MRC Medical Research Council

Economic Impact Report 2013/14

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1.0 Introduction

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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, Innovation and Skills (BIS). All of the MRC's Economic Impact reports are available on the MRC website[1].

The Research Councils have worked closely with BIS with the aim of streamlining the metrics that are presented in this report. The aim has also been to make reporting across the Councils more consistent and to provide more informative and robust metrics.

The list of metrics agreed between BIS and the Research Councils can be found in Annex 1, and supporting data is presented in Annex 2. Each Research Council also presents a small number of additional metrics and narrative information to ensure the report reflects the full range of activities undertaken by the council. The additional metrics for the MRC are noted in Annex 1.

This report should be read in conjunction with the MRC Annual Report and Accounts 2013/14 and the MRC Annual Review 2013/14, which provide a comprehensive summary of achievements over the period. These and all other MRC publications are available from the MRC website.

The MRC Economic Impact Report includes data covering the last four years, with some data extended further back where available.

2.0 Summary and highlights

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The heart of our mission is to improve human health through world-class medical research. To achieve this, we support research across the biomedical spectrum, from fundamental laboratory-based science to clinical trials, in all major disease areas. We work closely with key stakeholders and other research funders in the UK and internationally to deliver our mission, prioritising research that is likely to make a real difference to clinical practice and the health of the population.

Our stakeholders include the UK's health departments and other government departments and agencies, the six other Research Councils, Innovate UK, industry sectors such as pharmaceutical, biotechnology, nutrition, medical technology and informatics, the academic and charity sectors, and of course the public. Established in 1913 and incorporated by Royal Charter in 1920, the MRC's mission is to:

- Encourage and support research to improve human health.
- Produce skilled researchers.
- Advance and disseminate knowledge and technology to improve the quality of life and economic competitiveness of the UK.
- Promote dialogue with the public about medical research.

Our allocation from Government for 2013/14 was agreed under the 2010 Spending Review. The *MRC Delivery Plan 2011/12 – 2014/15*[2] details the MRC's spending priorities and intended activities for the spending review period. It describes how the MRC plans to use its resources to achieve its mission and contribute toward the Government's objectives for the science budget. Progress in implementing the delivery plan and achievements against the milestones are monitored routinely by the MRC Management Board. Progress is reported to Council and, via biannual meetings, to BIS. A summary of this progress is included in the subsequent annual delivery plan reporting framework document[3]. The MRC also reports on the outputs of MRC research in its annual outputs, outcomes and impact reports[4].

In 2009, we published our five-year strategic plan, *Research Changes Lives*[5], which defines our role in contributing to faster and more effective ways for medical research to flourish at all stages, from working to understand the fundamental science of how our bodies work to tackling some of the most pressing health issues facing society. In 2013 we published a refreshed strategic plan, Research Changes Lives 2014-2019, which continues our strategic direction, building on our strengths and achievements and also takes into account new scientific opportunities to secure tangible impact from MRC research.

The MRC's four strategic aims are:

- Picking research that delivers: setting research priorities which are most likely to deliver improved health outcomes.
- Research to people: bringing the benefits of excellent research to all sections of society.
- Going global: accelerating progress in international health research.
- Supporting scientists: sustaining a robust and flourishing environment for world-class medical research.

100 years of impact

The MRC celebrated 100 years of supporting ground-breaking research and innovation in 2013. Although the research landscape may have changed in the decades since the MRC was established in June 1913 to study tuberculosis, the primary aim — to improve the health and wellbeing of society — has remained the same.

From the discoveries of penicillin and the structure of DNA to demonstrating the links between smoking and lung cancer and high blood pressure and heart disease, MRC-funded research teams have been at the forefront of medical advances. A timeline of the MRC's key discoveries and achievements over the past 100 years can be found on the MRC Centenary website[6].

MRC research is generating world-leading knowledge

One of the key indicators of research quality is the extent to which publications arising from the work are cited in peer-reviewed literature. Despite having only 0.9 per cent of the world's population, the UK is home to 4.1 per cent of the world's researchers responsible for 15.9 per cent of the world's most highly cited research papers[7].

Since 2006, MRC-funded researchers have produced more than 70,000 publications, of which almost 45,000 are peer-reviewed articles or reviews. Almost half of these (49 per cent) are co-authored with international partners and a fifth of funding awards (20 per cent) are linked to deliver more than 16 publications. Most importantly, the quality of MRC-funded research is consistently high. In studies of normalised citation impact (NCI), MRC publications score more than twice the global average. In addition, MRC-funded research produces more highly cited papers than other UK-funded research (NCI >4, 11.5% versus 4.9%).

MRC research is highly collaborative and catalyses significant inward investment to the UK

Over half of all MRC awards involve collaboration, with a total of nearly 16,000 partner organisations. Collaborations might be evidenced by (but not limited to) outputs such as exchanging expertise, materials, access to facilities, co-authorship of papers, or obtaining joint funding.

The majority of awards with collaborations involve more than five individual collaborators (5.42 on average) and six per cent are highly collaborative, with ten or more different collaborators all working on the same shared goal. These collaborations are most often within academia, but 42 per cent of collaborations include other public sector organisations, hospitals, private sector and/or charitable organisations.

25 per cent of MRC funding is awarded in partnership with other organisations. In total in 2013/14 the MRC spent approximately £150m in biomedical research working with partners; £115m of this was from the MRC's own allocation and approximately £33m was leveraged from other funding and partner organisations. The partners include eight major medical charities, the European Commission and international co-funders, and partnerships with industry. Inter-governmental/ public partnerships include five of the seven Research Councils, Innovate UK, National Institute for Health Research (NIHR), Department of Health, Chief Scientist Office (Scotland), National Institute for Social Care and Health Research (NISCHR, Wales), Department for International Development (DfID) and the Food Standards Agency (FSA).

One example of multi-organisation research collaboration is the **UK10K project**. Established in 2010, this collaboration brings public sector (the MRC, Department of Health), charitable (Wellcome Trust) and academic (University of Bristol, King's College London) institutions together with one aim; to study the genetic code of 10,000 people to develop better understanding of the links between rare genetic mutations and human diseases. In 2013, **Professor Peter Scrambler** at **King's College London** became one of several MRC researchers to publish their findings from this project, identifying mutations involved in ciliopathy disorders such as jeune asphyxiating thoracic dystrophy (JATD), Mainzer-Saldino syndrome and primary ciliary dyskinesia.

Similarly, the **UK Regenerative Medicine Platform (UKRMP)** is a collaboration between the MRC, BBSRC and EPSRC to provide cross-institutional research hubs to address the key areas of research or technology development to support new treatments. In 2013/14 the full budget of £20m was committed, with further funding of £20m to provide state-of-the-art facilities for UKRMP hubs and beyond. In addition, the **University of Manchester** has received £5m in funding for a Centre for Doctoral Training in Regenerative Medicine to provide future scientists with expertise in this growing multidisciplinary field of research.

By providing funding, the MRC also contributed to the acquisition of further funding from other sources. From 2006 to 2013, MRC-funded researchers reported further funding to a total value of £3.2bn, with 46 per cent of awards reporting at least one instance of additional funding. Roughly two thirds (68 per cent) came from other UK funders, particularly the Wellcome Trust (£435m) and National Institute for Health Research (NIHR, £195m). A further fourteen per cent was obtained from the rest of Europe (£446m), particularly the European Commission (£120m), and another eleven per cent from North America (£364m). The largest private sector funder was Merck & Co Inc, providing £88.3m (largely via a collaboration with **Oxford University** and the **MRC/CRUK/BHF Clinical Trial Service Unit)**.

MRC translational research is bringing new treatments to the clinic and providing a rich pipeline of opportunities for commercialisation

In 2013, 12 per cent of MRC awards reported 809 products, interventions and clinical trials[8]. These are at all stages of development, from initial development to market authorisation and adoption. Approximately a quarter of these reported products were classified as potential therapeutic drugs, while 18 per cent were new non-imaging diagnostic tools. Of the products reported, just over half were in the earliest stages of development, and a further 31 per cent in early clinical stages of evaluation. A total of 16 per cent of products were in the marketplace or in the process of authorisation.

In addition to products, 31 per cent of MRC awards reported production of research materials for others to use. This includes any development that makes new lines of enquiry possible, or materials that significantly accelerate research progress. This area therefore covers research 'raw materials' such as new reagents, cell lines, or antibodies, and also new methodologies, disease models or techniques that can aid further studies.

To commercialise the developments they have made, MRC researchers reported 11 patent applications and 32 granted patents in 2013[9]. In addition, a further three spin-outs or new businesses were created in 2013, bringing the total number of new companies set up as a direct result of MRC funding to 77, accounting for a considerable contribution to the UK economy and creating at least a further 100 highly skilled jobs in the medical research sector.

For further details, see the relevant sections within this report. Some particularly noteworthy examples of product development, new treatments and commercial ventures are highlighted below.

Researchers at the **MRC Human Genetics Unit** at the **University of Edinburgh**, in collaboration with an international team of researchers, have become the first to use stem cells to develop three-dimensional cultures that resemble primitive human brain tissues. The development of 'organoids', defined structures of cultured cells, can be used to help better model neurological disorders, providing a platform for new therapies before progression to clinical trials[10].

Researchers at the **MRC Prion Unit** and the NIHR Queen Square Dementia Biomedical Research Unit (BRU) have developed and tested an integrated tool (the 'MRC Dementia Gene Panel') to diagnose early onset, genetic forms of dementia, bringing together for the first time all 17 genes known to play a substantial role in causing inherited forms of dementia. Using 'next generation sequencing', a modern method of analysing the DNA from a patient's blood sample, they were able to look for abnormalities in all of these genes simultaneously[11]. Their work shows that the technology is highly accurate and comprehensively identified the genetic abnormalities more efficiently and effectively.

Access to antiretroviral treatments (ART) for children in Africa is significantly lagging behind that of adults – by the end of 2011 only 28 per cent of the two million children who needed treatment were on it, compared with 51 per cent of adults in need. Furthermore, more than half of HIV-infected infants and young children die before their second birthday. The five-year ARROW trial[12] was set up in Uganda and Zimbabwe and co-ordinated by the **MRC Clinical Trials Unit** to assess whether replacing expensive routine lab tests to monitor ART with careful clinical care and follow-up could be safely implemented. By conclusively showing that this can be done, this trial greatly adds to the argument that resources are best spent extending access to life-saving treatment, rather than doing routine lab tests which add little benefit.

3.0 Inputs: investment in the research base

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3.1 Income and expenditure

In 2013/14 the MRC's gross research expenditure was £845.3m compared to £766.9m in 2012/13. The support for world-class medical research to improve human health and enhance the economic competitiveness of the UK included:

- £332.3m on grants and to researchers in universities, medical schools and research institutes.
- £328.0m on programmes within the MRC's own units and institutes including £7m on studentships.
- £104.4m on programmes within university units, including transfer of property, plant and equipment with a net book value of £29.2m.
- £62.9m on studentships and fellowships in universities, medical schools and research institutes. (There were approximately 1,800 postgraduate students and 390 fellows in March 2014).
- £17.7m for international subscriptions.

This is broken down in more detail in Annex 2 in Section 3.1: Income and expenditure.

3.2 Human capital (input)

The MRC's vision for training and careers is to train and develop the next generation of research leaders. The MRC aims to strengthen and sustain a world-leading medical research workforce equipped with contemporary skills across a range of basic science and clinical disciplines by:

- Supporting excellent individuals at critical points of their careers through continued investment in clinical and non-clinical research training ensuring a demanding and rewarding research experience at various career stages.
- Investing in areas with the most potential to deliver excellence and innovation for human health, with particular attention to national strategic research skills needs.
- Enhancing the development, support and career options for non-traditional highly-skilled technical researchers.
- Increasing support and skills development for research leaders of tomorrow including mentorship.

The capacity and skills spend for the financial year 2013/14 was £62.9m, with an approximate 35:65 split between studentships and fellowships: £22.5m for studentships and £40.4m for fellowships (including Clinical Research Training Fellowships[13]).

The MRC employs around 2,500 research staff in intramural MRC institutes and units and supports approximately 1,200 live grants on which researchers are employed. Further details are given in Annex 2 in Section 3.2 Human capital (input).

The MRC has transferred MRC units to university ownership, to capitalise on the added value and mutual benefit that closer integration between these units and world-class university research will bring. As a result of the university

units programme, 14 units, 970 staff and an MRC budget of approximately £62m per year have transferred from the intramural programme to the HEI sector, the bulk of which transferred in 2013/14. The MRC also set up two university units *de novo*. The MRC currently retains nine intramural units in the UK as well as two overseas units.

The MRC funds a range of fellowship award schemes for both clinical and non-clinical researchers, as well as specific fellowships schemes targeting strategically important research areas or skill-sets. There is further information on MRC schemes on our website[14] as well as comments from researchers showing how the MRC has supported them through their careers.

4.0 Outputs: research performance

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4.1 Knowledge generation

The data on the MRC's outputs and outcomes presented in this, and subsequent sections, was collected through Researchfish (previously MRC eVal)[15]. This is the system used by the MRC to capture information on outputs, outcomes and impacts from MRC-funded researchers. Researchfish is a federated system now used by more than 90 research organisations and funders[16]. In 2013/14, the MRC led work with RCUK to develop a common question set for use in Researchfish, ensuring that the same information on outputs and impacts can be collected by all of the funders using the system regardless of the research discipline. This will help RCUK gain an unprecedented view of the progress, quality and impact of the research all the Research Councils fund, giving us an insight into what works well and where there might be gaps.

Researchers can enter, amend and update information in Researchfish all year round, and must submit it to the MRC during an annual data-submission period. This means that numbers reported this year will be different to those reported last year as researchers can continue to add information retrospectively. 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 some data are presented here and in both the *MRC Annual Report 2013/14*[17] and *Outputs, Outcomes and Impact of MRC Research 2013/14*[18], there will be some slight differences in the figures reported.

2013 was the sixth year that researchers used the system, and 94 per cent of the MRC scientists who had held any funding from the organisation since 2006 submitted information relating to almost 5,000 awards in total (4,901 responses from an expected 5,226).

Analysis of the Researchfish dataset is providing a detailed picture of the progress, productivity and quality of the science we support. In particular, it is highlighting how MRC research contributes to the development of new medicines and technologies, improvements to clinical and public health policies and practices, and how MRC research encourages inward investment to the UK.

It is important to note that while counts of reports from Researchfish are listed here to illustrate the volume of output information collected, the MRC is primarily interested in the quality of reports received. Reports are reviewed in order to identify duplicate reports, and to consider whether they meet basic criteria such as being evidenced, justifiably linked to a core MRC programme, and occurring within the relevant timescale[19]. The main exception is published output where there is interest to benchmark output using a variety of more quantitative bibliometric approaches.

MRC-funded research carried out between 2006 and 2013 has contributed to:

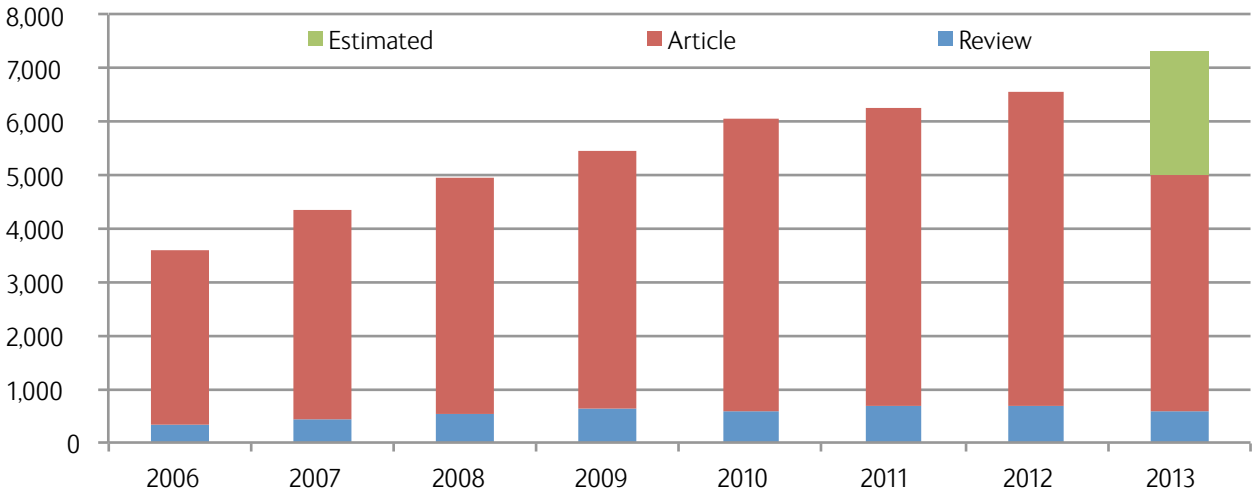
- More than 49,000 scientific papers (5,015 in 2013) with more than twice the world citation impact on average.
- The development of almost 4,000 instances of influence on policy and practice (536 in 2013), including more than 370 contributions to clinical guidelines.
- The development of more than 800 products and interventions (166 in 2013).

- The creation or growth of 77 companies (three in 2013).
- Approximately 850 patents (52 in 2013), with discoveries related to 227 (26 per cent) of these patents already licensed worldwide.
- Almost 15,000 instances of collaboration (1,242 in 2013) with researchers in more than 100 countries.

4.1.1 Paper outputs

Publications are an important primary output from research, and an integral part of the scientific method; they record new knowledge, methods or insights from a synthesis of existing work, and enable these to be used in other research. Figure 1 shows the number of unique publications for MRC-funded research, by year of publication; see Annex 2, Section 4.1 Knowledge General, for actual numbers.

Figure 1: *Numbers of unique publications submitted by MRC-funded researchers via Researchfish, by year of publication*



The data-gathering period for Researchfish in 2012/13 closed in November 2013. The number of unique publications submitted by MRC-funded researchers (both intramural and extramural) for 2013 is therefore incomplete (partial year numbers for reviews 577, articles 4,438) and will increase; as such, a projection has been estimated.

The citation of publications in further peer-reviewed research articles is often used as a measure of research productivity, quality and impact. These citation counts can be normalised by scientific field and year of publication to give a measure of normalised citation impact (NCI). An NCI score of 1 means that the paper is behaving as would be expected for that subject area in that year, and this is referred to as the world average. Therefore an NCI of above 1 means that the paper is cited more often than would be expected and is above the world average. (Normalised citation impact data and analysis: Evidence, Thomson Reuters UK.)

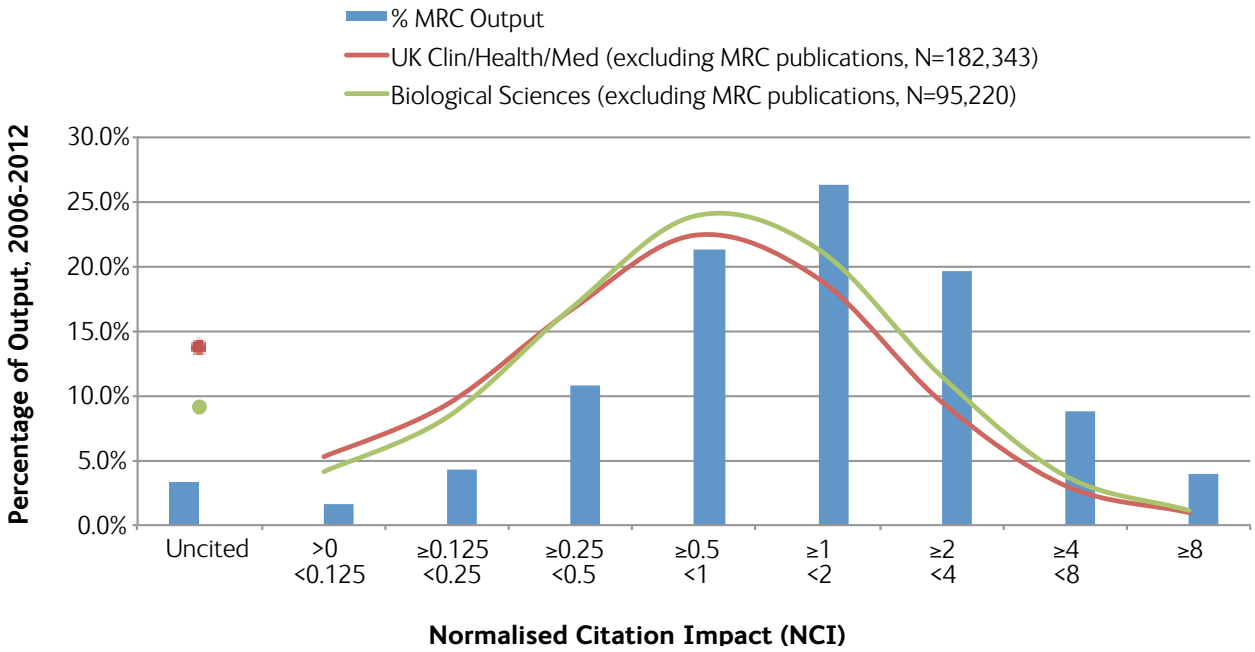
The average normalised citation impact for MRC publications from 2006 to 2012 is 2.1, more than twice the world average[20].

A further measure of the quality of publications is the number or percentage of articles that are either uncited or, conversely, those deemed as 'highly cited' (ie NCI≥4)[21].

For the UK in general, approximately 30 per cent of papers are never cited. This falls to between nine and fourteen per cent in biomedical fields and for MRC-funded research, this figure is approximately three to four per cent (as shown in the Impact Profile® - Figure 2).

MRC-funded research generates a greater percentage of highly-cited papers than other UK clinical and UK biological sciences research (11.5 per cent compared to four per cent and 4.9 per cent respectively). It also generates a greater percentage of 'very highly-cited' papers (NCI≥8) than UK clinical and UK biological sciences research (3.6 per cent compared to one per cent and 1.1 per cent respectively).

Figure 2: *Impact Profile® of citation scores*

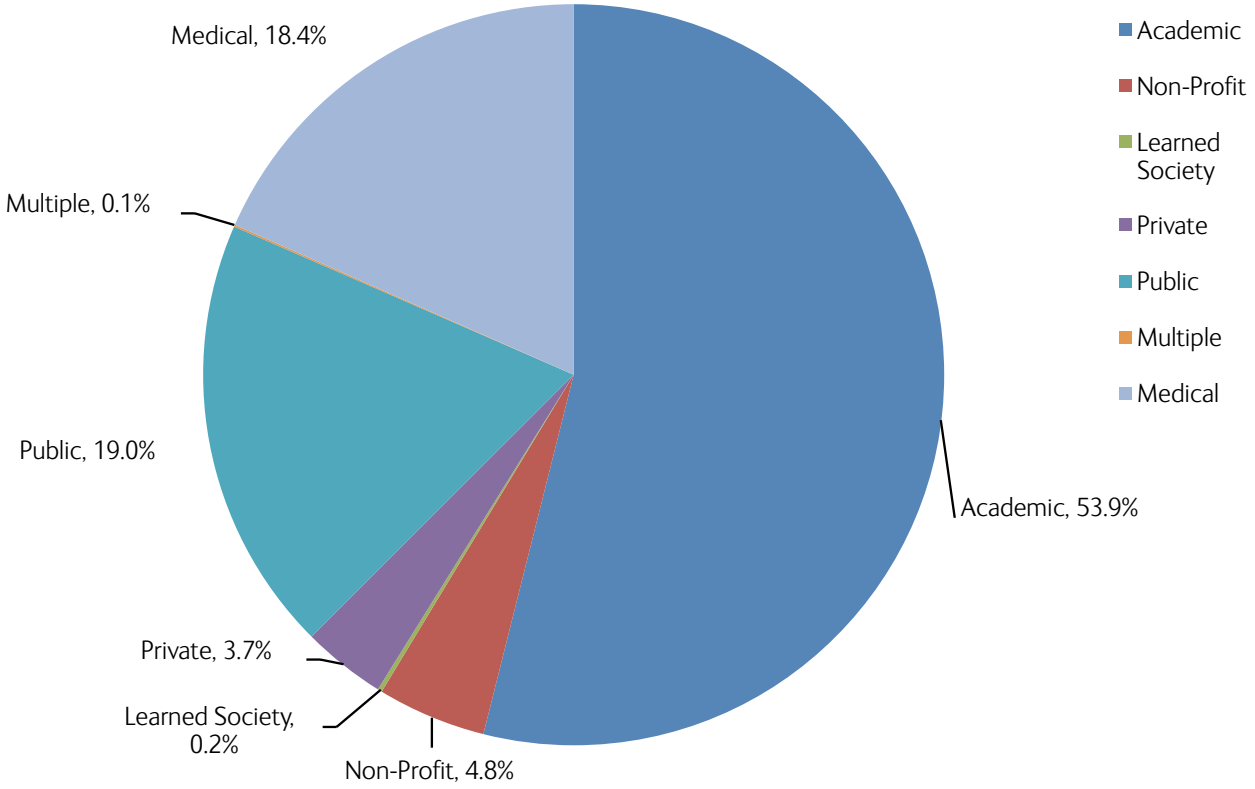


Co-authorship

Analysis of the authors who have contributed to a research publication can be used as an indicator of collaborative working.

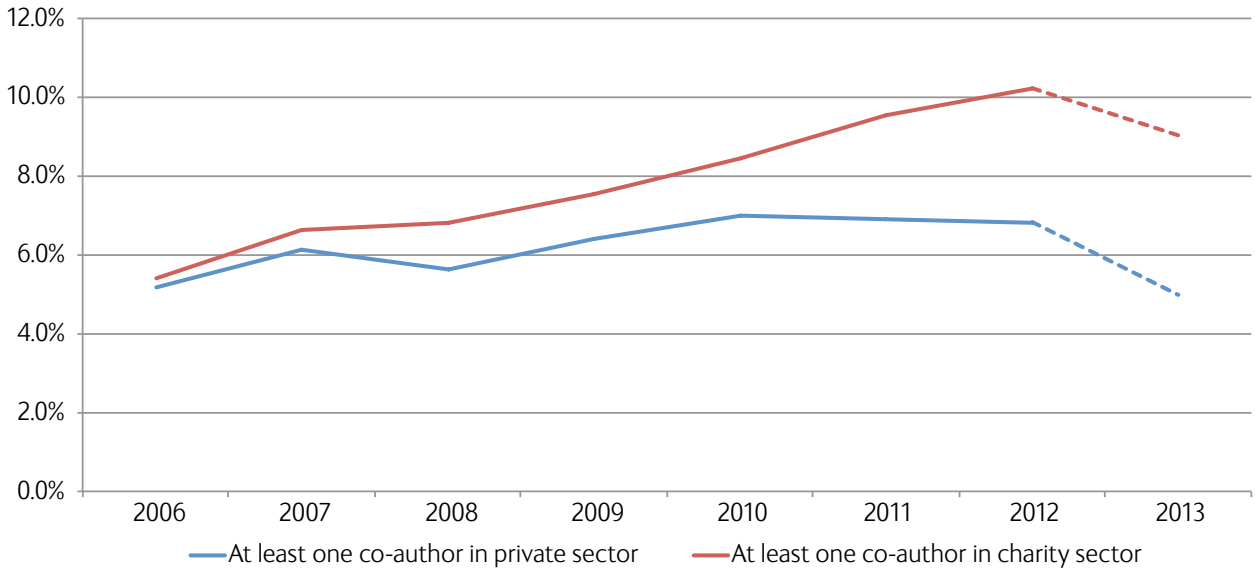
Analysis of these MRC-attributed papers also shows that 49 per cent have at least one author from outside the UK. Figure 3 shows the co-authorship of all of the MRC-funded papers reported by sector in Researchfish.

Figure 3: *Co-authorship of all MRC-funded papers by sector*



It is also useful to track the co-authorship of papers over time. Figure 4 shows the percentage of papers published by year with at least one author from either the charity sector or the private sector. Both charity and private sector authorships in 2013 appear slightly lower (<two per cent difference) than 2012, however it is important to note that changes in coding practice, natural variation and/or the fact that the 2013 is incomplete could all account for variations of this size.

Figure 4: *Percentage of papers with at least one author from either the charity or private sector, by year*



Papers published in 2013 already exhibiting high citation impact

In the bibliometric analysis, we included papers entered into the Thompson Reuters database between the years 2006 and 2012 with citation counts taken at the end of 2013, so that all papers had at least one year to accumulate citations. There are papers, however, published at the end of 2012 and during 2013 that have already rapidly been cited.

The following case studies show three papers published between the end of 2012 and 2013 that have already being cited at a rate that is more than 60 times the world average.

Innate lymphoid cells — a proposal for uniform nomenclature

NCI:	DOI:	Article:
100	10.1038/nri3365	Spits H *et al.* (2013) *Nature Reviews Immunology* **13:** 145-149[22]

Summary:

Innate lymphoid cells (ILCs) are a family of cells involved in immunity and tissue development. Several distinct members of the group have recently been identified; however, different names have been used to label them.

Dr Andrew McKenzie at the **MRC Laboratory of Molecular Biology**, together with international colleagues, proposes in this paper a classification system to define ILCs. This system is based on the type of cytokines — small proteins involved in cell signalling — the ILCs produce and the mechanisms for doing so. They define group 1 ILCs by their ability to produce interferon-γ (IFN-γ), an important activator of macrophages; group 2 by their ability to produce T helper 2 cell-associated cytokines such as interleukin-5 and interleukin-13; and group 3 by their ability to produce T helper 17 cell-associate cytokines interleukin 17 and 22.

The paper also credits funding from the NIH, Wellcome Trust and the Howard Hughes Medical Institute.

TREM2 variants in Alzheimer's disease

NCI:	DOI:	Article:
79	10.1056/NEJMoa1211851	Guerreiro R *et al.* (2013) *The New England Journal of Medicine.* **368**(2):117-127[23]

Summary:

This paper was reported by **Professor Julie Williams** at the **MRC Centre for Neuropsychiatric Genetics and Genomics** at **Cardiff University**, who was part of an international collaboration that examined gene mutations linked to Alzheimer's disease. The *TREM2* gene codes for the 'triggering receptor' protein found on myeloid cells produced in the bone marrow. The protein is located on the cell surface where it interacts with the protein encoded by the *TYROBP* gene forming a complex that activates the cell. The complex is found in osteoclasts — specialised cells involved in the normal process of bone remodelling, specifically, that break down and removes bone tissue that is no longer needed. The complex is also found in microglia — immune cells that protect the brain and spinal cord from foreign invaders and remove dead nerve cells and other debris.

Homozygous loss-of-function mutations in *TREM2* have previously been linked to a form of early-onset dementia called Nasu–Hakola disease[24]. This disease is associated with the presence of bone cysts and subsequent fractures. This research collaboration identified homozygous *TREM2* mutations in three Turkish

patients showing symptoms associated with frontotemporal dementia and leukodystrophy — a group of disorders associated with the degeneration of white matter in the brain — but without the bone-associated symptoms[25]. Additionally, a genome-wide analysis has identified eight linkage regions, including one on chromosome 6 — the site of *TREM2* — with significant associations to late-onset Alzheimer's[26].

To investigate further the researchers performed a case:control study of 1,092 patients with Alzheimer's disease and 1,107 controls. They found significantly more variants in a part of the *TREM2* gene in patients with Alzheimer's compared to those without the disease. The most commonly-associated variant rs75932628 — encoding R47H — showed significant association with Alzheimer's disease. The authors therefore conclude that the reduced function of *TREM2* is key to the pathogenic effect of these risk variants associated with Alzheimer's disease.

Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial

NCI:	DOI:	Article:
60	10.1016/S0140-6736(12)61963-1	Davies C *et al.* (2013) *The Lancet* **381**(9869):805-816[27].

Summary:

This paper presents the follow-up analysis of the Adjuvant Tamoxifen: Longer Against Shorter (ATLAS) randomised trial, led by **Dr. Christina Davies** at the **MRC Clinical Trial Service Unit**. For women with oestrogen receptor (ER)-positive early breast cancer, treatment with tamoxifen for five years substantially reduces the breast cancer mortality rate throughout the first 15 years after diagnosis. The study demonstrated that continuing tamoxifen to 10 years rather than stopping at five years produces a further reduction in recurrence and mortality, particularly after year 10. These results, taken together with results from previous trials of five years of tamoxifen treatment versus none, suggest that 10 years of tamoxifen treatment can approximately halve breast cancer mortality during the second decade after diagnosis.

The five-year survival rate for breast cancer has increased by 18 per cent between 1986-1990 and 2005-2009[28], predominantly due to the introduction of breast cancer screening[29] and improved treatment regimens such as this.

This trial also benefited from funding from Cancer Research UK, AstraZeneca UK, the US Army and EU-Biomed.

Non-paper outputs

The following outputs, outcomes and impacts that have arisen either wholly or partially from MRC-funded research were all reported through Researchfish.

The data and analysis in this report represents only a small amount of what MRC does with the information collected through Researchfish. Further analysis and stories of impact can be found on the MRC website; in particular in the *Outputs, outcomes and impact of MRC research: 2013/14* report[30], and case studies which are based on the outputs from MRC-funded research[31].

4.1.2 Collaborations

Collaborative work is of increasing importance in facilitating the delivery of all strands of the MRC's mission to improve the health of the nation through world-class medical research. Collaboration has been shown to be a driver of research excellence. In a period of constrained public finances it is even more important to have access to a wider range of facilities and equipment through a pooling of resources and expertise[32].

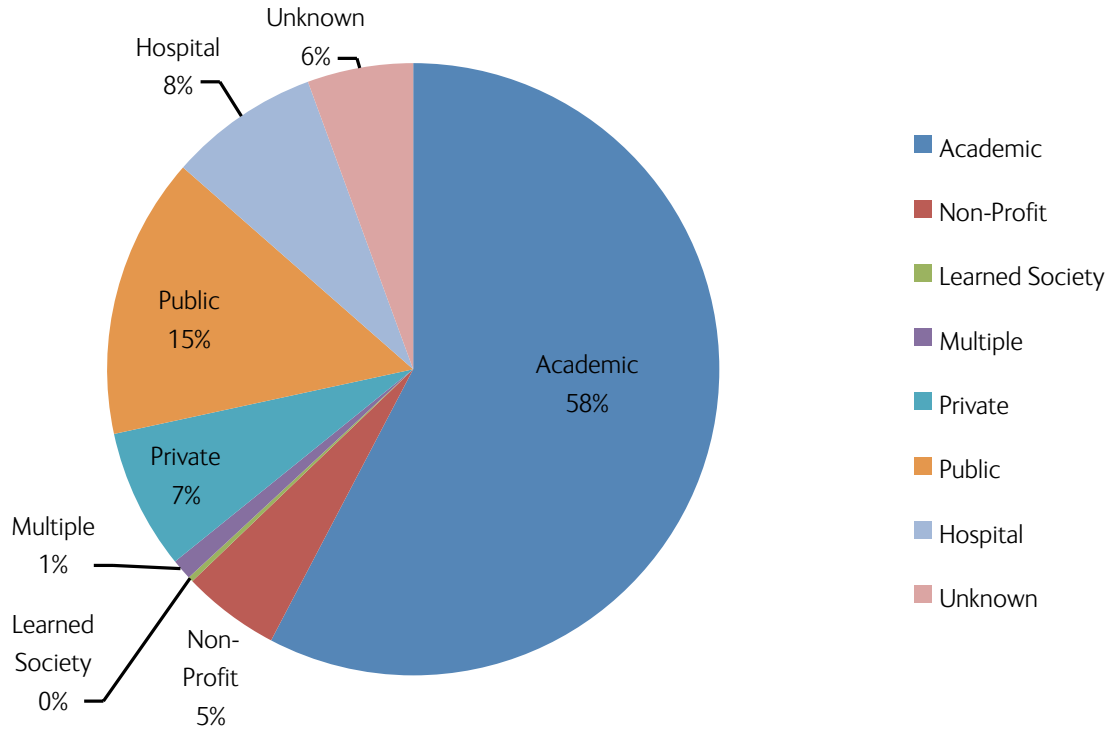
Recipients of 52 per cent of MRC awards reported that they had embarked on new collaborations as a result of their MRC-funded work. Each collaboration can include a number of partners across different sectors. These partners may be funded from multiple sectors (for example, charitable, public, and private sources) and are not confined to just the UK. Researchers reported a variety of purposes for engaging in a collaboration, including funding, access to equipment, and provision of analytical techniques and expertise.

- Recipients of 52 per cent of awards (2,917) reported that they had been part of one or more collaboration(s) between 2006 and 2013.
- There were 14,907 collaborations reported (1,242 in 2013), involving a total of 13,716 unique partner organisations.
- The average number of collaborators linked to awards reporting at least one collaboration was five (5.42), a slight increase on last year's average (5.28).
- Six per cent (339) of awards were highly collaborative, reporting links to more than ten different collaborators.

Researchfish data allow us to examine how researchers are engaging with partners from different sectors. The majority of collaborations reported were with academia (58 per cent), followed by the public sector (15 per cent), and then hospitals (eight per cent) and the private sector (seven per cent).

Figure 5 shows the proportion of MRC collaborations by sector; see Annex 2 Section 4.1 Knowledge generation for specific figures.

Figure 5: *Proportion of MRC collaborations by sector*



Examples of excellence through collaboration:

Smartphone app to monitor food intake

Researchers at the **University of Leeds** have developed a smartphone app in conjunction with Blueberry Consultants that enables users to monitor their food intake and exercise. My Meal Mate™ also allows users to set a weight loss target and sends them a weekly update on progress via text message[33]. In a pilot randomised controlled trial, the researchers compared the app to other ways of monitoring food intake - an online food diary and a traditional paper version. Over the six months of the study those using the app lost on average 4.6kg (10lbs), compared with the 2.9kg (6.5lbs) and 1.3kg (3lbs) lost by the paper-based and online diary users, respectively[34]. A link to the app has been placed on the NHS Choices website. Since its launch in 2013, there have been between 10-50,000 downloads[35]. This is the only weight loss app supported by published peer-reviewed evidence.

Investigating the emergence of novel MRSA strains in cattle and their transmission to man

Professor Mark Holmes at the **University of Cambridge** has formed collaborations with the Health Protection Agency (HPA) and the Statens Serum Institut (SSI) in Denmark to investigate the emergence of a new MRSA strain in cattle and humans. In 2011 MRSA strains with a *MecC* gene — a new form of the *MecA* gene, the gene present in MRSA that encodes a penicillin-binding protein — were identified to be present in cattle and humans[36]. The strain was undetectable by current diagnostic tests, a concern when trying to identify the source and transmission of infection. Professor Holmes has exchanged *S.aureus* isolates with both organisations, who have also undertaken functional analyses on the samples. Professor Holmes has conducted whole genome sequencing on the samples, which has led to the HPA implementing a diagnostic test based on this data in order to incorporate screening for *MecC* MRSA as part of their surveillance activity[37].

UK10K

The UK10K project is a major collaboration among several leading academic and research institutions including the MRC, Wellcome Trust, Department of Health, Bristol University and King's College London. The project, which started in 2010, aims to better understand the link between rare and low-frequency gene mutations and human disease by studying the genetic code of 10,000 people in great detail.

Several MRC researchers are involved in the project, including **Professor Peter Scambler** at **University College London** who has helped identify several new genes involved in ciliopathy spectrum disorders. These are genetic diseases of the cellular cilia, slender organelles that protrude from the larger cell body, such as those lining the windpipe, where they sweep mucus and dirt out of the lungs. Results include the identification of gene mutations causing jeune asphyxiating thoracic dystrophy (JATD), a sometimes lethal disease characterised by shortened ribs and long bones, accompanied by renal, liver and retinal disease[38], Mainzer-Saldino syndrome, characterised by retinal degeneration and kidney disease[39] and primary ciliary dyskinesia, that causes a defect in the action of the cilia lining the respiratory tract, the fallopian tube, and the flagella of sperm, resulting in respiratory infections and infertility[40].

Structure and function of AMPK

AMP-activated protein kinase (AMPK) functions in the regulation of cell energy. Evidence suggests that it may therefore play a role in human diseases characterised by defects in energy metabolism. **Professor David Carling's** current research at the **MRC Clinical Sciences Centre** focuses on the regulation of AMPK using structure/function analyses and the physiological role of AMPK using transgenic models. Professor Carling has identified the mode of action of small molecule activators of AMPK and will use this in order to determine whether there are any natural ligands that activate AMPK by a similar mechanism. As part of an industrial CASE studentship in 2013, AstraZeneca have synthesised a number of small molecular activators of AMPK. They have also produced a fluorescent analogue molecule for one of these activators that will be used as a probe to screen for natural ligands that compete with the binding.

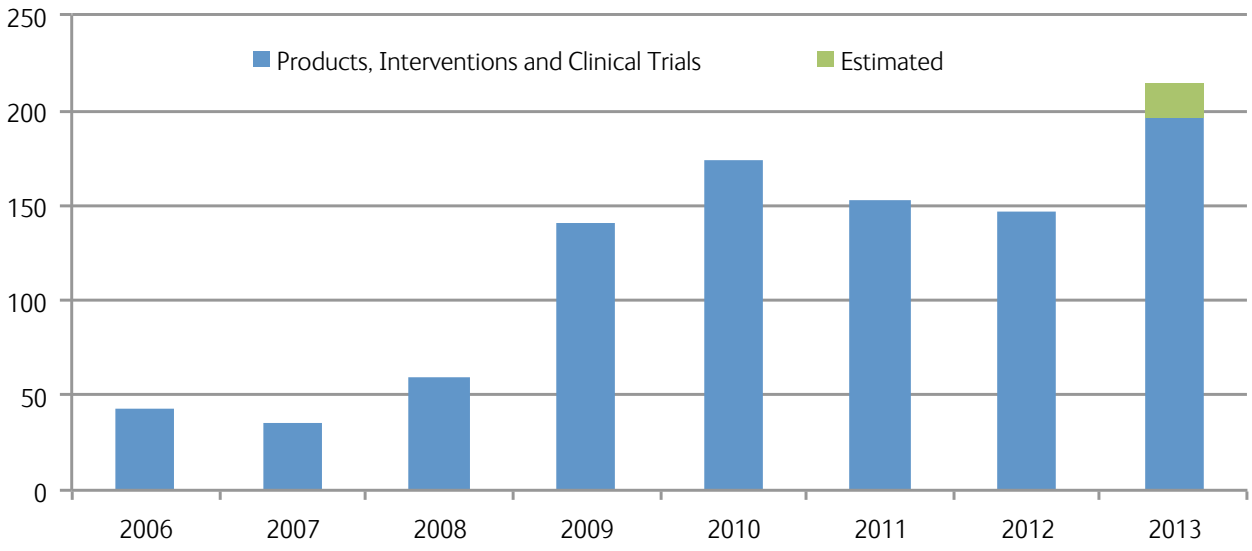
4.1.3 Products or interventions

Products or interventions include the development of diagnostic tools such as screening, therapeutic interventions including drugs, vaccines, medical devices or surgery, preventive interventions, health/social care services, and several others. Researchfish also records the current stage of development that the product or intervention has reached.

Reports detailing 809 products and interventions were entered into Researchfish in 2013, from approximately 12 per cent of awards. Note that data from 2013 is partial due to the timing of data collection. Therefore a projected total has been estimated. Figure 6 shows the products and interventions based on the year in which the most recent stage was completed; see Annex 2 Section 4.1 Knowledge generation for specific figures.

Please note that the values presented here show a steep increase from those reported in the last Economic Impact Report[41]. This variation is attributable to a change in reporting method. For data gathering in 2013, "Products or Interventions" was changed to "Products, Interventions and Clinical Trials". As such, numbers reported from 2006-2012 have increased by an average of 20, and the approximately 200 products attributed to 2013 could be a direct result of more clinical trials being attributed to awards in this manner.

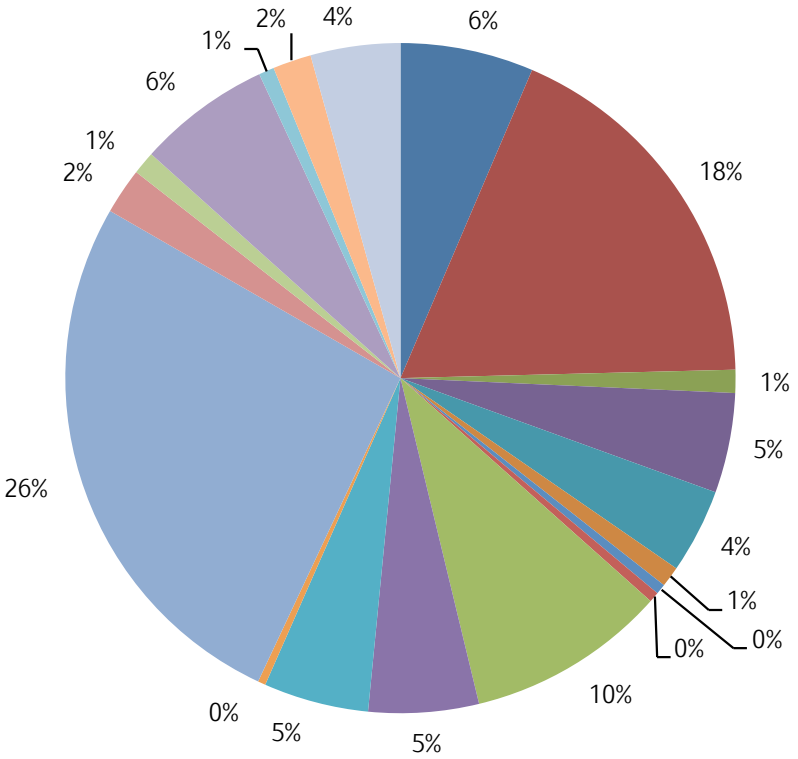
Figure 6: *Number of products and interventions by year at which most recent stage was completed*



Products and interventions by type

Figure 7 shows the percentage of each type of product or intervention reported between 2006 and 2013. The most common category of product or intervention in development was the *therapeutic intervention – drug*, reported by 213 awards (26 per cent of all products and interventions reported). See Annex 2 Section 4.1 Knowledge generation for specific figures.

***Figure 7**: Percentage of each type of product or intervention reported between 2006 and 2013*



- Diagnostic Tool - Imaging
- Diagnostic Tool - Non-Imaging
- Health and Social Care Services
- Management of Diseases and Conditions
- Preventative Intervention - Behavioural risk modification
- Preventative Intervention - Nutrition and Chemoprevention
- Preventative Intervention - Physical/Biological risk modification
- Products with applications outside of medicine
- Support Tool - For Fundamental Research
- Support Tool - For Medical Intervention
- Therapeutic Intervention - Cellular and gene therapies
- Therapeutic Intervention - Complementary
- Therapeutic Intervention - Drug
- Therapeutic Intervention - Medical Devices
- Therapeutic Intervention - Physical
- Therapeutic Intervention - Psychological/Behavioural
- Therapeutic Intervention - Radiotherapy
- Therapeutic Intervention - Surgery
- Therapeutic Intervention - Vaccines

Products and interventions by development stage

There were 251 reports of products and interventions in early- or late-stage clinical evaluation and 353 reports of products in initial or refinement stages. The inclusion of Developmental Pathway Funding Scheme (DPFS) projects in 2011 has significantly added to the number of projects in early developmental stages.

Table 1 shows the distribution of numbers of products and interventions by development stage.

Table 1: *Distribution of products and interventions by development stage*

	Therapeutic Intervention	Diagnostic Tool	Support Tool	Preventative Intervention	Management of Diseases and Conditions	Products with applications outside of medicine	Health and Social Care Services	Total (%)
Initial development	114	67	48	13	5	2	2	**251 (31%)**
Refinement (non-clinical)	44	29	20	6	0	0	3	**102 (13%)**
Refinement (clinical)	47	21	6	2	3	0	0	**79 (10%)**
Early clinical assessment	100	35	6	17	6	0	0	**164 (20%)**
Late clinical evaluation	57	7	1	3	16	0	3	**87 (11%)**
Market authorisation	7	5	5	0	1	0	0	**18 (2%)**
Small-scale adoption	11	20	26	3	2	0	1	**63 (8%)**
Wide-scale adoption	12	15	9	1	6	2	0	**45 (6%)**
Total (%)	**392 (41%)**	**199 (21%)**	**121 (13%)**	**45 (5%)**	**39 (4%)**	**4 (0%)**	**9 (1%)**	**809 (100%)**

The Researchfish data shows a range of different product types spanning all stages of product development. The progression of products from initial development to early clinical stages can involve a significant degree of attrition, so it is not surprising that more than half of the products are listed as pre-clinical here.

Supporting researcher-industry collaborations is one of the MRC's key strategic objectives. Methods to achieve this include the Biomedical Catalyst to align MRC translational research schemes with Innovate UK funding and the MRC translational response mode funding which provided £43.4m in 2013/14. This includes 'confidence in concept' awards aimed at getting more new product developments initiated and progressed.

Specific examples of products in development:

Campath as a treatment for multiple sclerosis

Alemtuzumab (Campath or Lemtrada) is a humanised rat monoclonal antibody used for the treatment of patients with resistant chronic lymphocytic leukaemia. MRC researchers **Professor Alastair Compston** and **Professor Alasdair Coles** at the **University of Cambridge** have conducted clinical trials demonstrating its effectiveness in the treatment of multiple sclerosis[42,43], an autoimmune condition in which the immune system mistakes myelin — the layer of protein surrounding nerve fibres in the brain and spinal cord — for a foreign substance and attacks it. The myelin becomes inflamed, disrupting the messages travelling along nerve fibres. Alemtuzumab works by binding to and killing the lymphocytes (immune cells) that attack the myelin. It is believed that the lymphocytes regenerated by the immune system following treatment with alemtuzumab do not include the subset that destroys myelin.

The origins of alemtuzumab date back to MRC-funded experiments on human lymphocyte proteins by **Professor Herman Waldmann** and colleagues in 1983. It was named

'Campath' after the pathology department of Cambridge University. In September 2013, alemtuzumab was licensed as a treatment of "adult patients with relapsing remitting multiple sclerosis with active disease defined by clinical or imaging feature" in Europe, including the UK. It is now also licensed in Canada, Australia and Mexico.

Biomarkers for deep brain stimulation in Parkinson's

Electrical deep brain stimulation is increasingly being used in the treatment of neurological disorders such as Parkinson's disease and dystonia. The technique involves inserting a wire into a particular part of the brain. A generator sends small electrical currents through the wire to the brain, where they block abnormal signals that cause many of the debilitating symptoms of Parkinson's like tremors, slowness, stiffness, and difficulty with speech.

The MRC has played a significant role in the development of deep brain stimulation. The breakthrough came via work by MRC-funded **Professor Tipu Aziz**, a neurosurgeon at **Oxford University/John Radcliffe Hospital**, who identified a target, the pedunculopontine nucleus by studying the brains in non-human primates[44]. When this target was stimulated, Parkinson's symptoms were alleviated, even in patients who were not responsive to drugs.

In a complementary study, **Professor Peter Brown** at the **University of Oxford** has conducted research into the brain signals that can be recorded by electrodes to identify biomarkers – signals that can be used as a way of determining when and how much stimulation is necessary, improving the clinical result and extending battery life. Professor Brown will further determine which biomarkers are linked to symptoms and how deep brain stimulation interacts with each patient's own brain signals to identify the most effective stimulation pattern in individual patients[45].

Drug for prevention of kidney transplant rejection

In a Phase II clinical trial, **Professor Steven Sacks** at the **MRC Centre for Transplantation** at **King's College London** has shown that the drug eculizumab could be effective at preventing severe antibody-mediated resistance in sensitised kidney transplant recipients.

Approximately 30 per cent of kidney transplant candidates on waiting lists are 'sensitised', or make antibodies, against potential donors. This can lead to severe kidney damage leading to loss of function and possible loss of the transplanted kidney. Conventional immunosuppressant treatments are ineffective in preventing antibody-mediated resistance. Eculizumab is a humanised monoclonal antibody currently licensed for the treatment of paroxysmal nocturnal haemoglobinuria. It works by inhibiting the activation of the terminal complement, part of the innate immune response that helps antibodies clear the body of pathogens.

The trial involved the treatment of 47 sensitised recipients of kidneys with eculizumab. At nine weeks after the transplant, the failure rate due to antibody-mediated resistance was 6.4 per cent, compared to an expected rate of 30 per cent.

LiverMultiscan

As many as one in ten adults in the UK have some form of liver disease, which is currently the fifth most common cause of mortality for both men and women. Early detection would be highly beneficial, as many patients only show symptoms in advanced stages. However the current procedure for diagnosing liver disease, a liver biopsy, only allows examination of only 0.002 per cent of the liver[46] and carries with it a high risk of severe bleeding.

Professor Stefan Neubauer at **Oxford University** developed the LiverMultiscan[47] in 2010, a device that combines three imaging techniques using magnetic resonance imaging (MRI) to stage liver disease accurately. This technique can replace the use of an invasive biopsy which saves money and provides a better patient experience.

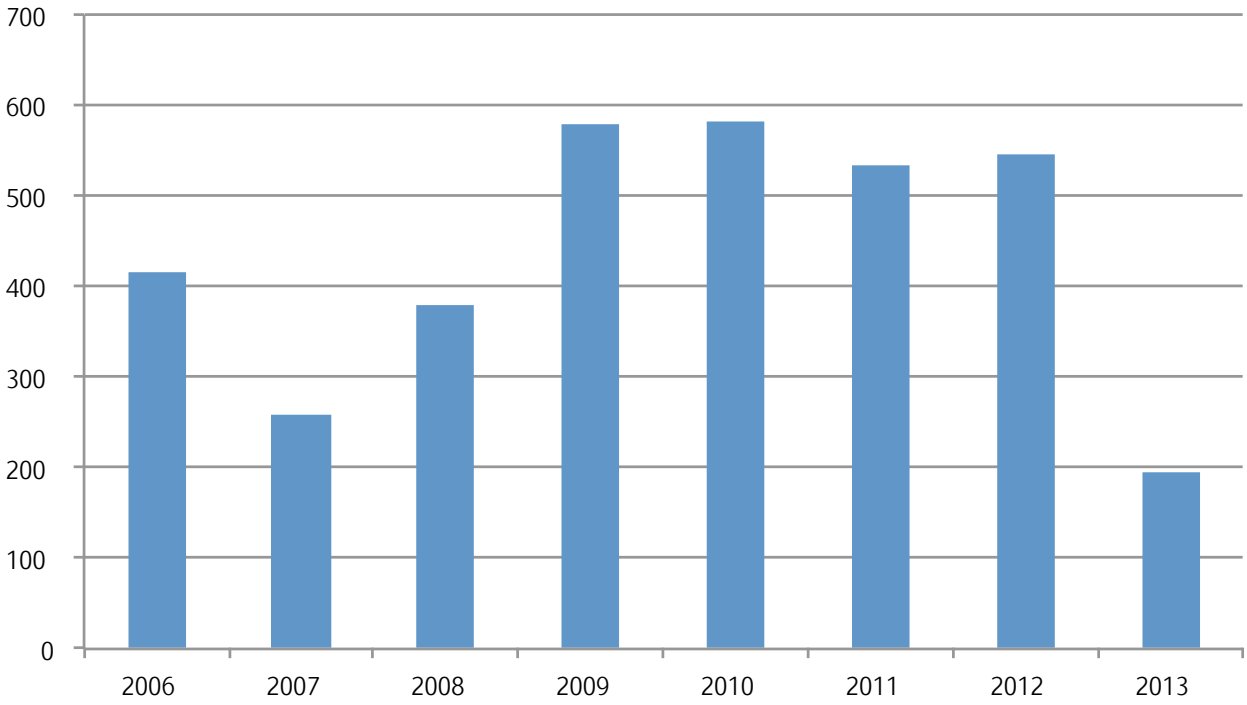
This has recently led to the establishment of spin-out company Perspectum Diagnostics which has raised seed fund capital of £0.5m and been awarded £1.2m in funding from the Innovate UK.

4.1.4 Research materials

Recipients of 31 per cent of awards reported that their work had produced research materials for others to use. The average number of research materials for awards reporting at least one instance was two (2.3).

Note that data from 2013 is partial due to the timing of data collection, and therefore a projected total is estimated. In addition, the *Research Materials* section has been subdivided into two categories; *Research Tools and Methods* and *Research Databases and Models*. As a result, reporting on outputs for 2013 in this area appears much lower than comparative years. We are reviewing this process and future reporting will see the new subdivisions handled separately. Figure 8 shows the combined numbers for both research materials subdivisions by the year in which they were realised - see Annex 2 Section 4.1 Knowledge generation for specific figures.

Figure 8: *Number of research materials by year realised*

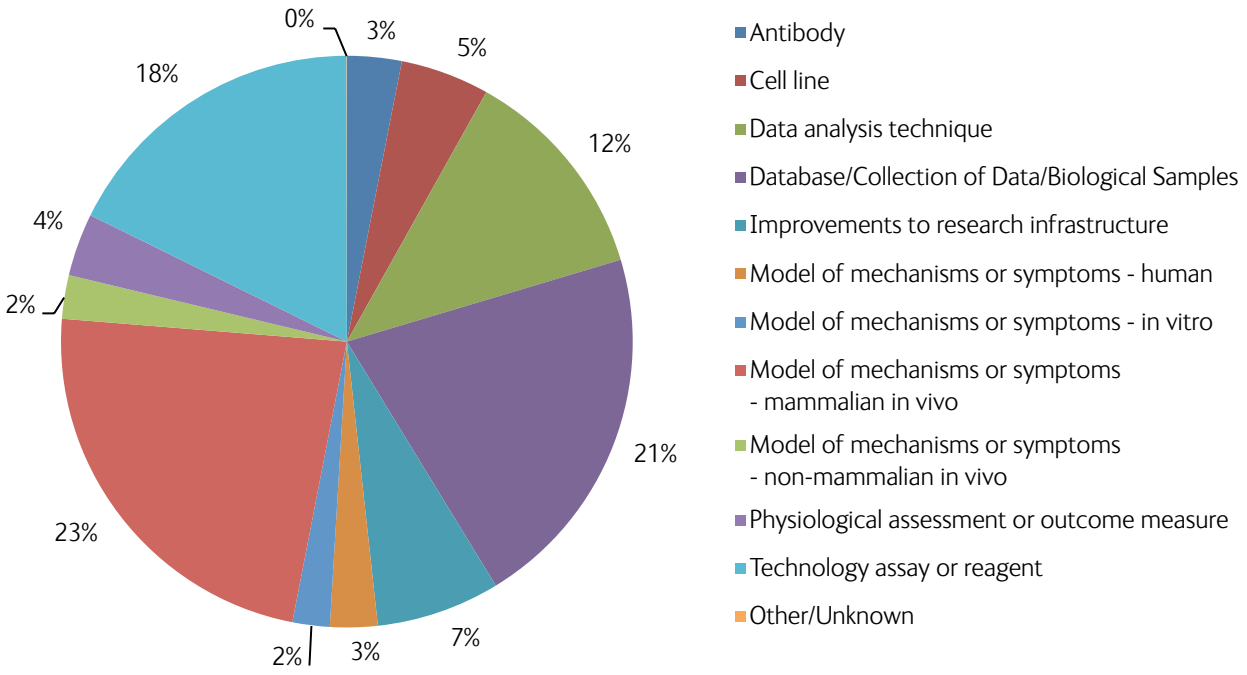


Research materials include reports of databases, data analysis techniques, cell lines, models of mechanisms or symptoms, and new equipment.

Models of mechanisms or symptoms – mammalian *in vivo* - were the most common research material (28 per cent), followed by database/collection of data/biological samples (19 per cent).

Figure 9 shows a breakdown of the distribution of type of research materials reported; see Annex 2 Section 4.1 Knowledge generation for specific figures.

Figure 9: *Distribution of type of research materials reported*



Specific examples of research materials:

Growth of 3D structure resembling human brain tissue

An international team of researchers, led by the Institute of Molecular Biotechnology in Austria, in collaboration with the **MRC Human Genetics Unit**[48] at the **University of Edinburgh** have for the first time used stem cells to grow a three-dimensional structure in the lab that resembles primitive human brain tissue[49].

This provides a unique new laboratory tool for studying human-specific features of brain development and neurological disorders in a way that has not been possible using animal models.

To create the brain tissue, the researchers began with human embryonic and induced pluripotent stem cells (IPSCs), which they used to produce neuroectoderm – the layer of cells in the embryo from which all components of the brain and nervous system develop. Fragments of this tissue were then embedded in gel droplets that provided a scaffold for complex tissue growth and placed into a spinning bioreactor.

After a month, the tissue fragments had organised themselves into primitive structures that could be recognised as developing brain regions such as retina, choroid plexus and cerebral cortex. Radial glial stem cells, pivotal in developing the central nervous system, were seen to generate neurons in an identical manner to that known to occur in normal development. At two months, the organoids had reached their maximum size of 4mm.

Using IPSCs from a patient, the researchers were able to model the development of microcephaly, a disease in which brain size is reduced. As expected, the organoids created using these cells grew to a smaller size. On further investigation, they found that genetic mutations in the patient cells cause neural stem cells to shift from self-renewal to differentiation into nerve cells at an earlier stage, leading to an overall reduction in cell number and size of the organoid.

Model systems like these are likely to become increasingly important for early testing of new therapies before they progress to human trials.

Müller glial stem cells

Researchers at **University College London** have produced a line of Müller glial cells derived from the donated eyes of people who have recently died. These cells have the ability to transform into the specialised cells at the back of the eye, so may be able to treat a wide range of sight disorders.

In 2014 the team, led by **Professor Astrid Limb**, stimulated these cells to differentiate into rod photoreceptor cells, which detect light in the retina[50]. Injecting these cells into the eyes of blind rats partially restored their sight and brain scans showed that half of the electrical signals between the eye and the brain were recovered following the treatment. It is hoped that the cells might be able to help patients with disorders such as macular degeneration or retinitis pigmentosa. There are currently clinical trials taking place using stem cells from embryos, however, there remains ethical debate around this process. In addition, it takes several months to prepare these cells whereas the Müller glial cells can be prepared within a week.

These cells are the only Müller cell lines available for retina research in this field and the group has given them to approximately 100 other research groups.

Adaptation of malarial parasite *Plasmodium knowlesi* to erythrocyte cells

Researchers at the **MRC National Institute for Medical Research** (NIMR) have successfully cultured the malaria-causing parasite *Plasmodium knowlesi* in human red blood cells, which means it is no longer necessary to use primate models[51]. *P.knowlesi* is a simian parasite; however it is closely related to *Plasmodium vivax*, the most important cause of human malaria outside Africa, so its study can provide insights into unique aspects of the biology of *P. vivax*. *P. knowlesi* has also recently been identified as a significant cause of often severe human malaria in south-east Asia.

Edinburgh Adipose Tissue Bank

Mesenchymal stem cells are adult stem cells that can differentiate into a variety of cells. They were originally identified in bone marrow, but have since been isolated from all adult tissues, including fat – adipose tissue. Adipose tissue is easily accessible and readily abundant, even in individuals of healthy weight. It therefore offers an excellent source of stem cells. Plastic surgeons routinely remove large volumes of adipose tissue through reconstructive and cosmetic procedures. Adipose tissue is also a good source of fat cells, endothelial cells and vascular smooth muscle cells.

Researchers at the **MRC Centre for Regenerative Medicine** at the **University of Edinburgh** have set up an adipose tissue bank, comprising adipose tissue from different parts of the body, including subcutaneous, visceral and brown adipose tissue. Since receiving ethical approval in 2010, the bank has collected samples from 58 patients[52]. It also stores genetic information and plasma samples from the subjects as well as details of sample lineage, all of which may prove important for tissue-specific drug delivery.

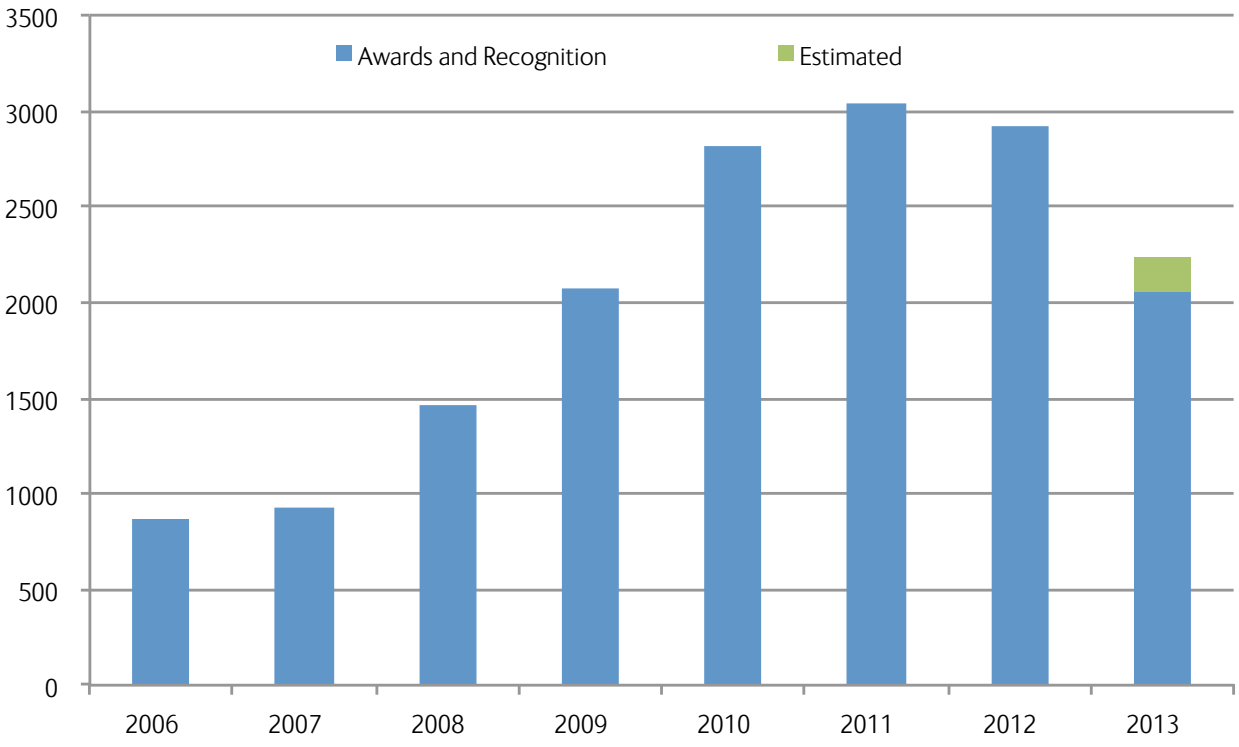
4.1.5 Awards and recognition

Measures of esteem can include awards and other evidenced forms of acknowledgement. It is an encouraging reflection of the reach and significance of MRC research that MRC researchers have secured the most highly prized awards in science including the Nobel Prize and the Louis-Jeantet Prize. Measures of esteem are also used internationally by some funders alongside citation analysis, peer review and research income as indicators of research quality[53].

In total, researchers made 14,520 reports in this section. Recipients of 50 per cent of awards reported that their work had resulted in such formal recognition for them personally, or for members of their MRC-funded team. The average number of reports per award (of those reporting recognition) was six (5.93). Ten or more instances of personal recognition were reported in seven per cent of all awards.

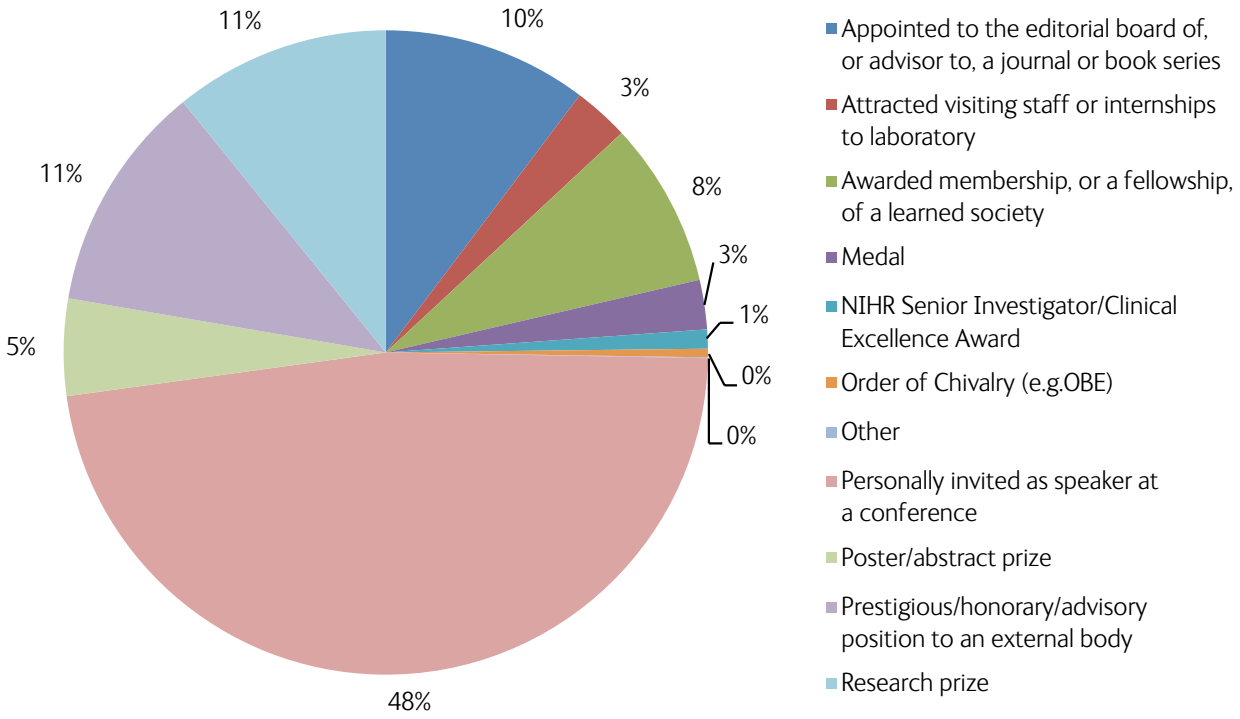
A breakdown of the number of reports of recognition by year is shown in Figure 10; see Annex 2 Section 4.1 Knowledge generation for specific figures. Note that figures for 2010-2012 appear to show a significant increase since the last Economic Impact report, suggesting a degree of lag in reporting. In addition, data from 2013 is partial due to the timing of data collection and is equivalent to 'current year' values in previous reports.

Figure 10: *Number of reports of recognition by year*



Researchfish captures information on the type of recognition reported; the most frequently reported type of recognition in 2013 was being personally invited as a speaker at a conference, in 48 per cent of awards reporting personal recognition. This was followed by being appointed to a prestigious/honorary/advisory position to an external body (11 per cent), research prize (11 per cent) and appointed to the editorial board or as an advisor to, a journal or book series (10 per cent). The distribution of types of recognition is shown in Figure 11; see Annex 2 Section 4.1 Knowledge generation for specific figures.

Figure 11: *Distribution of types of recognition*



Specific examples of awards and recognition:

BMJ Research Paper of the Year

Research led by **Professor Simon Griffin** and **Dr Rebecca Simmons** at the **MRC Epidemiology Unit, University of Southampton**, has won the *British Medical Journal*'s prestigious **Research Paper of the Year** award in 2013. The paper presents the results of the ADDITION study which was the first robust evaluation of diabetes screening and suggested that its effectiveness may have been overestimated[54]. The authors concluded that screening is only likely to benefit the small minority of people with undiagnosed diabetes and is unlikely to reduce deaths in the general population.

Waddington Medal

Dr Jim Smith, director of the **MRC National Institute for Medical Research** was awarded the 2013 **Waddington Medal.** The Waddington Medal is the only national award in developmental biology and is awarded for outstanding research performance as well as services to the subject community.

Bradford Hill Medal

Dr Conor Farrington at the **Open University** was awarded the Royal Statistical Society's **Bradford Hill medal** in 2013 for his development of the self-controlled case series method[55] and outbreak detection systems. Dr Farrington developed the world's first comprehensive, automated outbreak detection system which is capable of monitoring more than 3,000 infections and was used during the 2012 Olympics.

The Bradford Hill Medal[56] is awarded every three years to a Fellow of the Society in recognition of 'outstanding or influential contributions to the development, application or exposition of medical statistics'.

International Osteoporosis Foundation Medal of Achievement

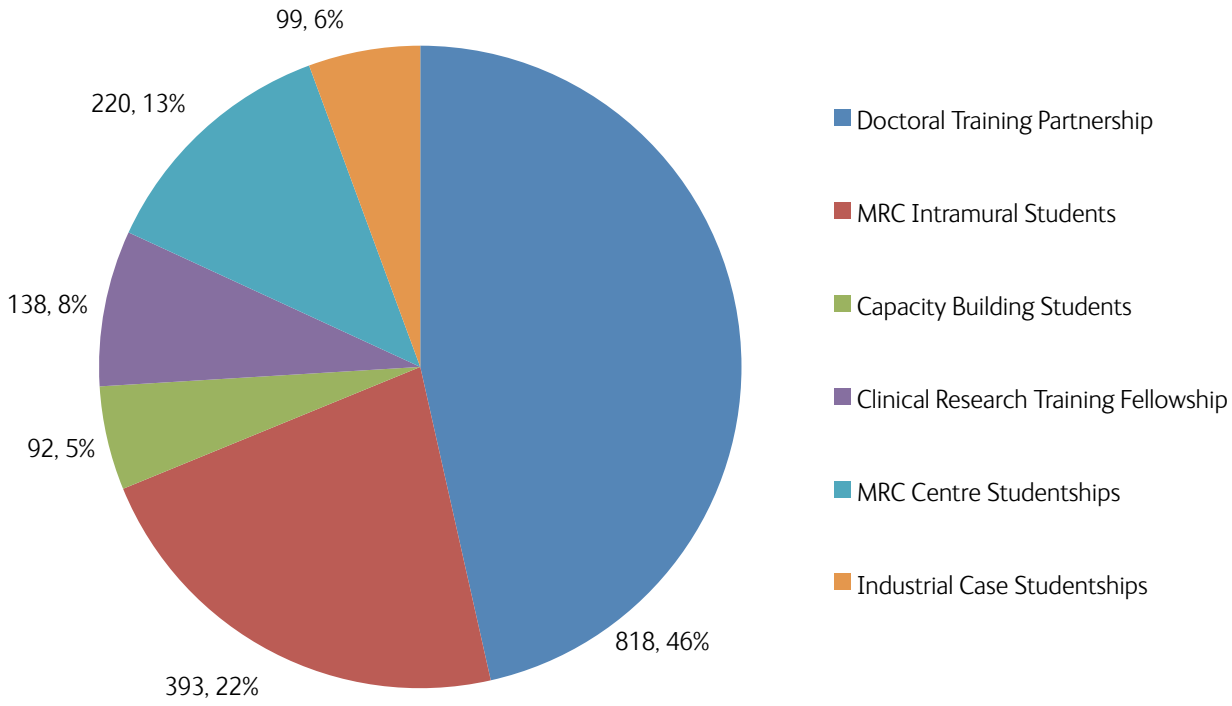
Professor Cyrus Cooper, director of the **MRC Lifecourse Epidemiology Unit** was awarded the **International Osteoporosis Foundation (IOF) Medal of Achievement** for significantly advancing the field of osteoporosis through original and outstanding scientific contributions. Professor Cooper's key research contributions include: discovery of the developmental influences which contribute to the risk of osteoporosis and hip fracture in late adulthood; demonstration that maternal vitamin D insufficiency is associated with sub-optimal bone mineral accrual in childhood; characterisation of the definition and incidence rates of vertebral fractures; leadership of large pragmatic randomised controlled trials of calcium and vitamin D supplementation in the elderly as immediate preventative strategies against hip fracture.

4.2 Human capital (stock)

MRC provides 46 per cent of its studentship funding to research organisations (ROs) and MRC institutes, units and centres as a block Doctoral Training Partnership (DTP). The award provides ROs with significant flexibility in managing their postgraduate studentship population. Many ROs leverage additional sources of funding to further increase flexibility and critical mass of PhD cohorts.

The total number of PhD studentships across the MRC's intramural and extramural programmes in March 2014 is estimated to be approximately 1,800[57], as shown in Figure 12. These are broken down by funding mechanism, showing the number and proportion of each.

Figure 12: *Number of live MRC studentships as at March 2014*



In addition to PhD studentships, the MRC also invests in a limited number of research masters. In 2013, Advanced Course Masters studentships[58] were awarded in the priority areas of biomedical imaging, advanced *in vivo* sciences and mathematics, statistics and computation. Table 2 shows the awards by skills priority area.

Table 2: *Awards by skills priority area*

Primary priority area	Students per intake year 2012-2015	%
Biomedical imaging	14	20%
Advanced *in vivo* sciences	16	23%
Mathematics, statistics and computation	40	57%

Industry CASE studentships

A shared vision for collaborative training has been agreed across all Research Councils.

Research Council Collaborative Training will provide doctoral students with a first-rate, challenging research training experience, within the context of mutually-beneficial research collaboration between academic and partner organisations in the private, public and civil society sectors.

Through Industrial CASE schemes, Research Councils promote studentships with a minimum of a three-month period of relevant training with a non-academic partner. MRC CASE studentships are awarded through an annual competition, with approximately 30 to 35 studentships awarded per annum to a wide range of research organisations and non-academic partners. Typically, 30 to 50 per cent of awards involve Small and Medium Enterprises (SMEs).

Research organisations have the flexibility to use their Doctoral Training Partnership to fund collaborative studentships with industrial or other partnership funders. Currently, only a few collaborative studentships are funded through this route (around 20 studentships). In April 2014, MRC awarded pilot 'flexible supplements' across all 24 Doctoral Training Partnerships to encourage, for example exceptional training opportunities in partnership with industry.

The MRC encourages collaborative studentships that are truly mutually beneficial projects likely to enhance students' training. The MRC therefore does not mandate a conversion rate of Doctoral Training Partnership to collaborative studentships.

A yearly breakdown of the number of students funded under this scheme and the partner organisations is shown in Annex 2 Section 5.1.

4.3 Knowledge transfer and exchange

A major focus for the MRC in recent years has been the translation of the results of basic science into improved healthcare, products and services. The MRC's translational research agenda aims – to drive innovation, speed up the transfer of the best ideas into new treatments, and improve the return on investment in fundamental research – and objectives are outlined in the MRC Strategic Plan.

The MRC works with the NIHR, NHS England, and the devolved health departments to ensure that we have integrated funding schemes, infrastructure and facilities to provide a pathway for research from laboratory to standard patient use.

Supporting collaboration between researchers and industry is an integral part of our strategy and at the heart of our mission to produce benefits for patients and growth in the UK economy. In 2013/14, we continued to develop and implement innovative new ways of working with companies to support this goal.

In October 2013, the MRC made two further stratified medicine awards totalling £8.8m to support partnerships between academic and industrial researchers in open innovation consortia targeting psoriasis and schizophrenia. These awards are part of the MRC's £60m commitment in the current comprehensive spending review to stratified medicine and build on seven earlier consortium awards totalling £28.8m. Combined, the nine consortia in the MRC's stratified medicine portfolio bring together 30 academic and 41 industrial partners from both the biopharmaceutical and diagnostics sectors.

In March 2014, MRC entered into a five-year initiative with AstraZeneca that will give academic researchers unprecedented access to over two million compounds and state-of-the-art high throughput screening facilities in

Cambridge. This collaboration will enable researchers to identify new drugs for the treatment of disease and chemical probes to better understand disease.

MRC translational response mode funding schemes made 55 awards totalling £43.4m in 2013/14. These included 'Confidence in Concept' awards ranging from £250k to £800k to 22 universities. These also included five awards to academics working with SME partners. The SME partners received funding from Innovate UK, as part of the Biomedical Catalyst partnership.

The Development Gap Fund, which provides seed funding to help exploit cutting edge science arising from the MRC's intramural programmes, provided £900k in funding to support 12 projects covering a range of disease areas and approaches.

See Annex 2 Section 4.3 Knowledge transfer and exchange for a breakdown of numbers of awards and commitment for the relevant grant schemes.

Examples of outputs/impacts in this area:

Floceleris

Floceleris is a spin-out from the **University of Cambridge** formed in 2012 by **Dr Damian Crowther** and colleagues. The company is developing a pre-symptomatic test for clinical samples to capture and measure the aggregation of amyloid beta peptides that occurs during neurodegeneration. The test will be used to find new drugs that inhibit disease progression and serve as a companion diagnostics tool to stratify patients and personalise treatments for Alzheimer's patients. In 2013 Dr Crowther was awarded the Carpe Diem Life Science Award[59] for the best start-up company in the University of Cambridge's Entrepreneurs Business Creation Competition.

Sannox Therapeutics

Sannox Therapeutics is a spin-out based on the research of **Professor George Baillie** at the **University of Glasgow**. Professor Baillie is developing novel therapeutic agents to treat a number of diseases which have an unmet clinical need. The ultimate aim is to progress potential drugs to such a stage that they would be attractive to pharmaceutical companies or investors to take forward to the marketplace. Professor Baillie's team have developed a system in which they can interpret the interfaces of protein:protein interactions and produce peptides that disrupt specific protein complexes. The lab uses screening techniques to convert peptides into conventional small molecules that could also disrupt protein:protein interactions. It is hoped that this platform will lead to drugs with fewer side effects as the compounds target the cellular location of a particular protein or enzyme rather than its overall activity.

Absynth Biologics

Antibiotics have been the conventional treatment for bacterial infection for 60 years. However antibiotic resistance is becoming a pressing concern. One alternative is to generate protective immunity through vaccination. Alternative approaches to treatment are a focus of theme two of the cross-council initiative to tackle antimicrobial resistance.

Fundamental MRC and BBSRC-funded research into the bacterium *Staphylococcus aureus* led to the creation of spin-out company Absynth Biologics in 2007. The company is now working, with support from the Biomedical Catalyst, to produce a vaccine against the bacterium, including methicillin-resistant *S. aureus*, or MRSA. *S.aureus* causes a wide range of infections, including septicaemia and wound abscesses.

In 2012, Absynth received a feasibility award through the Biomedical Catalyst to further develop the vaccine. Following that, in 2013 Absynth and **Professor Simon Foster** at the **University of Sheffield** received more than £2m from the Innovate UK and the MRC, again through the Biomedical Catalyst and part-administered through the MRC's Developmental Pathway Funding Scheme (DPFS), to take the vaccine to a pre-clinical stage.

The company is currently in a funding round with investors, which, if successful, will enable Absynth to grow and move to the next stage of product development.

4.4 Intellectual property activity

MRC Technology (MRCT) is a key partner in our translational strategy, working to translate cutting-edge scientific discoveries from MRC units and institutes into products, and managing our intellectual property such as valuable patent rights associated with the production of monoclonal antibodies.

During 2011/12, changes were made to MRCT governance to strengthen its independence from the MRC following the adoption of new articles of association, effective from 31 January 2012. The organisation now works with the MRC under contract, and the MRC paid MRCT management fees of £4.62m in 2013/14 (£4.2m in 2012/13).

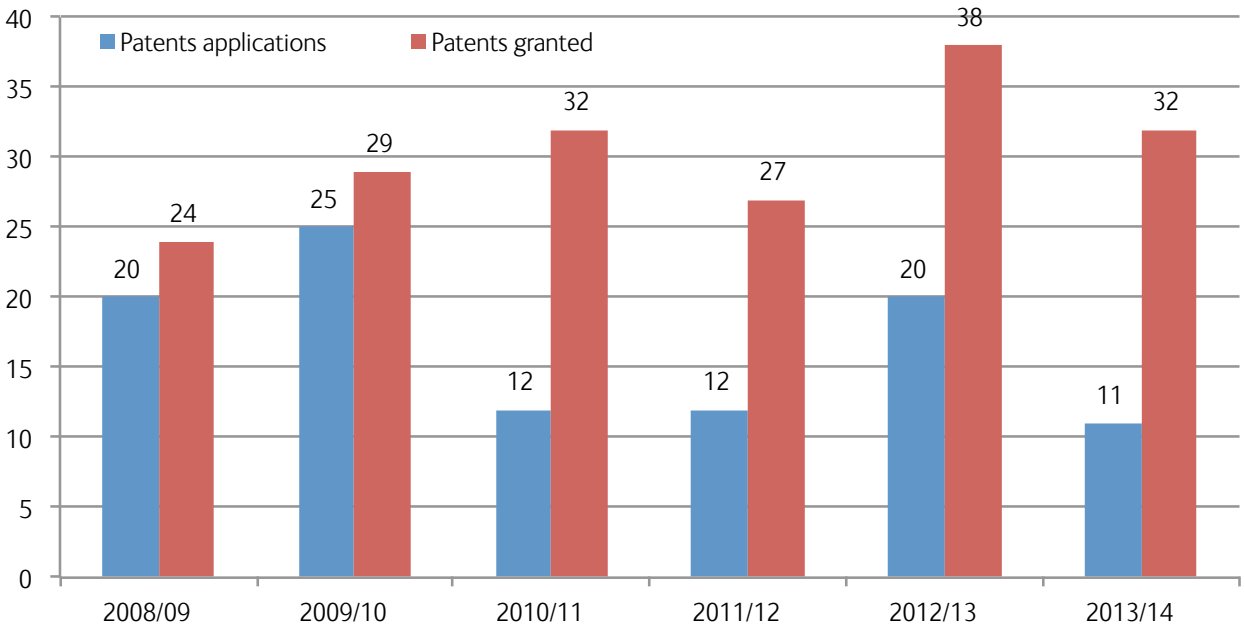
MRCT provides management of both new intellectual property and commercial opportunities arising from research by MRC staff, and the management of existing MRC intellectual property and on-going licensing arrangements. In 2013/14, 32 patents were granted, a slight decrease from last year (2012/13: 38 patents granted). Licensing income to the MRC from all MRCT-managed sources also fell slightly to £85.4m, from £91.7m in 2012/13. It is likely that the transfer of MRC units to university units, which includes transfer of employee contracts and materials will impact on both the reporting of patents and IP income.

4.4.1 Patent applications and patents granted

MRCT works with scientists from MRC-funded units and collaborating organisations to discover and protect healthcare innovations.

The data presented here and below are MRCT data and therefore represent the intramural part of the MRC portfolio only. There is a significant time lag in the process for patents to be granted, as such, there is no correlation between the number of patent applications and patents granted each year. Figure 13 shows the number of patent applications and patents granted by year.

Figure 13: *Number of patent applications and patents granted by year*



Patent information is also collected through Researchfish; the dataset contains details of 849 discoveries in the intellectual property section. These include 74 reports of copyrighted works, 210 reports of discoveries for which formal protection was not possible or required, and 565 reports relating to published and granted patents.

Twenty seven per cent of discoveries overall (227/849) were reported as 'licensed' by 2013. The proportion is slightly higher for patented discoveries (31 per cent, 180/579). This is similar to the proportions reported in the last three years. This calculation does not include the 11 per cent of reports where researchers indicated that details were 'commercial in confidence' and could not be provided (93/849); it would be reasonable to assume that some of these cases will translate into new licences in due course.

4.4.2 Spin-outs/new businesses created

MRCT has managed the creation of two new businesses in the last six years directly from the MRC's intramural programme.

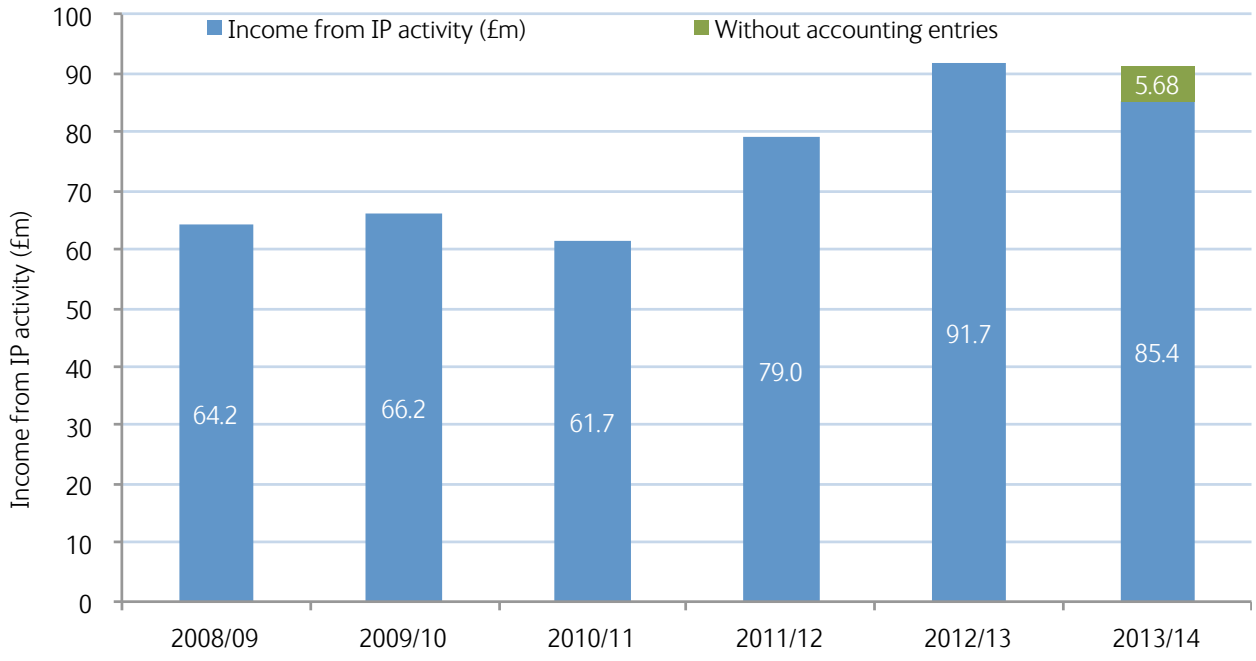
The MRC also collects data on spin-out companies through Researchfish. MRC funding has contributed to the set up or growth of 77 companies, 55 of which have been formed since 2006, including three in 2013. It is estimated that these companies represent at least 100 new highly skilled jobs in the UK.

See both Annex 2 Section 4.4a Intellectual Property Activity (MRCT-managed) and Section 4.4b Intellectual Property Activity (Researchfish data) for a breakdown of the data on patents and spin-outs.

4.4.3 Income from intellectual property

Figure 14 shows the income from intellectual property, including licence income and receipts from sales of shares in MRC companies.

Figure 14: *Income from intellectual property (IP)*



Specific examples of commercialisation (reported in Researchfish):

Treatment of disabilities following stroke

Acute stroke is the third largest cause of death in the UK and the leading single cause of severe disability. More than 110,000 people in England will have a stroke each year, costing the NHS £2.8bn. The number of years with a reduced quality of life due to the disabilities caused by stroke is larger than of any other disease in the elderly population except for dementia. Cognitive impairment is present in more than 30 per cent of long-term survivors of stroke.

Hemispatial neglect is one of the major cognitive disorders following stroke. This is caused by brain injury to the right cerebral hemisphere, resulting in visual neglect of the left-hand side of space. This causes a patient to behave as if the left side of the sensory space is non-existent. There are currently no reliable drug treatments for neglect, other cognitive impairments or motor deficits following stroke.

Professor Masud Husain at **University College London**, in conjunction with UCB Pharma, has applied for a patent for the use of rotigotine in the treatment of hemispatial neglect and other disabilities following stroke. Rotigotine is a dopamine agonist — a compound that activates dopamine receptors in the absence of dopamine — and an approved treatment for Parkinson's disease. Professor Husain has shown that treatment of stroke patients with rotigotine is associated with a significant improvement in the Mesulam shape cancellation task – a test whereby patients have to search visually for targets and mark these with a pen. The number of targets found on the left-hand side increased by 12.8 per cent after the patient was treated with rotigotine[60].

Antagonist of gene implicated in cancer

The gene Lrg1 codes for the glycoprotein LRG1, the expression of which is upregulated in cancer cells. Until recently however, its specific function was unknown. **Professor Stephen Moss** at **University College London** showed in 2013 that in the presence of the growth factor TGF- ß1, LRG1 promotes the division of endothelial cells – the cells lining blood vessels, and therefore angiogenesis, the formation of new blood vessels from pre-existing ones[61]. Angiogenesis is essential for tumour growth to provide the tumour with a supply of nutrients and oxygen and to remove waste, and so angiogenesis is one target for cancer treatment.

Professor Moss has patented, via **UCL Business plc**., antagonists of LRG1[62].

Enzyme replacement therapy for mitochondrial neurogastrointestinal encephalomyopathy

Researchers at St George's, University of London entered into a licensing agreement in 2013 with rare disease research and development company Orphan Technologies Ltd to develop an enzyme replacement therapy for mitochondrial neurogastrointestinal encephalomyopathy (MNGIE). MNGIE is a rare progressive disease with an average life expectancy of 38. It is caused by a defect in the gene responsible for producing the enzyme thymidine phosphorylase (TP). Without this enzyme, mitochondria cannot function properly resulting in problems with the nervous system and skeletal muscle. It causes symptoms such as diarrhoea, constipation, gastroparesis, nausea, vomiting, weight loss, muscle weakness and nerve damage.

The new therapy, Erythrocyte Encapsulated Thymidine Phosphorylase (EE-TP), is based on introducing TP directly into patients' erythrocytes (red blood cells). Encapsulating the enzyme in the red blood cells increases the period that the enzyme is most effective for and minimises an adverse immune reaction.

EE-TP has been granted orphan drug status in Europe and the United States. It has also already been used to treat several patients with urgent medical needs through compassionate use treatment. EE-TP has been found to be effective in reducing or eliminating the elevated plasma and urine concentrations of thymidine and deoxyuridine, toxic substances that accumulate in tissues of MNGIE patients.

Use of nitric oxide in prevention of ventilator-associated pneumonia

Ventilator-associated pneumonia (VAP) is the most common healthcare-linked infection contracted by patients in intensive care[63]; it is the basis for about half of all antibiotics given in this department[64]. The biggest risk factor for the development of the condition is the presence of a tracheal tube[65], a tube inserted into the windpipe to maintain a patient's airway. The tubes interfere with the normal protective upper airway reflexes, prevent effective coughing and encourage the entry of infected secretions from the respiratory and upper digestive tracts. It is estimated that over 60,000 patients are mechanically ventilated in UK intensive care units annually and the reported incidence of VAP varies from around 10 per cent to more than 30 per cent. It has been shown that oxides of nitrogen play a key role in the maintenance of host defence against various microbial pathogens. Ordinarily, oxides of nitrogen (NOx) are present in high concentrations in the stomach where they play an important role in maintaining sterility and preventing gastrointestinal infections.

Professor Charles Hinds at **Queen Mary, University of London**, has shown that during critical illness, the production of NOx is reduced. This predisposes colonisation of the stomach and oral cavity by pathogenic bacteria and therefore the subsequent development of VAP. Professor Hinds has patented a system for the external production and local delivery of nitric oxide (NO) and NOx[66]. The solution is designed to restore normal physiological activity of NOx by nasogastric and oral administration. In 2013 he entered into an agreement with EdixoMed to conduct a Phase I/II trial of this system[67].

The Imperial Antibiotic Prescribing policy smartphone app

The Imperial Antibiotic Prescribing Policy (IAPP) smartphone app was developed by Imperial College Healthcare NHS Trust's antibiotic review group and the UKCRC Centre for Infection Prevention and Management in 2011. The app helps healthcare professionals choose the most appropriate course of treatment to ensure antimicrobials are prescribed appropriately. The app has now been integrated into the Imperial College Healthcare NHS Trust's antimicrobial stewardship programme and has been recognised in the Department of Health's Antimicrobial Resistance five-year Strategy. It has also won an Outstanding Service Care and Research (OSC&R) award, Novartis antimicrobial stewardship award and was highly commended at the National Patient Safety Awards.

Mathematical model for TB and HIV control projections and costings

Dr Richard White at the **London School for Hygiene and Tropical Medicine (LSHTM)** developed a mathematical model in 2013 for tuberculosis (TB) and HIV control projections and costings. This tool will be freely available for download by TB and HIV policymakers around the world for decision-making on control strategies. It has been used to update The Sudan's National Strategic Plan in 2013 in a move to more decentralised provision of TB patient care. It is planned for it to be used in approximately five more high TB-burden countries in 2014 and rolled out globally in 2015. It will also be used in workshops run by UNAIDS, the Global Fund and WHO.


HLP
AL
5cm
MF 1.09
DIR
TR 480.0
TE 14.0
TA 01:31
BW 90.0
M/ND
HLP
AL
5cm
MF 1.09
DIR
TR 480.0

5.0 Outcomes

5.0 Outcomes

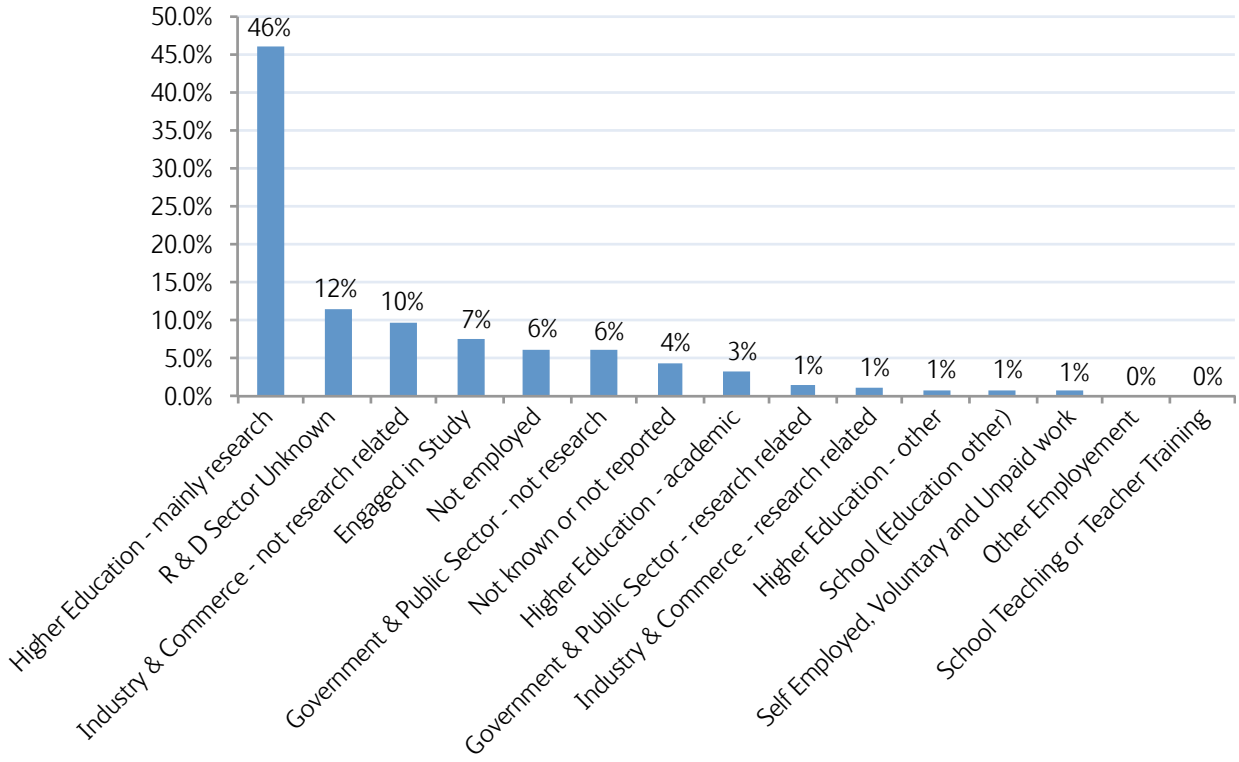
5.1 Human capital (flow)

Encouraging our students and fellows to establish mutually beneficial relationships with industry is key to ensuring that the UK has a skilled workforce that delivers for the UK in terms of both health benefits and economic returns.

The Higher Education Statistics Agency (HESA) DLHE (Destinations of Leavers from Higher Education) survey provides information about patterns of employment and further study or training six months after completion.

Figure 15 shows the first destination information for MRC PhD students who completed their programmes during the academic year 2012/13 (1 August 2012 to 31 July 2013).

Figure 15: *First destinations of MRC students who completed programmes during the academic year 2012/2013*



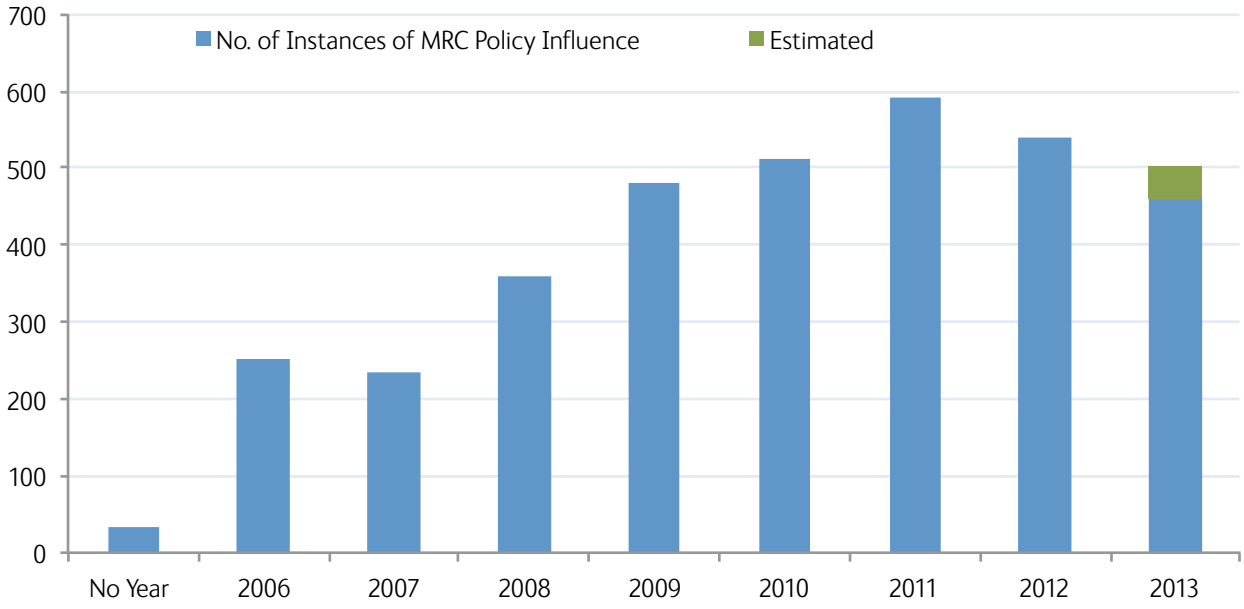
The data demonstrate that six months after completing an MRC PhD, 89 per cent of students are known to be in employment or engaged in further study. Around 46 per cent of MRC-funded students go into research related employment in Higher Education. Just over a fifth (22.7 per cent) enter industry or research and development related employment. Further data on this are available in Annex 2 section 5.1 Human capital (flow).

5.2 Public policy

Research in areas such as the relationship between health, diet and the choices we make, or the effect of the environment that we live in on health are areas that often result in public health interventions and policy changes rather than commercially exploitable 'products'. These are equally important outcomes to monitor as they often have a substantial impact on the public and result in significant impact. Information on influence on policy and practice is collected through Researchfish.

There were 3,911 reports of policy influences between 2006 and 2013. Figure 16 shows the number of reports of influence on policy by the year that it was realised[68]. Please see Annex 2 Section 5.2 Public policy for more specific figures. Note that data from 2013 is partial due to the timing of data collection, and therefore a projected total has been estimated.

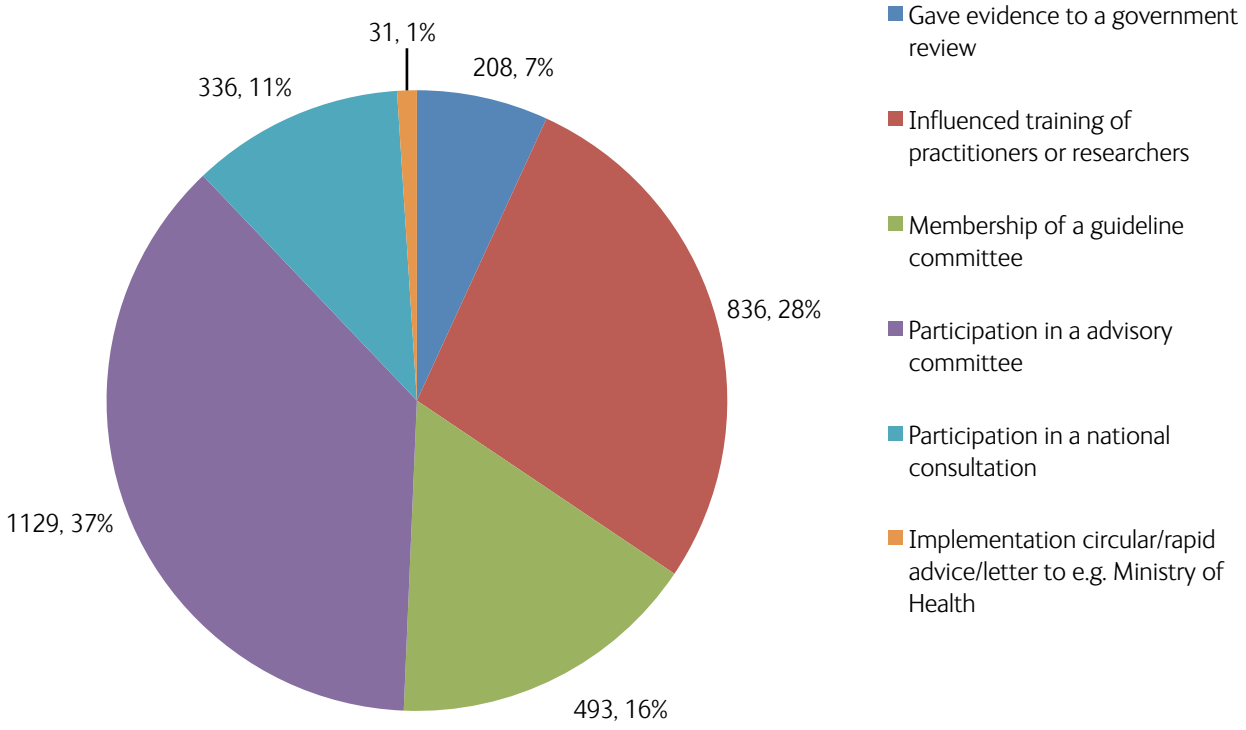
Figure 16: *Number of reports of influence on policy by year*



Each influence on policy is reported as a specific 'type', such as 'citation in clinical guideline' or 'participation in national consultation'. These types fall into two categories – 'influences on the policy setting process' and 'citations in key policy documents' and are shown in the metrics below.

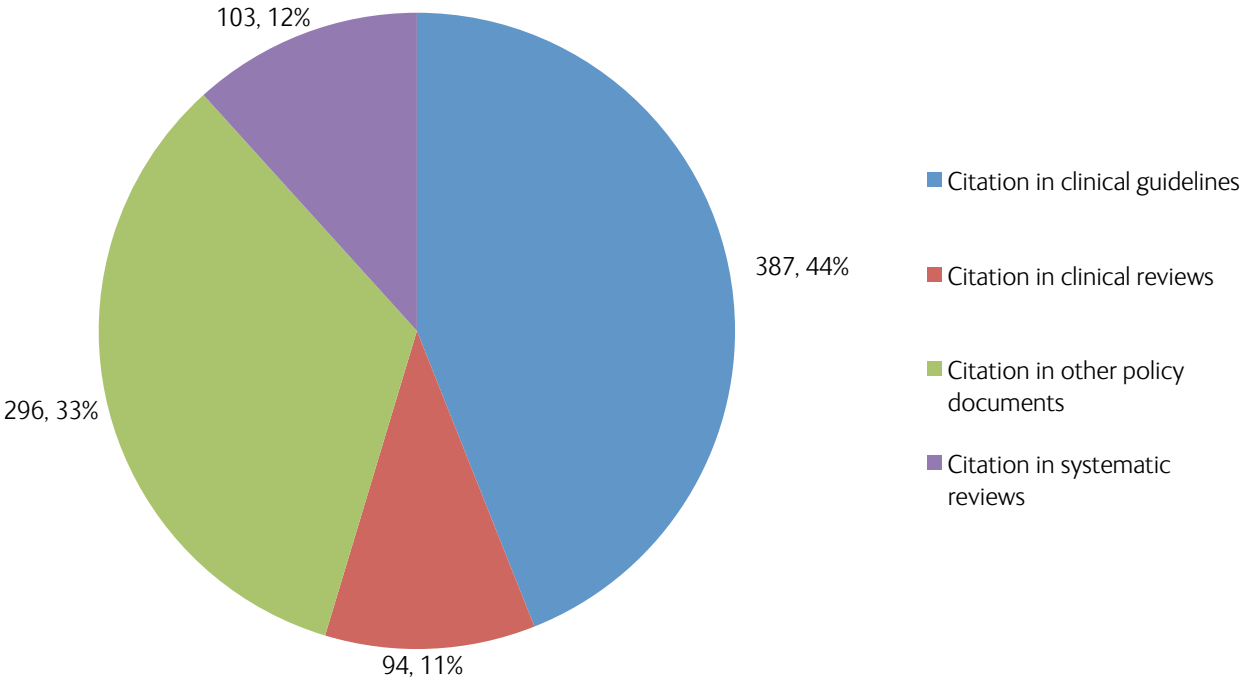
There were 3,033 reports of influences on policy setting processes reported between 2006 and 2013. Figure 17 shows the breakdown by type of policy setting process with specific numbers and proportion.

Figure 17: *Breakdown of type of policy setting process*



There were 880 reports of value/policy changes induced through citation in key policy documents reported between 2006 and 2013. Figure 18 shows the breakdown by type of policy document with specific numbers and proportion.

Figure 18: *Breakdown of type of policy documents*



Specific examples of influences on policy:

Importance of sufficient iodine intake during pregnancy

The MRC-funded **Avon Longitudinal Study of Parents and Children (ALSPAC)** showed in 2013 that iodine deficiency in pregnancy has an adverse effect on children's mental development[69].

Iodine is essential for producing the hormones made by the thyroid gland, which have a direct effect on fetal brain development. For many years, iodine intake in the UK was thought to be sufficient. A study conducted by researchers at the Universities of Surrey and Bristol has however shown that more than two-thirds (67%) of pregnant women are deficient.

The researchers assessed the mental development of the women's children by their IQ at age eight and reading ability at age nine. The researchers found that children of the women in the iodine-deficient group were significantly more likely to have scores at the low end of verbal IQ, reading accuracy and reading comprehension, even after adjusting for external factors likely to affect the scores, such as parental education and breast-feeding. The lower the mother's level of iodine, the lower the average scores for IQ and reading ability were.

As a result of this study, the British Dietetic Association (BDA) has produced a fact sheet on the importance and sources of dietary iodine[70], with a focus on the increased requirements of pregnant women.

Citation in NICE guidelines "Overweight and obese adults – lifestyle weight management"

In May 2014 the National Institute for Health and Care Excellence (NICE) published guidelines on lifestyle weight management[71] for overweight and obese adults. The guidelines comprise multi-component lifestyle weight management approaches that aim to change someone's behaviour to reduce their energy intake and encourage them to be more physically active in order to reduce the risk of the main diseases associated with obesity. In compiling the guidelines, the Guidelines Development Group drew on research from **Professor Susan Jebb** who, in 2011, showed that participating in commercial weight management programmes, such as Weightwatchers and Slimming World, can lead to a greater weight loss over a 12-18 month period than from following the advice of a doctor[72].

Addition of rotavirus vaccine into The Gambia's Expanded Programme of Immunization (EPI)

In August 2013 the Ministry of Health and Social Welfare of The Gambian government formerly introduced the rotavirus vaccine into its Expanded Programme of Immunization (EPI), the eleventh vaccine the country has introduced since it joined the global programme in 1979. The EPI was set up by the World Health Organization in 1974 to ensure that children in all countries receive life-saving immunisations.

Research conducted by the **MRC Gambia Unit** played a valuable role in ensuring the rotavirus vaccine was added to the programme. **Dr. Jahangir Hossain** at the **MRC Gambia Unit** was part of an international study that confirmed that rotavirus was the leading cause of diarrhoeal disease among infants in developing countries[73]. The Global Enteric Multicenter Study (GEMS), the largest study ever conducted on diarrhoeal diseases in developing countries, found that approximately one in five children under the age of two suffer from moderate-to-severe diarrhoea each year, increasing children's risk of death 8.5-fold and leading to stunted growth over a two-month follow-up period.

Rotavirus is responsible for the death of nearly 300 Gambian children under five each year, accounting for approximately one third of all under-five diarrhoeal deaths and diarrhoeal disease hospitalisations in The Gambia. If used in all GAVI-eligible countries[74], rotavirus vaccines could prevent an estimated 180,000 deaths and avert six million clinic and hospital visits each year[75].

Chief Medical Officer seminar on future public health policy for HIV research

Professor Sheena McCormack at the **MRC Clinical Trials Unit** is a clinical epidemiologist who specialises in the development and implementation of biomedical interventions to prevent, or reduce, the risk of acquiring HIV. In 2013 she took part in a Chief Medical Officer (CMO) seminar on future public health policy for HIV research. As a result of the seminar, the CMO outlined plans to update the UK's HIV policies in order to help people get diagnosed earlier. Following the seminar, Professor Dame Sally Davies wrote to all GPs advising them to test patients presenting with glandular fever symptoms for HIV. The ban on the sale of HIV self-testing kits was also lifted in April 2014 to encourage individuals to get tested as soon as possible.

5.3 Public engagement

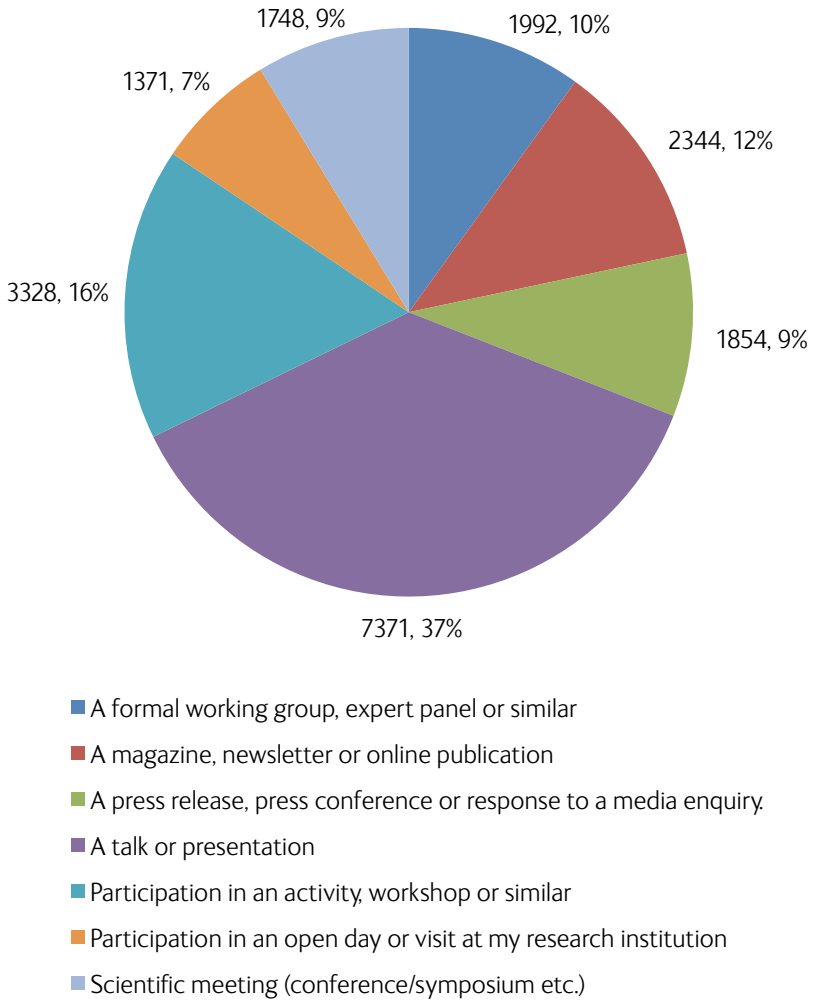
One of the aims in the MRC's strategic plan, *Research Changes Lives*[76], is to bring the benefits of excellent research to all sections of society, and this is supported by a specific objective to enhance engagement and communication with our scientists and partners, policymakers and parliamentarians and the public. This confirms our duty, as set out in the MRC's mission, to engage with the public and other groups, to give an account of our research, to ensure that public views and concerns are reflected in our decision-making, and to build public trust in the MRC and the research it funds.

Public engagement events by type

Researchfish collects information about public engagement and dissemination activities delivered by MRC-funded researchers. They are asked to report on their interaction with non-academic audiences. For example, giving a public talk about their research to a non-scientific audience, working with journalists to share research findings via the media or taking part in a public science festival. Between 2006, when data collection began, and 2013, MRC-funded researchers reported 23,292 distinct dissemination activities, from 56 per cent of awards. The average number of engagement activities per award (from awards reporting engagement activities) was seven (7.47). Eleven per cent of all awards reported more than ten engagement activities.

Figure 19 shows the breakdown by type of engagement activity with specific numbers and proportion. Further data on this can be found in Annex 2 Section 5.3 Public Engagement.

Figure 19: *Public engagement activity by type*



Funding for public engagement

Engagement with the public is delivered directly by MRC-funded researchers who interact with a wide range of audiences including patient groups, local communities and schools, and these activities are funded from core budgets. In addition, the MRC has a corporate budget for public engagement – £377k in 2013/14 – which includes small grants

for researcher-led public engagement projects such as taking activities to popular music festivals and creating resources for schools.

Researchers are supported in their public engagement work by a network of four MRC communications managers who offer help and advice and work with them to make the best use of available resource to achieve their public engagement goals. In 2013/14, the MRC delivered professional public engagement training to more than 130 researchers; all training was delivered before a public event to improve the quality of the scientist's interaction and experience, and to consolidate their learning. This does not include crisis communications and media training.

Face-to-face engagement

As 2013 was the MRC's centenary year, the programme of public engagement events was considerably larger than normal, and included a national MRC Open Week and a major public festival at the Science Museum in London, as well as MRC partnerships with the major UK science festivals. At the centenary events, more than 1,400 scientists and support staff funded by the MRC engaged face-to-face with members of the public by presenting their research in an accessible and interesting way, often using activities that facilitate discussion by demonstrating the impact research has on health, society and the economy. Collectively, these events reached more than 20,000 people of all ages and from all walks of life.

Public engagement activities and events generate considerable legacy in terms of building awareness, interest and support for the MRC and its work, as demonstrated by the pick-up of leaflets and magazines at events and increasing numbers of followers on social media. Legacy is also seen in the development of a cadre of researchers and support staff with improved awareness of the benefits of public engagement and increased advocacy for engagement within their institutions.

Media engagement

An integral part of the MRC's public engagement programme is the use of established media channels to reach public audiences and raise awareness of the MRC and its work. Between 2006, when data collection began, and 2013, MRC-funded researchers reported 1,854 separate media activities. Much of this work is driven and supported by the MRC press office, and in 2013 this resulted in 2,698 print and broadcast articles featuring the scientific achievements of MRC-funded researchers, of which around 1,000 appeared in national media.

The MRC encourages and supports its scientists to use social media to share research results, and this is an increasingly important medium which allows direct engagement between researchers and members of the public. The MRC community's social media presence is supported by a corporate Twitter account, Facebook page and blog site, *MRC Insight*, which alone has attracted 60,918 unique visitors since it was launched in June 2012.

Specific examples of engagement activities:

Association between consumption of sugar-sweetened beverages and cardio-metabolic risk factors in adolescents[77]

This paper, published in 2013 by the **MRC Human Nutrition Research** group, demonstrated a link between the high consumption of sugary drinks by teenagers and the risk factors namely lower levels of 'good' cholesterol and higher levels of the 'bad' triglyceride form of fat in their blood, for heart disease in later life. This paper received considerable media interest, including from the BBC, *The Guardian* and *The Telegraph*.

Science Inspired Tales

In 2012 **Professor Peter Openshaw** at **Imperial College London** gave a *Science Inspired Tales*[78] public stage performance at the Albert Hall Theatre in Brussels. During the lecture entitled "Our germs, our guns: an uneasy peace", he discussed infection and the immune system, recounting anecdotes and stories of his scientific inspiration.

Brain implant for Parkinson's disease

Researchers at the **University of Bristol** have developed a brain implant consisting of a system of tubes and catheters that allows them to pump protein therapy deep into the brains of patients with Parkinson's disease, potentially stopping the disease from progressing. Parkinson's, affecting around 127,000 people in the UK, occurs when a lack of a chemical called dopamine causes nerve cells within the brain to die. It is hoped that delivery of the protein — a growth factor called glial cell-derived neurotrophic factor (GDNF) — will encourage these cells to grow again. This new method of delivery will allow the protein to bypass the blood/brain barrier. A clinical trial[79], led by **Professor Steven Gill**, is on-going and has received publicity from Sky News, the BBC and *Daily Mail.*

Alzheimer's disease open day

Since 2006, **King's College London's Institute of Psychiatry** has held an annual open day hosted by Alzheimer's Research UK and the **MRC Centre for Neurodegeneration Research** to showcase its cutting edge research into Alzheimer's disease. In 2011 the event welcomed 150 members of the public, including carers and families of people with dementia, who engaged in workshops, talks and question and answer sessions.

Gene therapy to treat prostate cancer

In a Phase I clinical trial[80], researchers at the **University of Birmingham** are using gene therapy to treat prostate cancer that has relapsed after radiotherapy and hormone therapy. The AdUP trial uses a vector made from an adenovirus that has been modified to produce an enzyme called nitroreductase and GM-CSF — a growth factor that enhances the immune system by stimulating the number and function of white blood cells produced by the body. The vector is administered by way of an injection, which is then followed by treatment with CB1954 — a cytotoxic drug made active by the nitroreductase enzyme which kills cancer cells.

The BBC interviewed Bernard Ward[81], one of the first 20 patients undergoing this therapy, and the surgeons conducting the treatment. Mr Ward has suffered from prostate cancer for six years and standard treatments are no longer working. The clinical trial is designed to establish whether the treatment is safe for clinical use.

Science Museum Painless exhibition

As part of the Science Museum's Painless Exhibition[82] in 2013, **Professor Geoff Woods** at the **University of Cambridge** sequenced the genome of a man with congenital analgesia, a rare genetic disorder characterised by a total inability to sense pain. Worldwide, the prevalence of congenital analgesia is estimated to be around one in a million. At the exhibition, Professor Woods identified the patient's gene mutations, confirmed his diagnosis and was able to offer him genetic counselling. In 2006 Professor Woods discovered different mutations in the gene *SCN9A* responsible for this condition[83]. *SCN9A* encodes a subunit of a sodium channel expressed in neurons involved in the amplification of the pain signal; the gene mutations cause the protein to lose its function.

Annexes

Annex 1: Metrics Framework – BIS 2011/12

Key: =to include = optional = data not available

CATEGORY METRIC	UNITS	DEFINITION	
Total Funds Available	£m	Total funding available to the Research Council - Sum of Grant in Aid and Leverage	0
Budget Allocation	£m	Research Council Grant-in-Aid	0
Leverage	£m	Funding other than Grant-in-Aid. Sum of components below	0
of which Private	£m	Funding Leveraged from the Private Sector	0
of which from other Research Councils	£m	Funding Leveraged from other Research Councils	0
of which from other source	£m	Funding received from all other sources.	0
of which Private	%	As a percentage of Total Funds Available	
of which Other Research Councils	%	As a percentage of Total Funds Available	
of which Other	%	As a percentage of Total Funds Available	
Total Expenditure			
of which Responsive Mode Grant	£m	Accounts Expenditure on Responsive Mode Grants	0
of which Postgraduate Awards	£m	Accounts Expenditure on Postgraduate Student Support	0
of which Other components	£m	Residual Expenditure on other components as Total funding minus two above	0
of which Responsive Mode Grant	%	As a percentage of Total Funds Available	
of which Postgraduate Awards	%	As a percentage of Total Funds Available	
of which Other components	%	As a percentage of Total Funds Available	
Human Capital			
Principal Investigators	#	Total number of principal investigators directly supported on DATE	0
Research Leaders in Sponsored Institutes	#	Total number of research leaders in sponsored institutes where applicable on DATE	0
Research Fellowships	#	Total number of Research Fellowships on DATE	0
Knowledge Generation			
Number of Grants assessed for reporting	#	Number of grants assessed to which the outputs reported refer	0
Refereed Publications	#	Number of papers published in peer reviewed journals	0
Non Refereed Publications	#	Publications OTHER THAN those included under Refereed Publications	0
Co-authorship of refereed publications - International	#		0
Co-authorship of refereed publications - Industry	#		0
Human Capital			
Number of PhD Students Supported	#	Number of NEW PhD students supported on DATE	0
Number of Masters Students Supported	#	Number of NEW Masters students supported on DATE	0
Number of Other Students Supported	#	Number of New Non PhD or Masters Students supported on DATE	0
Finishing Rates	%	Percentage of PhD students submitting within 4 years of commencement of support (for example row 2007/08 refers to students who began in 2003/04)	0
Student funding/training schemes			

Knowledge Transfer and Exchange			
KE Spend	£m	Total spend for relevant year across all council KTE programmes	0
KE Programmes		Please State which KE programmes you support	0
Commercialisation Activities			
IP Activity (discretionary)			
Patents applications	#	Patent Applications to RC investments	0
Patents granted	#	Patents Granted to RC investments	0
Spin-outs/new businesses created	#	Number of new spin-outs created from RC investments	0
Income from IP activity	£m	Income from IP including areas such as licence income and receipts from sales of shares in RC funded companies	0
Human Capital			
Destinations of leavers		Total Number of leavers from Doctoral Programmes in this academic year (DLHE)	0
Of which University	%		0
Of which Wider Public Sector	%		0
Of which Third Sector	%		0
Of which Private Sector	%		0
Of which Unknown or Other	%		0
Of which Unemployed	%		0
Placements in user organisations	#	Count instances of funded placements in user organisations	0
Placements in user organisations		Examples of measured impact	0
Public Policy			
Instances of influence		Examples of influence in policy	0
Value/changes induced		Examples of measured impact	0
Public Engagement			
PE Schemes		Examples of PE Schemes	0

Additional MRC metrics

The MRC has also chosen to include additional metrics and/or narrative information on:

- Non-paper outputs (part of section 4.1 - Knowledge generation)
- Translational research and knowledge exchange (section 4.2 - Knowledge transfer and exchange)
- Public engagement (section 5.3 – Public engagement)

Annex 2: MRC metrics

Section 3.1 Income and expenditure

No.	Metric	Unit	2008/09	2009/10	2010/11	2011/12	2012/13	2013/14	Notes
1	Budget Allocation	£m	680.8	722.2	732.0	697.5	656.2	725.8	As per Annual Report – Financial Statement Section 3
2	Leverage (MRC definition)	£m	693.7	739.0	745.9	702.1	659.6	729.3	As per Annual Report i.e. budget allocation (metric 1) plus other income (metric 2c).
2	Leverage (BIS definition)	£m	63.4	77.1	67.6	56.5	68.3	66.9	As per BIS guidance i.e. external income (metrics 2a, 2b & 2c - excluding metric 2d).
2a	of which Private	£m	44.6	50.6	42.5	42.1	49.2	48.3	As per Annual Report – Financial Statement Section 5, total less metric 2b
2b	of which from other Research Councils	£m	5.8	9.6	11.2	9.8	15.7	15.1	As per Annual Report – Financial Statement Section 5
2c	of which from other source – Other Income[84]	£m	13.0	16.9	13.9	4.6	3.4	3.5	As per Annual Report – Financial Statement Section 6
2d	of which from other source - Licences and Shares[85]	£m	64.98	66.19	61.69	78.98	91.72	85.42	As per Annual Report – Financial Statement Section 2
3	Total Expenditure	£m	349.6	383.6	384.3	414.1	423.7	517.3	As per Annual Report (sum of metrics 3a to 3d)
3a	of which Responsive Mode Grant	£m	229.5	249.3	264.5	267.6	243.1	272.5	As per Annual Report – Financial Statement Section 11
3b	of which Postgraduate Awards[86]	£m	67.9	78.2	78.7	86.0	71.3	62.9	As per Annual Report – Financial Statement Section 2 & 13
3c	of which Other components - Other Research	£m	36.9	38.3	23.2	42.2	91.5	164.2	As per Annual Report – Financial Statement Section 12
3d	of which Other components - International Subscriptions	£m	15.3	17.8	17.9	18.3	17.8	17.7	As per Annual Report – Financial Statement Section 14

Section 3.2 Human Capital (input)

No.	Metric	Unit	2008/09	2009/10	2010/11	2011/12	2012/2013	2013/14	Notes
4	Principal Investigators on grants	#	1006	1081	1041	958	1050	1021	Data are expressed in terms of posts at December (for 2007/8 to 20011/12), August 2013 (for 2012/13) or March (for 2013/14). This is the number of distinct people. Where a person holds more than one grant they have been counted only once.
5	Research Leaders in Sponsored Institutes	#	349	346	289	237	239	246	Data are expressed in terms of posts at 31st December (2008/09 to 2012/13) or 31st March (2013/14).
6	MRC-funded fellows	#	368	362	387	376	351	384	Data are expressed in terms of posts at December (for 2007/8 to 20011/12) or March (for 2012/13 & 2013/14). This figure includes Clinical Research Training Fellowships. This is the number of distinct people: where a person holds more than one grant, they have been counted only once.

Section 4.1 Knowledge Generation

Paper outputs[87]

No	Metric	Unit										
7	Number of Grants assessed for reporting		4,614 submitted returns through Researchfish.									
8	Refereed Publications (publication year)	#	2006	2007	2008	2009	2010	2011	2012	2013	Total	The data gathering period for Researchfish in 2013 was October and November, therefore the figures for 2013 are partial. As such a projection has been estimated.
8a	Reviews	#	313	406	538	617	591	653	677	577	4,372	
8b	Articles	#	2,887	3,734	4,280	4,775	5,380	5,545	5,863	4,438	36,902	
8c	Total	#	3,200	4,140	4,818	5,392	5,971	6,198	6,540	5,015	41,274 (partial) 43,623 (estimate for full year)	
9	Co-authorship of refereed publications - International	#	20,050 (49%)					49% of MRC funded peer reviewed papers published between 2006 and 2013 which have at least one author from outside the UK.				
10	Co-authorship of refereed publications - Industry	#	2,618 (6%)					6% of all MRC funded peer reviewed papers published between 2006 and 2013 have at least one author from the private sector.				

No	Metric	
11	Collaboration	Number of collaborations reported with at least one partner in the relevant sector.

Sector	2013	%
Academic	8599	58%
Non-Profit	767	5%
Learned Society	40	0%
Multiple	163	1%
Private	1106	7%
Public	2213	15%
Hospital	1186	8%
Unknown	833	6%
Total	**14907**	**100%**

No	Metric	Unit	No Year	2006	2007	2008	2009	2010	2011	2012	2013	Total
12	Products, Interventions and Clinical Trials[88]	#	0	33	24	54	119	158	131	124	166 (partial) 181 (estimated)	809 (partial) 824 (estimated)

Type of Products & Interventions	2013	%
Diagnostic Tool - Imaging	52	6%
Diagnostic Tool - Non-Imaging	147	18%
Health and Social Care Services	9	1%
Management of Diseases and Conditions	39	5%
Preventative Intervention - Behavioural risk modification	33	4%
Preventative Intervention - Nutrition and Chemoprevention	8	1%
Preventative Intervention - Physical/Biological risk modification	4	0%
Products with applications outside of medicine	4	0%
Support Tool - For Fundamental Research	78	10%
Support Tool - For Medical Intervention	43	5%
Therapeutic Intervention - Cellular and gene therapies	41	5%
Therapeutic Intervention - Complementary	3	0%
Therapeutic Intervention - Drug	213	26%
Therapeutic Intervention - Medical Devices	18	2%
Therapeutic Intervention - Physical	9	1%
Therapeutic Intervention - Psychological/Behavioural	52	6%
Therapeutic Intervention - Radiotherapy	6	1%
Therapeutic Intervention - Surgery	15	2%
Therapeutic Intervention - Vaccines	35	4%
Total	**809**	**100%**

No	Metric	Unit	Pre-2006/ Unknown	2006	2007	2008	2009	2010	2011	2012	2013	Total
13	Research Materials[89]	#	1505	415	257	380	578	581	535	546	194 (partial) 212 (estimated)	4991 (partial) 5009 (estimated)

Type of Research Material[90]	2013	%
Antibody	154	3%
Cell line	251	5%
Data analysis technique	612	12%
Database/Collection of Data/Biological Samples	1043	21%
Improvements to research infrastructure	349	7%
Model of mechanisms or symptoms - human	134	3%
Model of mechanisms or symptoms - in vitro	105	2%
Model of mechanisms or symptoms - mammalian in vivo	1159	23%
Model of mechanisms or symptoms - non-mammalian in vivo	123	3%
Physiological assessment or outcome measure	177	4%
Technology assay or reagent	883	18%
Other/Unknown	1	0%
Total	**4991**	**100%**

No	Metric	Unit	No Year	2006	2007	2008	2009	2010	2011	2012	2013	Total
14	Awards and Recognition[91]	#	11	705	854	1285	1843	2603	2687	2548	1984 (partial) 2164 (estimated)	14520 (partial) 16361 (estimated)

Type of Award & Recognition	2013	%
Appointed to the editorial board of, or advisor to, a journal or book series	1493	10%
Attracted visiting staff or internships to laboratory	405	3%
Awarded membership, or a fellowship, of a learned society	1206	8%
Medal	360	2%
NIHR Senior Investigator/Clinical Excellence Award	139	1%
Order of Chivalry (e.g.OBE)	62	0%
Other award	6	0%
Personally invited as speaker at a conference	6904	48%
Poster/abstract prize	706	5%
Prestigious/honorary/advisory position to an external body	1666	11%
Research prize	1573	11%
Total	**14520**	**100%**

Section 4.2 Human Capital (stock)

No	Metric		
15	Number of PhD Students Supported		See narrative in section 4.2 of main body of report. The total number of live MRC studentships as at March 2014 was ~1,800. These are broken down below by funding mechanism, showing the number and proportion of each.

Funding mechanism	#	%
Doctoral Training Partnership	818	46.5
MRC Intramural Students	393	22.3
Capacity Building Students	92	5.2
Clinical Research Training Fellowship	138	7.8
MRC Centre Studentships	220	12.5
Industrial Case Studentships	99	5.6
Total	**1,760[92]**	

16	Number of Masters Students Supported		See narrative in section 4.2 of main body of report.

No	Metric									
17	Finishing Rates		Registration years 2004 to 2006 - Data from JeS Submission survey 2011, this therefore only includes students who completed the survey. Registration years 2007 & 2008 - Data from JeS submission survey 2013, however a significant proportion of students remain on the system without a definitive submission/award date, and are therefore classified as "unknown". As a result, percentages displayed here for unknown (*) are of all students on JeS for that registration year, whereas other percentages displayed are based on those with award dates available.							
18	Student funding/training schemes	Unit	2008/09	2009/10	2010/11	2011/12	2012/13	2013/14	Industry case studentships – funding by academic year.	
		£m	3.2	2.5	3.1	3.4	3.5	3.0		

Registration year	2004		2005		2006		2007		2008	
	#	%	#	%	#	%	#	%	#	%
Within 5 years	326	91.6	394	90.8	286	89.4	94	77.7	225	92.2
Greater than 5 years	9	2.5%	4	0.9	0	0.0	18	14.9	3	1.2
Delayed submission	6	1.7	9	2.1	25	7.8	0	0.0	0	0.0
Student will not submit	15	4.2	27	6.2	9	2.8	9	7.4	16	6.6
Total with Award Data	**356**		**434**		**320**		**294**		**484**	

Section 4.3 Knowledge Transfer and Exchange

No	Metric		
19	KE Spend		See narrative in section 4.3.
20	KE Programmes		Numbers of awards and total commitment values for some of the MRC translational schemes.

	2008/09		2009/10		2010/11		2011/12		2012/13		2013/14	
Scheme	#	£m	#	£m	#	£m	#	£m	#	£m	#	£m
Methodology Research Programme	18	6.1	23	7.4	9	3.5	14	5.0	11	3.5	8	3.9
Regenerative Medicine Research Committee[93]	12	6.4	13	7.3	10	7.6	7	4.5	6	3.9	4	3.2
Developmental Pathway Funding Scheme (DPFS)[94]	15	6.4	17	8.7	19	12.0	18	11.9	10	6.4	-	-
Developmental Clinical Studies (DCS)	-	-	3	5.3	10	13.7	20	22.3	-	-	-	-
Biomedical Catalyst Fund[95]	-	-	-	-	-	-	-	-	41	30.7	51	40.2
Stratified Medicine Initiative	-	-	-	-	5	12.0	1	6.0	4	15.9	2	9.0

Section 4.4a Intellectual Property Activity (MRCT managed)

No	Metric	Unit	2008/09	2009/10	2010/11	2011/12	2012/13	2013/14	TOTAL	
21a	Patents applications (MRCT managed)	#	20	25	12	12	20	11	100	This data is collected through MRCT and therefore only represents MRC's intramural programmes. Income from IP includes licence income and receipts from sales of shares in MRC companies.
22a	Patents granted (MRCT managed)	#	24	29	32	27	38	32	182	
23b	Spin-outs/new businesses created (MRCT managed)	#	0	0	2	0	0	0	2	
24	Income from IP activity (MRCT managed)	£m	64.19	66.17	61.69	78.98	91.72	85.4 (91.1)[96]	448.15 (453.85)	

Section 4.4b Intellectual Property Activity (Researchfish data)

No	Metric	Unit	unknown	2006	2007	2008	2009	2010	2011	2012	2013	Total
21b	Numbers of patents (Researchfish data)											
	Not licensed	#	30	11	34	74	111	116	60	54	39	529
	Licensed	#	40	12	26	17	40	35	19	27	11	227
	Commercial in confidence	#	7	4	9	6	13	23	16	13	2	93
	Total	#	70	27	69	97	164	174	95	94	52 (partial) 56 (estimated)	849 (partial) 853 (estimated)
23b	Spin-outs/new businesses created (Researchfish data)	Unit	Pre 2006	2006	2007	2008	2009	2010	2011	2012	2013	Total
		#	22	6	3	11	7	8	9	9	3	77

MRC funding has contributed to the set up or growth of 77 companies, 55 of which have been formed since 2006. It is estimated that these companies represent at least 100 new highly skilled jobs in the UK.

Data was collected based on company formation date following award start date, the de-duplicated based on company name (not ID#) for a unique count. Note that data for pre-2006 companies has been fully cleaned to remove business connections with constitute collaborations, not spin-outs/new businesses[97]. Data consolidated and corrected for duplications as of Researchfish SQL database extraction 17/11/14.

Section 5.1 Human Capital (flow)

No | **Metric**

25 Destination of leavers

The following data show the first destination of PhD students qualifying or completing their courses between 1 August 2008 and 31 July 2012.

Please note that this is an incomplete return and does not cover the total number of students funded by the MRC.

Taken from DLHE (Destination of Leavers from Higher Education) data 2013 which collects data on students who completed their courses between 1st of August 2012 and 31st of July 2013. The DLHE 2014 (i.e. data on students completing in 2013/14) is not yet available and will therefore be included in next year's Economic Impact Report (2014/15).

Category	2007/08	2008/09	2009/10	2010/11	2011/12	2012/13
Engaged in Study	12	19	17	9	22	25
Government & Public Sector - not research related	9	19	26	14	0	33
Government & Public Sector - research related	6	5	6	4	34	5
Higher Education - academic	3	9	7	15	6	11
Higher Education - mainly research	70	100	126	125	133	154
Higher Education - other	1	4	9	4	2	3
Industry & Commerce - research related	3	3	2	4	5	4
Industry & Commerce - not research related	11	23	16	27	22	33
Not employed	8	23	21	25	20	21
Not known or not reported	1	12	9	11	31	15
Other Employment	0	1	1	2	0	0
R & D Sector Unknown	25	27	49	39	43	39
School (Education other)	1	0	0	3	0	3
School Teaching or Teacher Training	1	1	2	1	1	0
Self Employed, Voluntary and Unpaid work	2	1	1	2	4	2
Total	**153**	**247**	**292**	**285**	**323**	**335**

26 Placements in user organisations

Unit	2008/09	2009/10	2010/11	2011/12	2012/13	2013/14
#	46	34	34	33	35	30

Numbers of Industrial CASE awards over the last four years, these are awarded in partnership with industry or policy making bodies. In 2013/14 MRC awarded 10 (out of 30) industrial CASE studentships to SMEs. The industrial partners for all 30 awards in 2013/14 are listed below:

Company	SME	Awarded
AstraZeneca	N	2
Bio Products Laboratory Ltd.	N	1
BioMoti Ltd.	Y	1
Boston Scientific	N	1
Critical Pharmaceuticals Ltd.	Y	1
Defence Science and Technology Laboratory (DSTL)	N	1
Domainex Ltd.	Y	1
Eisai Ltd.	N	3
Eli Lilly and Company Ltd	N	2
Essen BioScience	Y	1
GlaxoSmithKline	N	4
Immunocore Ltd.	Y	1
MedImmune	N	1
Medivir	Y	1
Nikon UK (Instrument Division)	N	1
Novartis Pharmaceuticals UK Ltd.	N	3
Optos PLC	N	1
Oxford Optronix	Y	1
Pharmidex Pharmaceutical Services Ltd.	Y	1
Redx Oncology Ltd.	Y	1
Touchlight Genetics Ltd.	Y	1
Total		**30**

Section 5.2 Public Policy

No	Metric	Unit	No Year	2006	2007	2008	2009	2010	2011	2012	2013	Total
27	Instances of Influence on Policy and Practice[98]	#	4	282	262	440	541	575	658	617	536 (partial) 585 (estimate)	3915 (partial) 3964 (estimate)
28	Instances of influence	Influences on policy setting processes, 3,033 reports between 2006 and 2013.										
29	Value/changes induced	Citations in key policy documents, 880 reports between 2006 and 2013. Please note that 2 instances of influence on policy were reported with a category of 'other'.										

Section 5.3 Public Engagement

No	Metric	
30	PE Activities	Below is a summary of the data by type of dissemination activity reported between 2006 and 2013. To reduce the burden on researchers they are advised to report just one of any type of activity within any given year therefore these figures are an underestimation of actual activity.

Type	Number	%
A formal working group, expert panel or similar	1992	10%
A magazine, newsletter or online publication	2344	12%
A press release, press conference or response to a media enquiry.	1854	9%
A talk or presentation	7371	37%
Participation in an activity, workshop or similar	3328	17%
Participation in an open day or visit at my research institution	1371	7%
Scientific meeting (conference/symposium etc.)*	1748[99]	9%
Total	**20,008**	**100%**

Endnotes

1. The MRC Economic Impact Reports can be found by using the search option or tag link "economic impact" at: http://www.mrc.ac.uk/news-events/publications/
2. www.mrc.ac.uk/Newspublications/Publications/DeliveryPlan/index.htm
3. www.mrc.ac.uk/news-events/publications/delivery-plan-reporting-framework-2013-14/
4. www.mrc.ac.uk/Achievementsimpact/Outputsoutcomes/index.htm
5. www.mrc.ac.uk/news-events/publications/strategic-plan-2009-14/
6. www.centenary.mrc.ac.uk/timeline
7. From the International Comparative Performance of the UK Research Base – 2013, an Elsevier prepared, Department of Business, Innovation and Skills published report on UK research.
8. Please note that in 2013 the Researchfish 'Products or Interventions' section was renamed 'Products, Interventions and Clinical Trials', and therefore represents a slightly different range of research outputs compared to previous reports.
9. Data from MRCT
10. Lancaster *et al.* (2013) Cerebral organoids model human brain development and microcephaly. *Nature* **501**(7467): p.373-9
11. Beck *et al.* (2014) Validation of next-generation sequencing technologies in genetic diagnosis of dementia. *Neurobiology of Aging* **35**(1): p.261-265
12. www.arrowtrial.org/
13. Clinical Research Training Fellows support clinicians undertake a higher degree (PhD or MD).
14. http://www.mrc.ac.uk/Fundingopportunities/Fellowships/index.htm
15. More information on Researchfish can be found at: www.researchfish.com and http://www.mrc.ac.uk/funding/guidance-for-mrc-award-holders/researchfish/
16. Value correct as at October 2014. An up-to-date list of organisations using Researchfish is at: https://www.researchfish.com/ourmembers
17. http://www.mrc.ac.uk/news-events/publications/annual-report-and-accounts-201314/
18. http://www.mrc.ac.uk/news-events/publications/outputs-outcomes-and-impact-of-mrc-research-2013-14/
19. In particular, in a slight modification to previous data analyses, outputs dated before award start dates are not included in the figures reported.
20. The normalised citation impact scores were taken at the end of 2013 for MRC publications published between 2006 and 2012 (as reported in Researchfish).
21. Normalised citation impact data and analysis: Evidence, Thomson Reuters UK
22. http://europepmc.org/abstract/MED/23348417
23. http://europepmc.org/articles/PMC3631573
24. Paloneva J *et al.* (2002) Mutations in two genes encoding different subunits of a receptor signalling complex result in an identical disease phenotype. *Am J Hum Genet.* **71**: 656–62.
25. Guerreiro RJ *et al.* (2013) Using exome sequencing to reveal mutations in TREM2 presenting as a frontotemporal dementia-like syndrome without bone involvement. *JAMA Neurol* **70**(1): 78-84.
26. Butler AW *et al.* (2009) Meta-analysis of linkage studies for Alzheimer's disease — a web resource. *Neurobiol Aging.***30**: 1037–47.
27. http://europepmc.org/articles/PMC3596060
28. Glover M *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.
29. Independent UK Panel on Breast Cancer Screening (2012) The benefits and harms of breast cancer screening: an independent review. The Lancet 380: 1778-1786.
30. http://www.mrc.ac.uk/news-events/publications/outputs-outcomes-and-impact-of-mrc-research-2013-14/
31. http://www.mrc.ac.uk/research/achievements/browse-our-achievements/
32. Growing the best and brightest – the drivers of research excellence. A report for the Department of Business, Innovation and Skills, (March 2014).
33. https://play.google.com/store/apps/details?id=com.mymealmate&hl=en_GB
34. Carter MC *et al.* (2013) Adherence to a Smartphone Application for Weight Loss Compared to Website and Paper Diary: Pilot Randomized Controlled Trial. *J Med Internet Res* **15**(4): e32.
35. As at September 2014, according to the Google Store.
36. García-Álvarez L *et al.* (2011) Meticillin-resistant Staphylococcus aureus with a novel mecA homologue in human and bovine populations in the UK and Denmark: a descriptive study. *The Lancet Infectious Diseases*, **11**(8): 595-603.
37. Pichon B *et al.* (2012) Development of a real-time quadruplex PCR assay for simultaneous detection of nuc, Panton–Valentine leucocidin (PVL), mecA and homologue $mecA_{LGA251}$ *J. Antimicrob. Chemother* **67**(10): 2338-2341.
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40. Onoufriadis A *et al.* (2013) Splice-site mutations in the axonemal outer dynein arm docking complex gene CCDC114 cause primary ciliary dyskinesia. *Am J Hum Genet.* **92**(1): 88-98.
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42. Cohen JA *et al.* (2012) Alemtuzumab versus interferon beta 1a as first-line treatment for patients with relapsing-remitting multiple sclerosis: a randomised controlled phase 3 trial. *The Lancet* **380**(9856): 1819-1828.
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47. Patent number WO2013088149
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49. Lancaster MA *et al.* (2013) Cerebral organoids model human brain development and microcephaly. *Nature* **501**(7467): 373–379.
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51. Moon RW *et al.* (2013) Adaptation of the genetically tractable malaria pathogen Plasmodium knowlesi to continuous culture in human erythrocytes. *PNAS* **110**(2): 531-536.

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53. E.g. Excellence in Research for Australia: http://www.arc.gov.au/era/
54. Simmons RK *et al.* (2012) Screening for type 2 diabetes and population mortality over 10 years (ADDITION-Cambridge): a cluster-randomised controlled trial. *The Lancet.* **380**(9855): 1741-1748.
55. http://statistics.open.ac.uk/sccs/index.htm
56. http://www.rss.org.uk/site/cms/contentviewarticle.asp?article=1074
57. Data collected from the Je-S student data portal (CRTFs collected by MRC in house system), information on students at MRC centres has been collected directly from the centres via email correspondence.
58. Numbers of students for the advanced course masters are notional numbers for three intakes across three years. As such, they do not take into account any leveraging by the RO.
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68. Note that two were reported without a year.
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81. www.bbc.co.uk/news/uk-england-birmingham-24635924
82. www.sciencemuseum.org.uk/visitmuseum/plan_your_visit/exhibitions/painless.aspx
83. Cox JJ *et al.* (2006) An SCN9A channelopathy causes congenital inability to experience pain. *Nature* **444**: 894-898.
84. Other income includes sales of laboratory and library services, as well as proceeds from the sales of radioisotopes etc.
85. Under "commercial activities" in the Annual Report. Income from IP includes licence income and receipts from sales of shares in MRC companies.
86. Please note that although the Annual Report financial statement section 13 gives a higher value (£69.9m), £7.0m is intramural (see section 2). Therefore this metric displays the extramural value (£62.9m) only.
87. From Thompson-Reuters data, via Researchfish. Values for metrics 7-10 are based upon paper outputs labelled as 'review' or 'article' under data type heading, extracted on 6th of October 2014.
88. Data obtained separately from Researchfish SQL database extraction on 11/11/14. Therefore these figures represent a revised dataset compared to other reports (eg Researchfish sample report, MRC Outputs Report, where data correct as of 27/04/14).
89. Data obtained separately from Researchfish SQL database extraction on 17/11/14. Therefore these figures represent a revised dataset compared to other reports (eg Researchfish sample report, MRC Outputs Report, where data correct as of 27/04/14).
90. Please note that the two new subcategories of research materials have been combined for this data. Therefore "data analysis technique" includes "data handling & control" and "computer model/algorithm".
91. Data obtained separately from Researchfish SQL database extraction on 11/11/14. Therefore these figures represent a revised dataset compared to other reports (e.g. Researchfish sample report, MRC Outputs Report, where data correct as of 27/04/14).
92. This denotes an increase of 178 submissions on the same SDP database since the production of the MRC's Annual Report (n=1,444, data collected in April 2014). The annual report dataset was also studentships only, and therefore excluded Clinical Research Training Fellowships (n=138). Data correct as of 17/09/14.
93. Regenerative Medicine Research Committee was previously the Translational Stem Cell Research Committee (TSCRC). Drawing on the experience and expertise of the MRC's TSCRC, the MRC has established the Regenerative Medicine Research Committee, to provide support for high quality proposals aiming to develop regenerative medicine therapies to improve human health.
94. In early 2012/13 the DPFS and DCS schemes were merged into one scheme. The revised DPFS provided one round of funding in May 2012.
95. Biomedical Catalyst (BMC) commitment includes awards made through the DPFS Panel and Major Awards Committee from Sept 2012 onwards, academic costs on Early and Late stage business-led BMC awards and awards made under the Confidence In Concept scheme. 2013/14 data includes both BCF & DPFS funding.
96. MRCT reports a total of £91.1m from all invoices raised in the 2013/14 financial year. The figure of £85.4m seen in the MRC Annual Report 2013/14 includes all invoices and accounting entries.
97. This resulted in a reduction in comparison to previous MRC reports, particularly from earlier (pre-2006) data collection periods.
98. Data obtained separately from Researchfish SQL database extraction on 11/11/14. Therefore these figures represent a revised dataset compared to other reports (e.g. Researchfish Sample Report, MRC Outputs Report, where data correct as of 27/04/14).
99. Please note that this 'type' of public engagement has only been included in Researchfish data gathering collection since 2011, as such this number will be under representative when compared to the other 'types' in the table above.

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