can be spread across a bacterial population very quickly. For this reason, outbreaks of hospital acquired infections where traditional antibiotics no longer work effectively, such as MRSA (methicillin-resistant *Staphylococcus aureus*), are becoming more common and are a serious risk to current medical practice. As such, studying the genes involved in this process, understanding how antibiotic resistance arises and more importantly, how it spreads has never been more important. **Professor Timothy Walsh** at **Cardiff University** is a world renowned expert in studying this process in a group of bacteria known as Gram-negative bacteria. In 2010, Prof Walsh was part of a team that reported a newly identified gene¹⁹, **NDM-1**, that confers multi-drug resistance against all but a select group of 'last resort' antibiotics such as colistin. Spread of NDM-1 bacteria was linked to travel between Europe and South Asia, especially for medical tourism, and <u>made headlines</u> around the world as a new "superbug".

Since 2011 Prof Walsh has been supported by MRC to study antibiotic resistance (**G1100135**), and received two further awards in 2015/16 for work on drug resistance in both Vietnam and China (**MR/P007295/1** & **MR/N028317/1**). In 2015, Professor Walsh and his team, along with collaborators in China identified another new gene²⁰, **MCR-1**, that allowed bacteria to survive the 'last resort' colistin treatment. This ground-breaking discovery means that certain bacterial infections could be impossible to treat with any of the antibiotics currently available. Although originally identified in China, MCR-1 has been subsequently reported in more than 30 countries including the UK, spanning four continents.

But with new knowledge comes a renewed effort to tackle antibiotic resistance. China is one of the world's highest users of colistin in agriculture, and it is likely that colistin resistance evolved in this context. Since the discovery of MCR-1, Professor Walsh and his team have worked closely with the Chinese Government to examine the use of colistin in agriculture. In July 2016, the Ministry of Agriculture in China announced that colistin will be **banned** from animal feed in agriculture use, effective from 1st November 2016. This significant policy shift will lead to withdrawal of more than 8000 tonnes of colistin as a growth promoter from the Chinese veterinary sector. In Europe, colistin remains the fifth most used antimicrobial for food-producing animals in the 26 EU/EEA countries. However in June 2016 the European Medicines Agency (EMA) **re-evaluated their advice** on the use of colistin, recommending that colistin sales for use in animals should be reduced to the minimum feasible.

¹⁹ Kumarasamy et al. (2011) Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. The Lancet – Infectious Diseases 10(9): p597-602. DOI: <u>10.1016/S1473-3099(10)70143-2</u>
 ²⁰ Liu et al. (2015) Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. The Lancet - Infectious Diseases 16(2): p161-168. DOI: <u>10.1016/S1473-3099(15)00424-7</u>





Foundations of innovation

Foundations of innovation

Shared ideas - Publications

In the past 350 years there have been many changes to how researchers access existing knowledge and report new discoveries. However the core motivations behind publishing research findings communicating information, building a knowledge base and validating research quality - have remained largely unchanged.

The majority of publications (>99 per cent) reported by MRC researchers (and from biomedical research in general) are classified as 'journal articles'. Journals will normally decide whether to accept an article for publication based on review by experts in relevant fields, although other publishing models (post publication peer review and the publication of pre-print articles) are increasingly being used to accelerate the reporting of results.

In the last five years, 62,607 journal articles have been reported via researchfish®, with 91 per cent of MRC awards having resulted in a publication within five years (Figure 4, below).

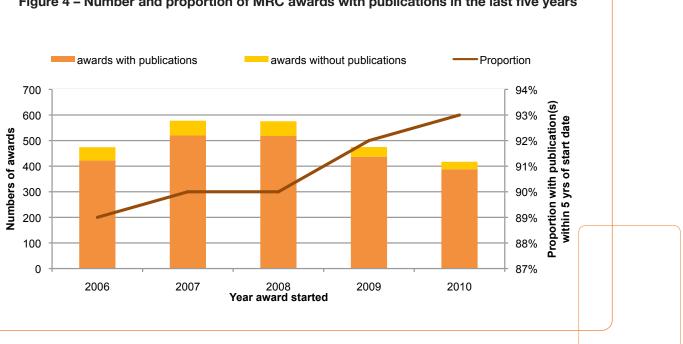


Figure 4 – Number and proportion of MRC awards with publications in the last five years

Bibliometrics

As all research is dependent on past discovery, 'Citations' - references to previous work in new publications - are often used as a metric to measure the attention that articles receive in the wider literature. Over time these bibliometrics can indicate how influential the original article was to the wider field of research.

Bibliometric measures are often used by funders, research organisations, publishers and researchers to quickly compare the citation of different bodies of work. However, the MRC, alongside other funders, recognises the need to use metrics responsibly, with recognition of the limitations of how such data can be interpreted. Internationally supported statements such as the **San Francisco Declaration on Research Assessment** (DORA) and the **Leiden Manifesto** highlight the care that should be taken over the use of metrics in research assessment. The UK's own expert review of the area published as the "Metric Tide" report²¹ sets out a comprehensive set of recommendations to improve research assessment and management.

The most recent citation information available to the MRC was sourced from the Scopus database provided by Elsevier²². By benchmarking each publication's citation record against publications in similar research fields, a 'field weighted citation impact' (FWCI) score is derived. A FWCI score of 1 indicates the paper is behaving as would be expected for that subject area, and this is referred to as the world average. Therefore an FWCI of above 1 means that the paper is cited more often than would be expected and is above the world average.

The mean FWCI for all MRC publications is 2.73, almost three times the world average.

In comparison, the average FWCI for the UK, USA and Germany is 1.46, 1.45 and 1.36 respectively, although such figures include all areas of research, not just biomedical. In parallel the publication output from a set of international research institutes with a biomedical focus was obtained (see Figure 5).

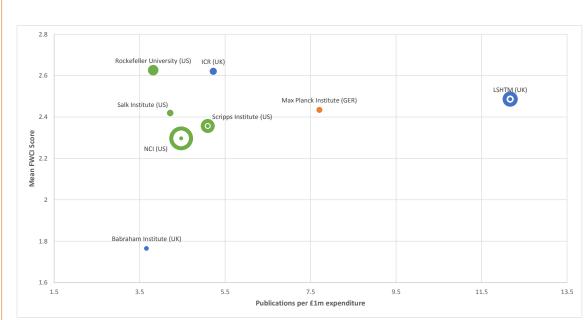


Figure 5 – Bubble chart of mean FWCI score and publications per £1m expenditure for nine comparator institutions

Figure Note: Comparator institution publications (2006-2014) includes 72,326 journal articles after de-duplication of publications attributed to MRC funding, with citation data correct as at August 2016. "Publications per £1m expenditure" is calculated from total number of publications divided by number of years covered (see above) to provide an average number of publications per year. This is then divided by the total operating expenditure for FY 2013/14 (collated from institutional 2013/14 financial reports) to provide an estimated publications per million pound figure. Bubble sizes are proportional to total number of publications, with UK, European and US institutions in blue, orange and green respectively.

A total of eight institutions were selected based on scientific discipline, publication output and/or annual expenditure. Citation analysis shows the overall MRC publication output FWCI score of 2.7 falls at the top of comparator institute range of 2.6 (Institute of Cancer Research & Rockefeller University) to 1.7 (Babraham Institute). Analysis of combined publication and expenditure data shows between 3.7 (Babraham Institute) and 12.2 (London School of Hygiene and Tropical Medicine (LSHTM)) publications per million pounds spent across the eight institutes. In comparison, the MRC portfolio overall delivers 6.4 papers per £1million expenditure although it should be noted that this calculation is based on a larger number of awards and linked publications.

²¹ Wilsdon et al. (2015) The Metric Tide: report of the independent review of the role of metrics in research assessment and management. Publisher: HEFCE, London, UK. DOI: **10.13140/RG.2.1.4929.1363**

²² Citation data accumulates following publication, and we require a minimum of 12 months before journal articles are included in our analysis. The following figures represent all publications attributed to MRC research via researchfish® from 2006-2014; a total of 56,607 articles, with citation information gathered through 2015.

Collaborations

The MRC works in partnership with other funders to jointly support programmes, bringing together complementary interdisciplinary expertise, infrastructure, and greater resources to address societal and scientific challenges. More than 25 per cent of MRC expenditure on research is committed jointly with other funding organisations. Notable examples include support for UK Biobank with Wellcome Trust, and support for the Francis Crick Institute with Cancer Research UK and others. Researchers also extensively collaborate to share ideas, expertise and facilities. We gain a view of these collaborations via the feedback collected annually via **researchfish@** and evidence in grant applications and research papers.

The MRC is keenly aware that research does not happen in isolation, it is a highly collaborative and global endeavour. Many breakthrough discoveries happen when there is interaction between disciplines, such as the interaction between engineering and biomedical sciences²⁵. Likewise collaborations outside of academia with the private and charity sectors are important.

The MRC has a number of funding mechanisms aimed to promote industrial collaborations, such as the MRC Industry Collaboration Agreement (MICA), Collaborative Awards in Science and Engineering (CASE) studentships, Proximity to Discovery: Industry Engagement Fund (P2D:IEF) and, in partnership with Innovate UK, the Biomedical Catalyst (BC). Currently more than a quarter of MRC awards (25.5 per cent) have at least one non-academic partner organisation already associated with the research at the point of application.

Likewise the MRC is an active participant in a number of national and international efforts to encourage and coordinate collaboration with other research funders, including:

- Lifelong Health and Wellbeing a cross-council initiative used to bring medical and social sciences together to meet the challenges and opportunities of an ageing population.
- <u>Compound Sharing Initiatives</u> 2015/16 also saw further awards made under MRC's award winning initiative, the most recent phase of which, involving six global biotechnology/pharmaceutical companies, was launched in July 2014.
- **<u>Biomedical Catalyst</u>** delivered in partnership with Innovate UK, the Biomedical Catalyst encompasses MRC's primary response-mode schemes focused on developing and testing next-generation therapeutics, diagnostics and devices. In 2015/16, MRC translational funding schemes made 42 awards totalling £40.9 million including **<u>'Confidence in Concept'</u>** awards.
- **Newton Fund** the MRC is an active partner in a range of international research and innovation programmes, including the Newton Fund, partnering the UK with emerging knowledge economies.
- Horizon 2020 the European Union's largest ever research and innovation programme with nearly €80 billion of funding available over seven years (2014 to 2020)²⁶.

In whatever form it appears, collaborations within the field of medical research all share a common goal; working collectively to maximise the potential for discovery to create real world benefits.

²⁵ EPSRC (2014) The importance of engineering and physical sciences research to health and life sciences. Published online, last accessed 25/10/16 <u>http://bit.ly/2lbsjhe</u>

²⁶ Note: Keyword searching of researchfish® data suggests at least £76m of funding has been reported by MRC researchers 2013-2016. In August 2016, HM Treasury agreed to underwrite Horizon 2020 funding for UK researchers following the EU referendum vote: <u>http://bit.ly/2boR025</u>



Collaborations and response to the Zika outbreak

In February 2016, the MRC was one of more than 30 organisations to sign an agreement committing to sharing data and results relevant to the current Zika crisis - and future public health emergencies - as rapidly and openly as possible. This follows from work begun following the global Ebola outbreak in 2014 and identifying a need for rapid and transparent sharing of research and public health data. In September 2015, a **consensus statement** arising from a WHO consultation affirmed that *"timely and transparent pre-publication sharing of data and results during public health emergencies must become the global norm."*

This international collaboration announcement coincided with the MRC's own announcement of a new 'rapid response' call for applications aimed at tackling the risk posed by the Zika virus through investigation of the nature of the virus, its transmission and the potential links to neurological conditions including microcephaly.

In 2016, the MRC and the Foundation for Science and Technology of the state of Pernambuco (FACEPE) in Brazil agreed to jointly fund a research proposal to investigate the viral features and host responses to Zika virus with a view to designing new preventative strategies. Genetic techniques will be used to support diagnostics and vaccine development studies as well as helping to understand the biology of the Zika virus during infection (MR/N017552/1).

In a parallel project, researchers at the University of Birmingham will also be in Brazil collecting Zika virus samples and genotype them_ (MC_PC_15100). They will use the latest technology in point-of-collection sequencing technology, the <u>Oxford Nanopore</u> <u>MiNION</u> sequencer (pictured). These USB-stick sized sequencing filters were donated to this study by the manufacturer, Oxford Nanopore Technologies, a spinout from MRC funded research in 2005 (G0300122).



Photo: Using the Oxford Nanopore MiNION device in front of the minibus lab in Joao Pessoa, Brazil. Source: University of Birmingham, photo by Ricardo Funari

Highlight:

Oxford Nanopore Technologies

Oxford Nanopore Technologies (ONT) was created to take advantage of the economic opportunities of IP derived from Professor Bayley's MRC-funded research at Oxford University in the early 2000's. The spin out company has now expanded to over 300 employees and has received external investment of £341 million over the last decade including £100 million announced in Dec 2016. Products developed by ONT have been used on the international space station, in the response to the Ebola epidemic in 2014-15, and in a wide variety of applications where rapid field diagnosis is key. Technology development now exploited by ONT was the result of cross-disciplinary funding from MRC, EPSRC and BBSRC for a variety of research programmes.

The Farr Institute

The Farr Institute of Health Informatics Established in 2012, The Farr Institute is a UK-wide research collaboration involving 24 academic institutions and two MRC units, with initial funding of £19

million from a consortium of ten organisations led by the MRC. The Institutes' key aim is to deliver high-quality, cutting-edge research using 'big data' to advance the health and care of patients and the public.

The Farr Institute exemplifies how coordinated working can allow all areas of the UK to benefit from MRC support. The four centres of the Farr Institute are located in:

- Centre for Improving Population Health through E-Health Research (CIPHER) at Swansea University
- Health e-Research Centre (HeRC) at the University of Manchester
- University College London, and
- University of Dundee

These Centres formed the cornerstones of a research network tasked with optimising the safe and trusted use of clinical, environment and population data in health research.

Prof Will Dixon from the University of Manchester has made good use of the new collaborative networks the Farr provides. Following from an MRC-funded fellowship examining steroids use in inflammatory disease (G0902272), Prof Dixon secured a Confidence in Concept award to support the *cloudy with a chance of* pain' study; the world's first smartphone-based study to investigate the association between arthritic or chronic pain and the weather. App development (pictured) was carried out in collaboration with digital company **uMotif**, and the study was formally launched in association with the Farr @ HeRC (MC PC 13042) in early 2016, with more than 12,000 patients already signed up.

The study aims to combine patient input, local weather information and the phone's GPS and accelerometer data to develop an algorithm for disease severity. This can be used to help optimise management in the clinic and provide a baseline for early and long-term intervention assessments. It will also provide the first scientific evidence for a phenomenon that has been discussed for the last 2,000 years.

Not only this, but the use of 'Citizen Science', i.e. the ability of anyone signed up to not only collect but also explore the data, has made for a popular news story, with TV interviews on BBC Breakfast, featured in an episode of Trust Me, I'm a Doctor and appearances in most national newspapers.



Photo: Screenshot of the UMotif app. Source: credited to UMotif.

While funding initiatives can encourage collaboration from the outset, there are many ways in which collaborations may arise as a result of the research. In the last five years of reporting, researchers reported new collaborations from 43 per cent of awards as a result of their MRC funding.

While the majority of the new collaborations made are within the UK, 42 per cent of collaborations are with international partners. The most common collaboration locations are within Europe (16 per cent) or the United States (14 per cent), see Figure 6 (red bubbles). The remaining 12 per cent (blue bubbles) account for a further 1,882 new collaborations across 76 countries.

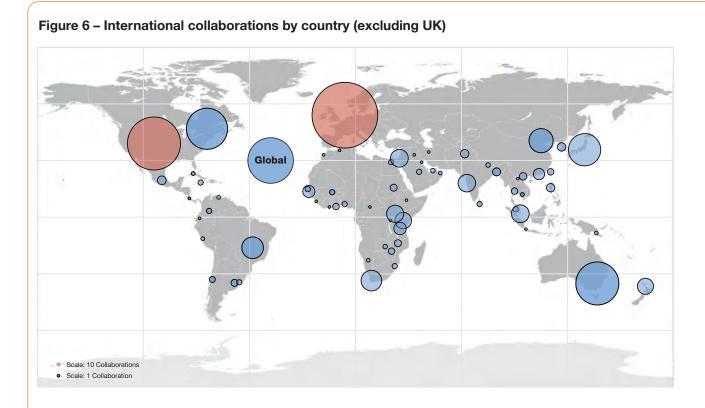


Figure Note:

This geographic bubble chart shows the number of collaborations reported by MRC researchers. Bubbles for Europe and USA are shown in red at 10x scale of other countries (blue). The 'global' total indicates collaborations with organisations classified as international, such as the United Nations or World Health Organisation.

Maintaining momentum – further funding

In addition to establishing and maintaining collaborations, researchers need to obtain on-going financial support to continue or expand on their work. Financial aid can also help develop research in new directions, such as the translation of outcomes into practical applications. This also demonstrates the extent to which MRC investments can 'crowd in' investment from external sources (e.g. other public funders, the private sector or non-profits/charities). In the last five years, 60 per cent of MRC awards have resulted in further funding within five years and since 2006, an estimated £5.84 billion of additional support²⁷ has been obtained as a result of MRC research (see Figure 7, below).





The 'crowding in' of funding by MRC researchers is an estimated at £4.38 billion of expenditure between 2011 and 2015, from more than half of all MRC awards. Over the same period, the MRC budget allocation from Government was approximately £3.58 billion, and in rough comparison, MRC researchers are able to access a further £1.2 in funding for every £1 of MRC support.

In 2015 a UK Government report, investigating the relationship between public funding for research and private investment in science²⁸, used a number of different data sources to £1 of public funding for research leverages between £1.1 and £1.6 in private sector funding²⁹. Likewise the recent assessment of spillover benefits of health research, published in 2016, suggested a return of £0.83-1.07 from the private sector for every £1 spent by public/charity funders, with a total rate of return between 24-28 per cent³⁰. The level funding derived from MRC funded research matches these analyses.

Of the further funding obtained, almost a third comes from outside the UK. Assessment of the location of further funding sources shows that of the ~ \pm 5.9 billion expenditure to date, \pm 1 billion comes from within Europe, with \pm 934 million (87 per cent of Europe total) directly from the European Union. A further \pm 840 million comes from outside Europe, primarily from the United States (\pm 607 million, 72 per cent), global organisations³¹ (\pm 128 million, 15 per cent) and Canada (\pm 35 million, 4 per cent).

http://bit.ly/1MvWLam

 ²⁷ Expenditure of reported further funding covers the period for which we have researchfish® data; 1 May 2006 to 1 April 2016.
 Estimates of expenditure of further funding are based on the assumption that the spending is distributed evenly over the period reported.
 ²⁸ Economic Insight (2015). What is the relationship between public and private investment in science, research and innovation?:

A report commissioned by the Department for Business, Innovation and Skills. Published online, accessed 01/10/16

A report continues of the Department for Dusiness, innovation and Okins. I doilsned online, ad

²⁹ In this study, and according to Organisation for Economic Co-operation and Development (OECD) definitions, charity funding for research was considered as part of the 'private' sector.

³⁰ Sussex et al. (2016) Quantifying the economic impact of government and charity funding of medical research on private research and development funding in the United Kingdom. BMC Medicine 14(32): DOI: <u>10.1186/s12916-016-0564-z</u>

³¹ In this context, 'Global' refers to international (or international schemes/programmes within) public bodies (e.g. WHO, UN), multinational companies (e.g. GlaxoSmithKline) and international non-profit/charities (e.g. UNICEF, Marie Curie Actions).

The value of economic evaluation

The Team for Economic Evaluation and Health Technology Assessment (TEEHTA) specialises in the economic impact of healthcare technologies at the University of York. In February 2015, the team published MRC-funded research (G0901498) suggesting that the £20,000 per quality-adjusted life year (QALY) threshold for cost-effectiveness used by the National Institute for Health and Clinical Effectiveness (NICE) may be too high³². This is a complex area of health economics. NICE generally considers interventions less than £20,000 as being cost effective, although interventions that cost £20-£30,000 may be considered cost effective if certain criteria are satisfied. Around 15 per cent of interventions approved by NICE are cost saving to the NHS. The TEEHTA researchers provided new estimates that showed the NHS currently delivered an additional QALY from just £13,000 of resource, and that this central estimate may be an over-estimate. The authors concluded that treatments more expensive than this would have an opportunity cost to the rest of the health service. This research received considerable media coverage³³ highlighting the importance of research that helps to support and improve effective resource allocation in the health service.

Dr Cynthia Iglesias is part of the TEEHTA and was the recipient of an MRC fellowship (**G0501892**). In 2014, Dr Iglesias received one year award of £102,000 from Innovate UK to investigate the economics of stratified medicine in rheumatoid arthritis. Dr Iglesias identified evidence to show that stratified approaches to treating a patient with rheumatoid arthritis may be cost-effective. However, there were gaps in the economic evidence base needed to support introducing stratified medicine in rheumatoid arthritis into healthcare systems. There was also uncertainty about how stratified approaches will impact future patient preferences, outcomes and costs when used in routine practice³⁴. While more research needs to be done to provide detail on the potential cost savings, as a result of her MRC fellowship, Dr Iglesias' research and new knowledge has also attracted further funding from the Luxemburg Institute of Health (€220,000) and the European Commission's Horizon 2020 programme (€6m) to continue her excellent work in the field of health economics.

³² Claxton et al. (2015) Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold. Health Technology Assessment 19(14): DOI: <u>10.3310/hta19140</u>

³³ Reported in the **BBC**, **The Telegraph**, **The Guardian** and **The Independent**

³⁴ Gavan et al. (2015) Economics of stratified medicine in rheumatoid arthritis. Current Rheumatology Reports 16:468. DOI: **10.1007/s11926-014-0468-x**



Shaping the future

Shaping the future

Behind great research are great scientists

To continue to reap the economic and societal benefits of research requires not just funding the buildings and the projects, but the dedicated scientists themselves. The expertise of senior clinicians and academics, with years of experience and unique understanding of their research, must be supported to ensure a new generation of researchers can continue in their footsteps.

Those at the start or early in their research careers are supported via the MRC capacity and skills programmes, with a net expenditure for the financial year 2015/16 of £71.0 million. This includes:

Studentships (£28.8 million, 40 per cent) funding 1,422 active PhD students (see Figure 8 below), with 403 new doctoral students starting study in the academic year 2015/16.

Fellowships (£42.1 million, 60 per cent) on 342 research fellows, including 167 Clinical Research Training Fellowships (CRTFs)³⁵.

In addition grants awarded via our strategic and response mode programmes from our various **boards** and panels provide support for principal investigators (PIs) and co-investigators (Co-Is) named on the proposal. At 1 April 2016 these programmes supported 1,149 PI a further 1,882 Co-I researchers. The MRC also supported a further 319 PIs as research or programme leaders across MRC **institutes** and units.

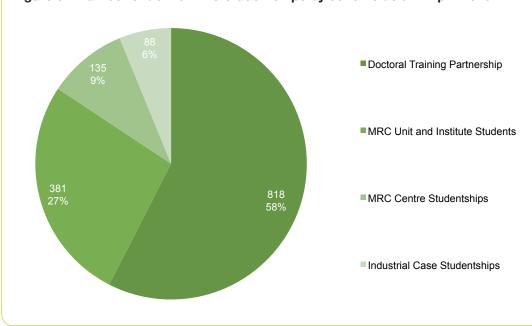


Figure 8 - Number of active MRC studentships by scheme as at 1 April 2016

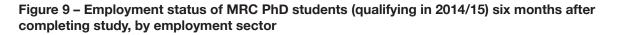
³⁵ Clinical Research Training Fellowships (CRTFs) support clinicians undertake a studentship leading to a PhD or other higher research degree but are counted under fellowships as they are personal awards to the individual.

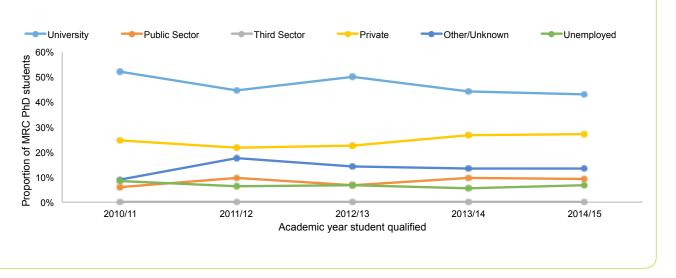
Career mobility

Researchers acquire many transferable skills with the ability to solve complex problems in creative ways; key attributes in a world where technology and innovation are in high demand. Even at the earliest stages as PhD students, researchers can find their skills sought after in both the research sector and as innovators in business.

Approximately 98 per cent of MRC PhD students will submit a thesis and attain their PhD, the majority (85 per cent in the last five years) within their expected submission period. Figure 9 (below) shows that six months after graduating³⁶, 89 per cent of students³⁷ are known to be in employment, higher than average graduate / postgraduate employment rates of 86 / 87 per cent respectively³⁸.

Just under half of students (43 per cent in 2014/15) remain in the higher education sector (Figure 9). Overall just over 55 per cent of MRC students went on to research-related employment and around a quarter of students (27 per cent in 2014/15) employed in the private sector. These data remain consistent with previous academic years, showing that MRC studentships continue to be desirable qualifications for future employment with a high propensity for research-related activities.





The MRC captures data on the PIs and Co-Is who receive direct and indirect support for their work at the point of application. However research is, by its nature, driven by the need to work collaboratively. Senior researchers recruit a variety of support to their projects; postdoctoral researchers to run experiments, technicians to manage the laboratory/equipment and support staff to help with administration.

MRC-funded researchers provide details on the staff who contribute to their work, and how the roles within the team change over time via researchfish[®]. Analysis of the top six researcher roles (see Figure 10, page 31) shows that overall 60 per cent of those employed as a result of MRC awards stay in the academic sector, while 10 per cent move into the private sector.

³⁶ Data from the Higher Education Funding Council for England (HEFCE)'s Destinations of Leavers from Higher Education

⁽DLHE) survey, which provides information about all graduates six months after they complete their studies.

³⁷ This includes students listed as 'self-employed' and 'other employment', in addition to those in university, public, third or private sector employment.

³⁸ BEIS (2016) Graduate Labour Market Statistics: 2015. Published online in April 2016. <u>http://bit.ly/1N2xzNN</u>

Post-doctoral researchers (largest group, 36 per cent, in Figure 10) tend to continue in careers in biomedicine, more than half attaining another post-doctoral research post and almost a fifth progressing as research fellows or project leaders. The researchfish® data on students (third largest group, 19 per cent) is reassuringly similar to the separate DLHE survey, where the majority leaving MRC support will continue in research (63 per cent). As a whole, these data help the MRC better understand how MRC support allows research teams to evolve and research careers progress; both of which helps us ensure our training support is meeting the needs of the research community and maximising our training's potential impact.

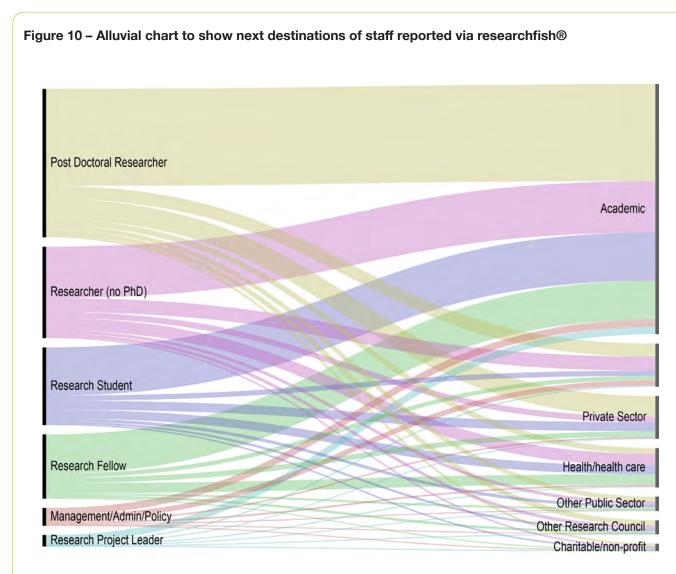


Figure Note: Next destination (role, sector and country) of for staff members leaving a role supported by an MRC award is reported by the award principal investigator via researchfish® 2006-2015. Collated data for the top six researcher roles being vacated is compared shown with the against the broad sector within in which their new role resides. Graphic created using RAWGraphs software³⁹.

³⁹ RAW is an open source project by DensityDesign Lab and Calibro, used under Apache Licence 2.0 URL: http://app.rawgraphs.io/ last accessed 01/02/2017.

Recognising research excellence

Measures of esteem can include awards and other evidenced forms of acknowledgement that researchers receive over their careers. For the MRC, we celebrate the awards and wider recognition won by our researchers, particularly where past and/or continuing MRC support has helped develop their career.

The <u>American Society of Human Genetics</u> (ASHG) has named **Professor Dame Kay Davies**, Director of the **MRC Functional Genomics Unit at the University of Oxford**, the 2015 recipient of the annual William Allan Award, presented annually to recognize substantial and far-reaching scientific contributions to human genetics.

Since the 1980s, Professor Davies has led research into Duchenne Muscular Dystrophy (DMD), a genetic disorder marked by muscle weakness that causes patients to become wheelchair-dependent early, while damage to the heart muscles means premature death is likely. Professor Davies and her team were involved in the first identification of the role of dystrophin in DMD. Dystrophin is a vital to the protein complex that links muscle fibres together and the absence or shortening of the protein through mutation leads to muscle weakening, fibrosis (scarring) and necrosis (wasting).

In her most recent MRC-funded work, Professor Davies' research group have shown that both recovery of even a smaller, quasi-functional dystrophin gene **(G0801763)** and increasing utrophin, a relative of dystrophin levels (**MR N010698/1**) can prevent disease progression, pioneering the development of potential new treatments for DMD.

Professor Davies' role as Director of the MRC Functional Genomics Unit facilitates the extension of her research beyond the understanding and treatment of DMD. These include the role of oxidative stress genes in Amyotrophic lateral sclerosis (ALS), mutations in mice as models for schizophrenia and how the genetic basis for neurodegenerative diseases like Alzheimer's are linked to sleep abnormalities (**MC U137761449** & **MC UU 12021/2**).

The Royal Society is the UK's premiere scientific academy, with a fellowship of more than 1,600 of the world's most eminent scientists. In December 2015 **Professor Sir Venki Ramakrishnan** became the 62nd President of the **Royal Society**, following in the footsteps of Isaac Newton and Humphrey Davey. Prof Ramakrishnan joined the MRC Laboratory of Molecular Biology in Cambridge in 1999 (**MC_U105184332**) and became Deputy Director. He currently retains an active research role as a programme leader. In recent years, Prof Ramakrishnan has been awarded both the **Louis-Jeantet** and **Nobel Prize**, among the most prestigious awards in science, for his work on the structure and function of the ribosome; a vital part of the cellular machinery of DNA replication/translation.



Celebrating science

Celebrating science

The MRC's mission includes promoting public dialogue on research. We rely on the support of taxpayers to continue funding for medical research and encourage MRC funded researchers to communicate their interests, approaches and results as widely as possible.

Engagement Activities

The MRC **encourages and supports its researchers** by creating engagement opportunities via open days, science festivals and our annual Max Perutz science writing competition. These events are, in part, directly supported by our corporate budget for public engagement – £170,000 in 2015/16 – which includes small grants for researcher-led public engagement projects such as taking activities to popular music festivals and creating resources for schools. The MRC Press Office also helps our scientists disseminate to the media with more than 8,900 articles on their scientific achievements in 2015. The MRC also has an ever-growing social media presence, through our Facebook, YouTube, Twitter accounts and **our blog**, *Insight*.

But public engagement is not limited to MRC-run events. We encourage our scientists to participate in their own organisations' engagement activities and, of course, their own ideas on how to engage, educate, and inspire the public. Over the past five years, more than 62 per cent of MRC awards have generated at least one example of public engagement, varying from traditional talks and lectures to open days to TV appearances to podcasts.

It is encouraging that so many of the MRC's researchers use their skills as public speakers, honed by scientific conferences and teaching duties, to engage with non-academic audiences; Almost of third of the audience (30 per cent) for engagement activities are the public, with a further 12 per cent aimed at policymakers and parliamentarians and another 12 per cent in schools (see Figure 11, below). The addition of patient engagement to researchfish® has also been a source of encouragement; MRC researchers often interact with patients, carers and patient groups with a specific interest in their particular area of research but it is only now that detailed information on these interactions has become available.

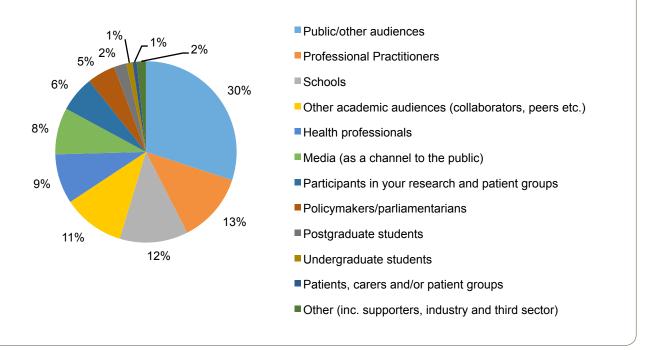


Figure 11 – Public engagement activities by MRC researchers classified by audience type

Case study:

Research by the pint

"If people want to come to labs to meet scientists, why not bring scientists to people?... What could be a more suitable place for an event like this than the most traditional institution in the UK – the pub?" - Praveen Paul & Michael Motskin⁴⁰, Founders, Pint of Science

Since 2012, the **Pint of Science** festival, a twist on the traditional 'science talk in a public venue', has been entertaining and informing the public. Attendees can chose from a selection of researchers and topics on offer... alongside a selection of beers, wines and spirits. The festival has grown considerably since the first festival, with 45 events in 15 pubs across three cities, to 500 events in 150 pubs in 50 cities across 9 countries.

Talking to researchers will often give you a feel for how enthusiastic they are about their work, and how much they enjoy sharing their findings with others. As a result it is no surprise that many MRC-funded researchers have organised and/or presented at Pint of Science events, such as students and scientists from the MRC Clinical Sciences Centre at Imperial College London who were <u>keenly</u> involved the 2015 festival, particularly the 'Beautiful Minds' event focused on neuroscience.

Within researchfish® there are several examples of MRC researchers organising and contributing talks, with a diversity of topics discussed:

- Dr Hendrik Huthoff's research focus is in the metabolism of immune cells and how this is disrupted following infection by HIV virus (<u>MR/J008125/1</u>). In his talk on <u>'Why haven't we cured HIV yet?</u>', Dr Huthoff discussed the difficulties of developing lasting cures and vaccines to a target virus with a long history of outwitting scientists.
- Public health specialty registrar Conall Watson, working on an MRC-funded doctorate in epidemiology, applied his knowledge of managing typhoid outbreaks to discuss how to stop a zombie epidemic in <u>"Models vs</u>
 <u>Zombies: Can maths stop an epidemic dead?"</u> which also resulted in an article in *The Lancet*⁴¹.
- Dr Ella James from the MRC Cognition and Brain Sciences Unit (MCUP 0901/1) presented how use of the computer game 'Tetris' may help reduce the build-up of flashbacks in post-traumatic stress disorder (PTSD).

By using pop culture references and an informal setting, such talks provide an excellent mechanism for wider dissemination, where the most basic questions can be asked without judgement. This is reflected in the success of Pint of Science, and the manner in which it has grown from a single event to a non-profit organization with an increasing global presence.

⁴⁰ Paul & Motskin (2016) Engaging the public with your research. Trends in Immunology 37(4): p.268-271. DOI: <u>10.1016/j.</u> it.2016.02.007

⁴¹ Watson et al. (2014) Waking the undead: bringing zombie epidemiology to life. The Lancet Infectious Diseases 14(10): p929. DOI: **10.1016/S1473-3099(14)70934-X**



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Getting creative

For many, the pairing of medical research and the arts seems unlikely. However over the last two years, the combined use of researchfish® across both medical and arts/humanities research funders has provided MRC researchers with the opportunity to report on their more creative endeavours. While relatively few in number, just 141 reports in the past five years, it has been interesting for the MRC to see less conventional means by which scientific achievements can be expressed. Around 35 per cent of these are films, videos or animations, which includes advocacy work, often created directly by researchers themselves, on social media video channels like YouTube. Also included are exhibits in science museums and artistic installations. Photographs, often taken for the purposes of research (e.g. captured by microscopy) can be subsequently used for more artistic purposes, such as the cover of books or magazines, or public display.

Case study:

Monitoring brain performance – via trapeze

Dr Petra Vertes is an MRC fellow in Biomedical Informatics at the Brain Mapping Unit (BMU), University of Cambridge and co-founder and organizer of the **Cambridge Networks** <u>Network</u> (CNN).

Dr Vertes' research (MR/K020706/1) focuses on networks within the brain and how these change as we age. Understanding the processes involved in brain organisation and development has implications not just for ageing, but for improving cognitive performance and treating disorders where alteration of brain networks are a critical component, such as schizophrenia.

In addition to her research, Dr Vertes has acted as consultant to an aerial performance theatre group, Scarabeus. Their latest production **'Depths of the Mind'** is an innovative performance that combines aerial skills with visual theatre, to bring to life the latest developments in neuroscience and neuroimaging connected to the adolescent brain. This not only raises the profile of neuroscience but, being specifically aimed at teenagers, will highlight the issue of mental health to a demographic experiencing a sensitive period of brain development and a high incidence of mental health issues.

Case Study:

From START to Finish

The **<u>Strategic Timing of AntiRetroviral Treatment</u>** (START) study is a randomised trial across 36 countries aiming to determine the best point at which to start anti-HIV drug treatments. Organisation for START comes through **<u>INSIGHT</u>** (International Network for Strategic Initiatives in Global HIV Trials) and is supported in part by the **<u>MRC Clinical Trials Unit</u>** (CTU) at University College London (<u>MC U122886352</u>, <u>MC UU 12023</u>).

Recruitment for the START study began in 2009 running until 2013, with follow-up assessment, such as impact on disease progress and mortality, continuing into 2016. However in **May 2015**, initial results from the START trial were released ahead of schedule, as the body of evidence gathered provided sufficient support for offering HIV treatment earlier to people diagnosed with HIV⁴². Applying treatment earlier reduces the damage to the patient's immune system, leading to reduced risk of developing serious illness.

In addition to the main study findings, community representatives - including Ugandan dancer, musician and HIV activist Moses 'Supercharger' Nsubuga - working with INSIGHT and the START trial have written two songs, with accompanying videos. <u>"Nobody Knows"</u> was released before the START results were announced, with <u>"Now I Know"</u> released a few months later. These songs help the wider work of advocacy for HIV/AIDS research, particularly in disseminating research findings to the communities most affected.



Annexes

Annex 1 – Reporting Requirements and Methodology

Introduction

The MRC Economic Impact Report has been published each year since 2005 and is part of the research councils' performance management framework implemented by the Department for Business, Energy and Industrial Strategy (BEIS). All of the MRC's Economic Impact reports are available on the MRC website⁴³.

In 2014, the Research Councils established a harmonised method for the collection of research outputs and outcomes data via researchfish®⁴⁴. This provided a good opportunity to review the common indicators in the Impact Reports, with a view particularly to extending the harmonisation of quantitative data. In April 2016 the Research Councils agreed a revised set of common indicators for our Economic Impact reporting which while similar to previous reporting requirements benefit from a more uniform methodological approach.

The list of common indicators currently agreed between BEIS and the research councils can be found in Annex 2. Each research council also presents a number of additional metrics and narrative information to ensure the report reflects the full range of activities undertaken by the council. The MRC Economic Impact Report includes data covering the last five years, with some data extended further back where available.

In addition to the raw metric data, this report also includes further details on the inputs, outputs and outcomes required, including some example case studies. Further information on each study can be found on the Research Councils UK (RCUK)'s information portal — the Gateway to Research⁴⁵ — by entering the project reference number listed under each case study in the search field or following the link provided.

It is important to note that the data and case studies featured in this report represent only a small proportion of the data collected annually by MRC. More details and further case studies can be found in other MRC publications, in particular the MRC Annual Report and Accounts 2015/16⁴⁶ and the Outputs, Outcomes and Impact Report 2015/16⁴⁷. All MRC publications can be found on the MRC website.

Data collection and analysis: researchfish® and the use of outputs, outcomes and impact data

The MRC's evaluation programme focusses on capturing evidence to track the progress, productivity and quality of the research the MRC funds. One route for doing this is through **researchfish®**, the online system used by researchers to feed back on the outputs and impact of their work. Outputs and outcomes include **publications** and academic **collaborations**, new **medical products** and technologies that advance understanding and provide evidence for **policy** improvement. Economic impacts may arise, such as obtaining **further funding** for continued research, commercialising **intellectual property** and establishing **spin-outs**. Our approach to capturing feedback about output is shared across all seven research councils and many other UK and international funders, providing the capability to identify a wide range of outputs across the UK research base, and better understand how these contribute to economic and societal impact.

⁴³ The MRC Economic Impact Reports can be found by using the search option or tag link "economic impact" at: <u>http://www.mrc.</u> <u>ac.uk/news-events/publications/</u>

⁴⁴_researchfish® is a registered trademark of Researchfish Limited: https://www.researchfish.com/

⁴⁵ Research Councils UK Gateway to Research. <u>http://gtr.rcuk.ac.uk/</u>

⁴⁶ MRC Annual Report and Accounts 2015/16: <u>http://www.mrc.ac.uk/publications/browse/annual-report-and-ac-</u> <u>counts-2015-16/</u>

⁴⁷ MRC Outputs, outcomes and impact of MRC research 2015/16: <u>http://www.mrc.ac.uk/successes/outputs-report/</u>

The MRC uses this detailed view of research output to communicate the benefits of medical research to Government, the public and other stakeholders, to evaluate funding mechanisms (e.g. schemes and units), and to review its portfolio. Examples of evaluation projects include the 2015/16 MRC-led evaluation of the multi-funder National Preventative Research Initiative (NPRI)⁴⁸, ongoing work to assess the benefits of establishing the Francis Crick Institute, and to evaluate the benefits of transferring MRC Units to University ownership. This Economic Impact report, an annual summary of Outputs, Outcomes and Impact⁴⁹ and The MRC Annual Report and Accounts⁵⁰ are examples of publications that include a broad range of case studies highlighting how MRC research influences wider society.

In 2014 all seven research councils joined researchfish®, become part of a community consisting of over 72,000 researchers reporting in, over 110 research organisations tracking outcomes on 100,000 awards and over £40 billion worth of funding⁵¹.

Researchers can enter, amend and update information in researchfish® all year round, but the MRC requires researchers to submit a return in the system once a year⁵² for the lifetime of the award and a number of years beyond. This means that numbers reported this year will be different to those reported previously as researchers can continue to add information retrospectively to provide a fuller account of research progress.

It is also important to note that there will some variations in analysis between reporting periods, as the modifications to the researchfish® question sets, data processing/cleaning (de-duplication, disambiguation etc.) and changes in coding practice will affect some data outputs. Therefore, while data presented here may be found in other researchfish® reports⁵³ and MRC publications⁵⁴, there may be some slight differences in the figures reported.

The latest reporting year (2015) was the eighth year that MRC researchers used the system, with a new data collection period running in February and March 2016. Since 2006, 92 per cent of the MRC scientists who have held any funding from the organisation have submitted information relating to more than 5,600 awards in total (5,684 responses from an expected 6,162).

It is important to note that while counts of researchfish® data help illustrate the volume of output information collected, the MRC is primarily interested in the quality of outputs received. We are most interested in how MRC research contributes to the development of new medicines and technologies, improvements to clinical and public health policies and practices, and how it encourages inward investment to the UK. Therefore outputs reports are extensively reviewed to identify duplicates and to consider whether they meet basic criteria such as being evidenced, justifiably linked to a core MRC programme and occur within the relevant timescale⁵⁵. The main exception to these internal duplication checks are published outputs. The primary aim with publications is to benchmark outputs using a variety of more quantitative bibliometric approaches such as citation indexing.

Finally, while researchfish® data is used for the majority of outputs within this report, MRC collects data from additional sources to provide further information on our activities. These include bibliometric data from Elsevier, studentship information from the Joint Electronic Submission (JeS) service and Higher Education Statistics Agency (HESA) and internal MRC grant/financial systems.



⁴⁸ NPRI Scientific Review Group (2015). NPRI: Initiative outcomes and future approaches. Published by MRC online,

September 2015. Last accessed 31/10/16. <u>http://www.mrc.ac.uk/publications/browse/national-prevention-research-initia-</u> tive-npri-report-2015/

⁴⁹ The most recent report, from 2014/15 is available online. The 2015/16 report's expected publication will be in early 2017:

http://www.mrc.ac.uk/successes/outputs-report/

⁵⁰ https://www.mrc.ac.uk/about/what-we-do/spending-accountability/annual-report/

⁵¹ The researchfish® system is owned and operated by Researchfish Ltd., and is available to all research funders on a subscription basis; <u>http://www.researchfish.com/</u>

⁵² The researchfish® submission period for 2015 closed in March 2016.

⁵³ MRC Official Researchfish® Sample Data Report 2015: <u>http://www.mrc.ac.uk/documents/pdf/official-mrc-research-</u><u>fish-report-sample-data-21-07-15/</u>

⁵⁴ Principally MRC Annual Reports and Outputs Reports: <u>http://www.mrc.ac.uk/publications/browse/</u>

Annex 2 – Common Indicators

The Research Councils have agreed a revised set of common indicators drawn from information from grants databases and researchfish[®]. Please note that any reporting lines marked with # indicate this is additional MRC-specific data, not part of the harmonised common indicators.

Table 1: Total Funds Available

Financial Year	201	1/12	201:	2/13	201	3/14	201	4/15	201	5/16
1.1 Budget allocation	69	97.5	65	6.2	72	5.8	70	3.5	79	7.8
1.2 Leverage total amount (BEIS defined) (£m)	56.5		68.3		66.9		6	1.7	65.7	
1.2.1 Leverage from other Research Councils (BEIS defined) (£m)	9.8	17.3%	15.7	23.0%	15.1	22.6%	16.6	26.9%	16.6	25.3%
1.2.2 Leverage from private sector (BEIS defined) (£m)	42.1	74.5%	49.2	72.0%	48.3	72.2%	41.6	67.4%	39.6	60.3%
1.2.3 Leverage from other sources (BEIS defined) (£m)	4.6	8.1%	3.4	5.0%	3.5	5.2%	3.5	5.7%	9.5	14.5%
1.3 Total further funds leveraged by projects	6	6.7	42.		32	2.2	9.	7.7	4().4
1.3.1 Funds leveraged by projects – private (£m)	0.8	11.6%	16.3	38.5%	24.6	76.2%	55.6	56.9%	22.0	54.3%
1.3.2 Funds leveraged by projects – public (£m)	2.0	30.1%	5.1	12.0%	2.8	8.8%	34.7	35.5%	11.2	27.7%
1.3.3 Funds leveraged by projects – non-profit	0.0	0.0%	0.1	0.2%	0.7	2.1%	2.6	2.6%	7.2	17.8%
1.3.4 Funds leveraged by projects – academic sector	3.9	58.3%	20.9	49.2%	4.1	12.8%	4.9	5.0%	0.1	0.2%

Notes:

 Figures for Sections 1.1 and 1.2 come directly from the <u>MRC Annual Report 2015/16</u>, see sections 2,4 and 5 of the 'Financial Statements' section (pages 105-107).

1.2 Note that the MRC also generates income leveraged from other Government sources and our (MRCT-managed) commercial activities; in 2015/16 these figures were £44m and £96m respectively. Combined with leverage, our total operating income for 2015/16 was £206m.

1.3 Figures for Section 1.3 have now been standardised across Research Councils. This indicator reports the cash and in-kind contributions from partner organisations that were listed on the original research proposal. It does not include any further leverage funding that may have arisen during the course of the award. It does not include additional funding leveraged by intramural investments.

Financial Year	201	1/12	201	2012/13 2013/14 2014/15 20		201	5/16			
2.1 Research expenditure	581.6	70.3%	630.2	74.5%	663.4	76.1%	676.4	76.2%	846.3	79.1%
2.2 Training expenditure	86.0	10.4%	79.5	9.4%	69.9	8.0%	71.1	8.0%	71.0	6.6%
2.3 Other expenditure	159.7	19.3%	135.7	16.1%	138.4	15.9%	140.6	15.8%	152.9	14.3%

Table 2: Total Expenditure

Notes:

Figures for Sections 2.1-2.3 come directly from the MRC Annual Report 2015/16 (Financial Statements, Section 2, page 105). 'Research expenditure' includes research grants, MRC institutes and units and other dedicated research expenditure such as funding for the Francis Crick institute.

Table 3: Human Capital

Financial Year	201 ⁻	1/12	201:	2/13	201:	3/14	2014	4/15	2015	5/16				
3.1(a) Number of PIs (on 1st April)	10	58	97	78	10	28	10	45	114	49				
3.1(b) Number of PIs at MRC institutes and units (on 1st April) #	23	37	23	39	24	16	35	357		357		357		9
3.2 Number of Research Fellowships (on 1st April)	37	77	35	58	33	36	34	18	34	2				
3.3 Number of PIs and CO-Is on research grants (on 1st April)/ the number of Research Organisations (including Independent Research Organisations)	# of Pls and CO-ls 2867	# of ROs 58	# of Pls and CO-ls 2754	# of ROs 62	# of Pls and CO-ls 2898	# of ROs 66	# of Pls and CO-ls 3090	# of ROs 68	# of Pls and CO-ls 3373	# of ROs 86				

Notes:

Figures for Section 3.1(a), 3.2 and 3.3 have now been standardised across Research Councils to report the number of Principal Investigators (Pls)/Co-investigators (Co-I)/Fellows/Research Organisations (ROs) supported on the 1 April of each reporting year. This standardised reporting excludes supported through intramural investments, unless they are in receipt of a research grant. However as MRC supports a significant number of researchers at our institutes and units, we also report these figures here (as additional Section 3.1(b)).

Table 4: Human Capital – postgraduates

Financial Year	2011/12	2012/13	2013/14	2014/15	2015/16
4.1 Number of new doctoral students within that financial year	411	414	452	387	403

Notes:

This indicator denotes the number of MRC-funded PhD students newly registered on the Joint Electronic Submission (Je-S) system within the financial year. Please note that records of MRC studentships on the Je-S database are provided directly by research organisations funded by MRC studentship programmes. These including DTPs and CASE PhD studentships, but may not include all intramural and centre studentships.

Reporting Year	2010/11	2011/12	2012/13	2013/14	2014/15
4.2 Doctoral submission rate ('within expected')	89.4%	77.7%	92.2%	92.5%	74.2%
4.2.1 Submission rate ('outside expected') #	7.8%	14.9%	1.2%	5.0%	24.2%
4.2.2 Overall submission rate (total)#	97.2%	92.6%	93.4%	97.5%	98.4%
4.2.3 Without submission data#	n/a	58.8% ²³	49.6% ²³	35.2% ²³	17.6% ²³

Notes

Research councils obtain submission data on students via an annual submission survey completed by the student's host research organisation⁶⁷. Students on research council studentships are encouraged to complete their studies by an expected submission date, although this varies depending on the nature (e.g. part/full time) and duration of the studentship undertaken. At MRC, expected submission dates **are defined as** 'no more than six months after the funding end date', where the duration of funding can range from three to four years. However submission of a thesis can also be affected by career breaks, changes in research direction, changes in supervisory arrangements and other situations outside of the student or research organisation's control. As such the submitting research organisation can adjusted the expected submission date to accommodate such changes. In general, more than 94 per cent of students submit a thesis within one year of their funding end date.

4.3 Destination of Higher Leavers from	Academic year programme was completed								
Education	2010/11	2011/12	2012/13	2013/14	2014/15				
4.3.1 of which University	47.8%	48.5%	55.3%	45.0%	44.7%				
4.3.2 of which Wider Public Sector	5.6%	8.0%	3.7%	8.8%	7.2%				
4.3.3 of which Third Sector	0.0%	0.0%	0.0%	0.0%	0.0%				
4.3.4 of which Private Sector	28.9%	19.0%	20.1%	26.9%	28.0%				
4.3.5 of which Unknown or Other	10.0%	18.0%	13.9%	14.4%	13.5%				
4.3.6 of which Unemployed	7.8%	6.5%	7.0%	5.0%	6.6%				

Notes:

Post-submission, the Higher Education Funding Council for England (HEFCE)'s **Destinations of Leavers from Higher Education** (DLHE) survey provides all research councils with information about all graduates six months after they complete their studies. This survey is a condition of funding for HEFCE-supported higher education institutions (HEIs) in England, which individual HEIs must fund and administer themselves, using materials provided by the Higher Education Statistics Agency (HESA). As such the data provided by HESA to all research councils on their PhD students is limited to those who successfully completed the survey request, so may not account for all studentships in our portfolio.

Collaborations,				Yea	r the a	award st	arted			
partnerships and secondments	201 ⁻	1/12	201	2/13	201	13/14	201	2014/15		5/16
5.1.1 Instances of collaborations and partnerships reported at point of application and % of awards reporting at least one partner organisation	376	1.5%	655	22.4%	661	20.1%	675	30.5%	715	25.5%
Collaborations, partnerships and	Year the collaborations, partnerships or secondments were first reported									e first
secondments	20	11	20)12	2	013	20	014	20)15
5.1.2 Instances of new	15	14	16	690	1	619	10	350	12	265
collaborations and partnerships reported in researchfish®	(22	32)	(28	368)	(2	405)	(19	928)	(16	648)
5.2 Instances of secondments reported in researchfish®	4	3	1	01	1	172	3	05	2	32

Table 5: Collaboration, partnerships and secondments

Notes:

Data on collaborations and partnerships at the point of application (5.1.1) come directly from the MRC's grant

management systems. Data on new collaborations (5.1.2) and secondments (5.2) is provided by researchers via researchfish[®]. Collaborations can involve multiple partners, hence the number of partnerships, shown in (), will always be higher than number of collaborations.

⁶⁶ Submission data is supplied by research organisations but this information, particularly the verified submission date, is often incomplete. As a result submissions rates are displayed as a percentage of the total studentships with completed award data, and studentships without submission data are left as 'unknown' until submission information is completed by the research organisation.
⁶⁷ Records of MRC studentships on the Joint Electronic Submission (Je-S) database are provided directly by research organisations receiving MRC studentship programme funding. See the <u>JeS handbook on PhD</u> submissions for more details. Please note that these data includes MRC Advance Course Masters, Doctoral Training Partnerships (DTPs) and CASE PhD studentships, but do not include intramural and limited Centre studentships.

Table 6: Knowledge Generation

	Year outcome realised								
Publications	2011	2012	2013	2014	2015				
6.1.1(a). Number of journal articles	11,543	12,346	13,226	13,335	12,157				
6.1.1(b). of which unique#	8,613	9,388	10,178	10,148	9,478				
6.1.2. Number of books	10	17	28	31	23				
6.1.3. Number of book chapters	50	109	134	123	86				

Publications:	Year the award started									
Number / proportion of awards	2006		2007		2008		2009		2010	
6.1.4 Number / proportion of awards that gave rise to at least one example of a publication within five years of award start date	422	89%	520	90%	518	90%	437	92%	388	93%

Notes:

A publication may have arisen from more than one award. Duplicate publication outputs are removed, where possible, using system-generated codes to indicate when an individual researcher has attributed an output to more than one award. This automated process cannot identify duplicate outputs where different researchers have entered similar information independently of one another. However the MRC encourages researchers to provide unique identifiers (e.g. a Digital Object Identifier, a PubMed ID) wherever possible, and works with Researchfish Ltd. and suppliers of bibliometric data to populate unique IDs to all MRC-affiliated publications. As a result, the MRC can also provide an additional total of unique publications for each reporting year (see 6.1.1(b)).

	Year outcome realised								
Other outputs	2011	2012	2013	2014	2015				
6.2.1 Instances of artistic and creative outputs	6	9	18	53	55				
6.2.2 Instances of research databases and models reported	13	32	63	94	81				
6.2.3 Instances of software and technical products reported	9	15	31	73	70				
6.2.4 Instances of research tools and methods reported	539	539	216	196	134				
6.2.5 Instances of medical products, interventions and clinical trials	133	136	208	139	78				

Notes:

Instances of other types of outputs listed here may have arisen from more than one award. Duplicate outputs are removed, where possible, using system-generated codes to indicate when an individual researcher has attributed an output to more than one award. This cannot identify duplicate outputs where different researchers have entered similar information independently of one another.

Intellectual Property (includes patents, copyrights,	Year outcome realised								
trademarks)	2011	2012	2013	2014	2015				
6.3 Instances of IP reported (researchfish® data)	119	122	94	53	48				
6.3.1 Instances of IP reported (MRCT data)#									
Patents applications	12	20	11	9	13				
Patents granted	27	38	32	42	33				
Non-patented IP disclosures	n/a	19	13	14	12				
6.3.2 Income from IP activity (MRCT managed) (£m)#	79.0	91.7	85.4	94.9	96.0				

Notes:

Information on intellectual property from two sources; MRC Technology (MRCT) is responsible for managing intellectual property and commercial opportunities arising from MRC's intramural programme (MRC directly supported Units and Institutes) (6.3.1, 6.3.2), in addition all researchers supported by the MRC report intellectual property arising from this funding through researchfish® (common indicator 6.3). The statistics gathered via researchfish® will include the output from both extramural and intramural programmes.

Spin-outs/start-ups created and significantly		Year outcome realised								
supported from the outset	2011	2012	2013	2014	2015					
6.4 Instances of spin-outs/start-ups	20	10	13	10	8					

Notes:

MRCT also has some capacity for managing the creation of spin-outs, and oversaw the creation of two new companies in 2010/11.

Table 7: Further Funding

Further Funding Number / proportion of awards	Year the award started											
	2006		2007		2008		2009		2010			
7.1.1 Number / proportion of awards with at least one instance of further funding within 5 years of the start date	302	64%	356	61%	369	64%	294	62%	214	51%		

Table 8: Engagement activities

Engagement activities Number / proportion of awards	Year the award started											
	2006		2007		2008		2009		2010			
8.1.1 Number / proportion of awards with at least one instance of engagement within 5 years of the start date	299	63%	372	64%	362	63%	294	62%	245	59%		

Table 9: Influence on Policy and Practice

Influence on Policy and Practice Number / proportion of awards	Year the award started											
	2006		2007		2008		2009		2010			
9.1.1 Number / proportion of awards with at least one instance of policy influence within 5 years of the start date	98	21%	146	25%	152	26%	129	27%	95	23%		

Notes:

Instances of further funding, engagement and policy influence listed here are reported via researchfish® and may have arisen from more than one award. Duplicate outputs are removed, where possible, using system-generated codes to indicate when an individual researcher has attributed an output to more than one award. This cannot identify duplicate outputs where different researchers have entered similar information independently of one another.

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