Medical Research Council

Exploring the breadth of impacts arising from MRC-funded research

An analysis of MRC's contributions to non-academic impacts submitted to REF2021

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Executive Summary

This report highlights a selection of research impacts submitted by UK higher education institutions (HEIs) to the 2021 REF assessment. Impact case studies (ICS) were identified that had a connection to MRC investments. As MRC institutes do not report impacts from their research to the REF assessment, impacts from this part of MRC's portfolio do not feature in the report.

The Research Excellence Framework (REF) is a national assessment of the research taking place across UK HEIs. REF takes place approximately every six to seven years. The REF is a process of expert review, carried out by expert panels for each of the 34 subject-based units of assessment (UOAs), under the guidance of four main panels (Panel A to D). Expert panels are made up of senior academics, international members, and research users.

As part of REF2021, UK HEIs submitted 6781 impact case studies intended to demonstrate the impact of their research on wider society and the economy. Automated and manual searches of the database were used to obtain 569 REF2021 ICS associated with MRC funding (hereafter referred to as MRC-ICS). These records were screened to focus on 60 exemplar MRC-ICS which are detailed in this report.

In this report, we provide 35 short summaries (based on 60 exemplar MRC-ICS selected from the 569 MRC-ICS) that demonstrate the breadth of impacts arising from MRC funded research, highlighting where MRC funding has made a significant contribution to realising the impacts. These have been grouped where common themes emerge. We have also highlighted, where possible, instances where these are relevant to the themes of MRC's new Strategic Delivery Plan.

We reveal clear evidence that MRC funded infrastructure and underpinning research is associated with high quality impact case studies. We show that MRC funding held by Universities across the UK contributes to diverse impacts submitted to a broad range of UoAs, and that these impacts are almost always the result of collaboration between multiple universities.

All 569 case studies from REF2021 identified as MRC-ICS have been added to our new searchable case study database (launching soon), which includes outcomes and impacts from the breadth of the historical MRC funding portfolio including ICS from REF 2014 and from MRC institutes. This resource is used to quickly locate published evidence of impacts arising from MRC research.

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Introduction

The selection of impact case studies was chosen from the REF2021 submission to best highlight the contribution of MRC funded research towards non-academic impact. The case studies were adapted from the REF2021 ICS online database, the introductory text was summarised to highlight key impacts and MRC funded contributions were identified. The following sections provide examples of MRC associated ICS (MRC-ISC) and quantitative analyses of these 569 case studies:

- Distribution of MRC linked impact across the main panels and UoAs
- Impact Quality Profiles for ICS associated with MRC
- Cross-discipline impacts
- Distribution of HEI's
- Identification of collaborators and networks involved in the impact
- Impacts in specific disease areas
- Breadth of impacts occurring from MRC research
- Analysis of the contribution of specific grants, programmes, long term investments and Units/Centres towards the research and impact claimed (highlighting impacts arising from historical investment in 22/25 Strategic Delivery Plan focus areas).

Distribution of MRC linked impact across the main panels and UoAs

REF is reviewed by subject experts in 34 different Units of Assessment (UoA), overseen by experts in four Main Panels. Around 9% of the total ICS submitted had readily identifiable references to MRC funding or MRC funded research. These MRC-ICS were distributed across all four main panels, Figure 1A, and 76% of the UoAs, Figure 1B, highlighting the diversity of impacts arising from MRC funded research. Main Panel A covers biomedical research (Clinical Medicine: UoA 1, Public Health, Health Services and Primary Care: UoA 2, Allied Health Professions, Dentistry, Nursing and Pharmacy: UoA 3, Psychology, Psychiatry, and Neuroscience: UoA 4, Biological Sciences: UoA 5, and Agriculture, Food, and Veterinary Sciences: UoA 6).

Impact Quality Profiles for ICS associated with MRC

The REF scoring system allocated 1 through 4* for each impact case study depending on the reach and significance of the described impact, (see annex for definitions of "reach" and "significance"). The individual ICS scores for a HEI submission were combined for each UoA (weighted by number of HEI staff within the research area) to form a HEI impact quality profile. Therefore, although individual ICS scores were not published, an overall indication of quality could be deduced using the UoA HEI impact quality score. In Main panel A, about 33 % the total ICS submitted were associated with the MRC, see Figure 1C. A higher proportion (42%) of known "Outstanding" (4*) ICS in Main Panel A were associated with MRC funding, as shown in Figure 1D, indicating a link between high quality REF scores and MRC funding.

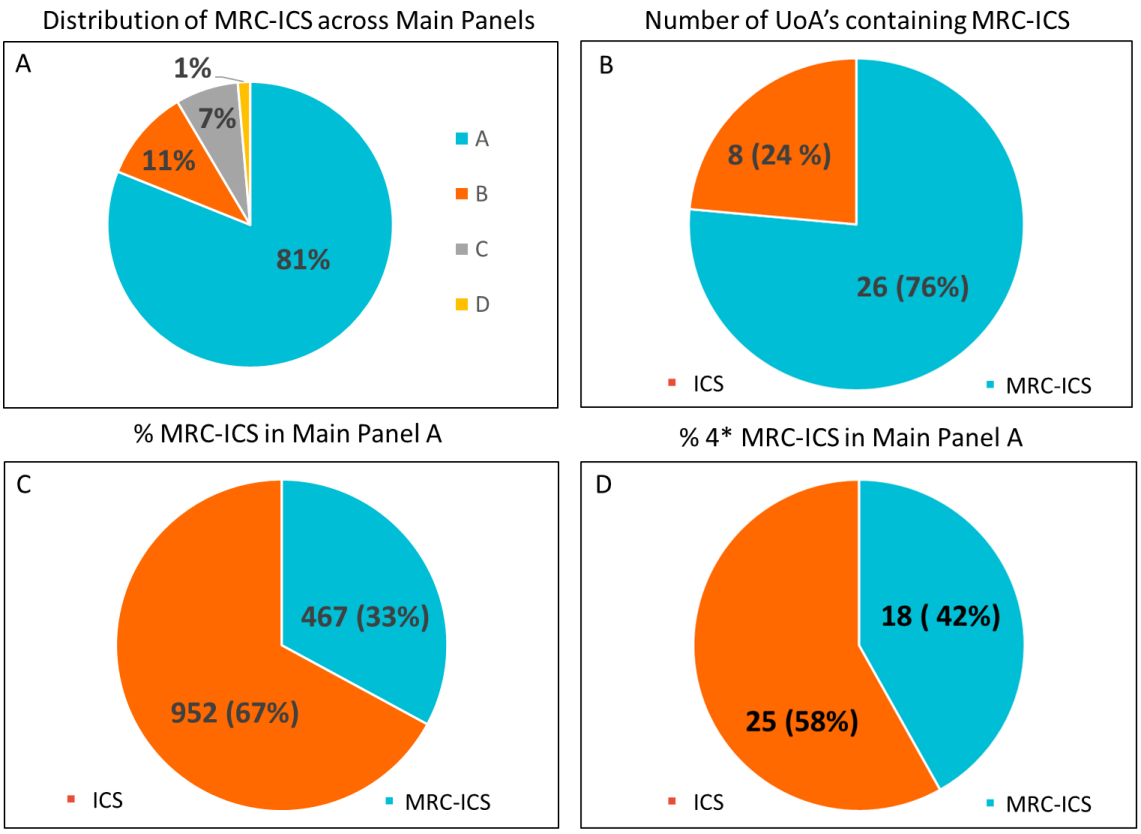


***Figure 1**: (A) Distribution of MRC-ICS across the Main panels and (B) Number of UoAs containing MRC-ICS. (C) Proportion of ICS in Main Panel A associated with MRC funding (MRC-ICS) and (D) proportion of known outstanding (4*) MRC-ICS in Main Panel A.*

Cross-discipline impacts

REF2021 case studies provide valuable insights into how MRC funded research has contributed to disciplines of research outside the UoAs where we would expect to see mention of MRC funded research. Our analysis identified case studies where MRC funded research has had an impact in these cross-disciplinary areas of study. The eight exemplar case studies below showcase the breadth of impacts arising from MRC funded research.

UoA11: Computer Science and Informatics

1. Development of effective communication tools has improved mental healthcare

Treatment outcomes for mental illness depend on the quality of doctor-patient communication. Researchers at Queen Mary University of London have developed a novel communication training programme for clinicians for psychosis treatment (TEMPO) which is used by 12 NHS Trusts across the UK and 43 international institutions. Since 2016, the team's communication support tools (DIALOG+) are now part of the NHS Outcomes Programme and recommended for use with all early intervention teams in England (>18,600 patients) and all patients receiving mental health services in London (>100,000 patients). When DIALOG+ is repeatedly used over six months, it has been shown to improve patients' quality of life and reduce treatment costs.

This research is underpinned by MRC funding in 2006, which showed how improved communication between patient and psychiatrist can influence treatment adherence in schizophrenia. The team subsequently built upon these findings to develop TEMPO training and the DIALOG+ mobile app.

UoA13: Architecture, Built Environment and Planning

2. Creating Step Changes in Cycling Policy and Infrastructure Planning across the UK

Researchers at the University of Westminster have identified evidence-based measures to enable greater uptake of cycling in the UK. The research has empowered city planners to influence changes to Transport for London and national infrastructure design guidance. The team have also provided the evidence base for the wider expansion of, and investment in, the mini-Holland scheme in London, a £90 million scheme which has demonstrably increased cycling uptake. A study investigating the early impact of the programme discovered that people in high-dose areas were 24% more likely to have done some cycling in the previous week than those where such improvements have not yet been made.

The health impact of this research programme was evidenced by research from collaborators at the MRC Epidemiology Unit, University of Cambridge. An MRC grant awarded in 2013 led to the development of the Propensity to Cycle Tool (PCT), an open-source online system for sustainable transport planning. Funding in 2017 for two modelling projects at the MRC Epidemiology Unit (METAHIT and TIGTHAT) led to the development of a range of tools to estimate the health effects (such as changes in physical activity, road traffic injury risk, and exposure to air pollution) of transport policies. These tools subsequently informed the development and integration of health impact pathways to evidence the expansion of and investment in cycling in the UK.

UoA14: Geography and Environmental Studies

3. Protecting human health from infectious diseases in low-resource settings

Research from the University of Brighton has helped the National Institute of Cholera and Enteric Diseases to prioritise effective public health interventions in urban slum districts in India (home to >100,000 people) and the Kenyan Medical Research Institute to protect 1,170 rural inhabitants. The team have provided low-cost bacteriophage-based tools to strengthen WHO and UNICEF sanitation protocols. The work has reduced human health risk from diseases including cholera, Ebola, typhoid, and childhood diarrhoea in regions of Africa, Asia, and South America.

This research was supported by MRC in 2017 in a project which quantified microbial contamination pathways between livestock and drinking-water. The team developed an affordable test using bacteriophages to test for micro-organisms that are specifically found in livestock faeces. The team used the test to investigate the importance of different sources of faecal contamination of drinking-water and manage the safety of rural drinking-water sources like wells and rainwater.

UoA12: Engineering

4. Development of applied cell engineering in knee joints: from the bench to a NICE-approved treatment for early osteoarthritis

A team of researchers including clinicians, engineers, and scientists at the University of Keele have developed a cell therapy for knee joints to treat defects in cartilage. The development of this applied cell engineering treatment has had impact on public policy, health and quality of life, and the economy. If left untreated, these defects can progress to osteoarthritis. The therapy, known as autologous chondrocyte implantation (ACI), received NICE approval in 2017.

MRC funding has supported this work since 2004 through the ACTIVE trial which provided the evidence base that led to NICE approval in 2017. Health-economic modelling showed ACI to be cost-effective, with an estimate of £8,000 per quality adjusted life year, as compared to alternative treatments. MRC funding in 2013 led the team to develop a prognostic tool to aid treatment decisions for both the surgeon and patient, helping identify those patients who will benefit most from ACI. In 2019, the team began investigating allogenic cell therapy, which would reduce cost and improve patient outcome as it would use an 'off the shelf' treatment using cells from different donors, while establishing GMP protocols for cartilage cells for this treatment.

5. Instantaneous Wave-free Ratio (iFR) for the Diagnosis of Coronary Heart Disease

Engineers and clinicians at Imperial College London have developed a diagnostic tool called Instantaneous wave-free ratio (iFR) to assess whether a narrowing in a coronary artery is limiting blood flow to heart muscles. It is used to stratify selection of patients for surgery, stenting or medical management. The approach has reduced procedural time and costs by 10%, compared to the leading alternative (Fractional Flow Reserve), while also improving patient comfort. iFR received FDA approval in 2014, has been licensed to Volcano-Philips and used in over 5,000 clinical cardiac catheter labs in more than 30 countries.

The underpinning research has been supported by MRC funding since 2010, where study of the blood pressure changes in grafted blood vessels provided insight into why some grafts last longer than others. Subsequent funding to the team in 2011 improved their understanding of aortic stenosis by using non-invasive measurements to aid the timing of aortic valve replacement before symptoms occurred.

UoA20: Social Work and Social Policy

6. Harnessing the draw of professional sports clubs to deliver improvements in health and wellbeing among at-risk groups

University of Glasgow researchers have developed and evaluated a weight management and healthy lifestyle programme delivered through professional football clubs, called Football Fans in Training (FFIT). FFIT is effective, cost-effective and reaches high-risk groups. Subsequent collaborations and agreements have resulted in over 10,000 men in 11 countries benefitting from healthy lifestyle programmes delivered in professional sports clubs. On average, participants have lost at least 3kg with subsequent health and wellbeing benefits including reductions in blood pressure, improvements in self-reported dietary intake, and self-esteem.

MRC funding contributed to this research in 2015 via the MRC/CSO Social and Public Health Sciences Unit at the University of Glasgow where the project provided evidence that the FFIT programme is acceptable to participants and Scottish Premier League coaches. This allowed the

team to evaluate the approach in a randomized controlled trial funded by NIHR in 2015 and subsequently launch the programme more widely.

7. HIV policy formulation and prevention: driving the decision for and implementation of publicly-funded pre-exposure prophylaxis in Scotland

University of Glasgow researchers have helped shape HIV prevention policy by supplying key data needed by Scottish Government policymakers to plan and fund pre-exposure prophylaxis (PrEP) for HIV prevention. In July 2017, Scotland became the first UK nation to fund PrEP on the NHS which led to a fivefold reduction in HIV incidence in groups with the highest risk of contracting HIV in the UK.

MRC funding has supported this research for over three decades since 1987, during which the Gay Men's Sexual Health survey (1996 to 2014) provided an estimate of HIV prevalence and undiagnosed infection among the gay and bisexual men who took part. MRC funding in 2013 supported the PROUD trial which showed that PrEP treatment is highly protective against HIV infection in a real-world setting. MRC funding in 2015 subsequently showed that understandings of PrEP effectiveness and concerns about maintaining regular adherence were barriers to potential PrEP uptake and use. This work allowed policymakers to optimise intervention delivery.

UoA32: Art and Design: History, Practice and Theory

8. The impact of user centred design on health, wealth and innovation culture

Cardiff Metropolitan University's User Centred Design (UCD) research has influenced strategies, working practices and product ranges in 1,023 international companies in sectors including engineering, medical devices, and banking. This influence, through a collaboration between Cardiff School of Art & Design with Cardiff University Medical School, led to the development of a trauma pack for rural Zambia capable of deployment by untrained, illiterate users. Zambia was chosen because trauma caused by road traffic incidents cost up to 5% of the country's GDP. The pack designed by the team was 80% cheaper than existing solutions with no drop in performance.

MRC supported the deployment of the Cardiff Trauma Pack in 2017 by funding an early phase study in Zambia to provide the evidence necessary for the larger-scale study mentioned in this impact. MRC has a rich history of funding research into understanding traffic incident trauma and treating traumatic brain injuries (TBIs) such as the MRC CRASH Trial funded in 2000. The study was carried out in in 52 hospitals in 14 countries and was the largest head injury trial ever conducted at the time. Subsequent international trials such as CRASH-3 funded in 2014 provided the first evidence of a drug which can prevent death from TBI by as much as 20% depending on severity of the injury.

Distribution of HEI's

The location of institutions submitting impacts associated with MRC funding is shown in Figure 2. The data demonstrates a spread of funding that is distributed across the length and breadth of the UK. There were 157 submitting HEI to REF2021 overall and MRC research is linked to impacts reported by 85 HEI's (55%) covering all four nations of the UK.

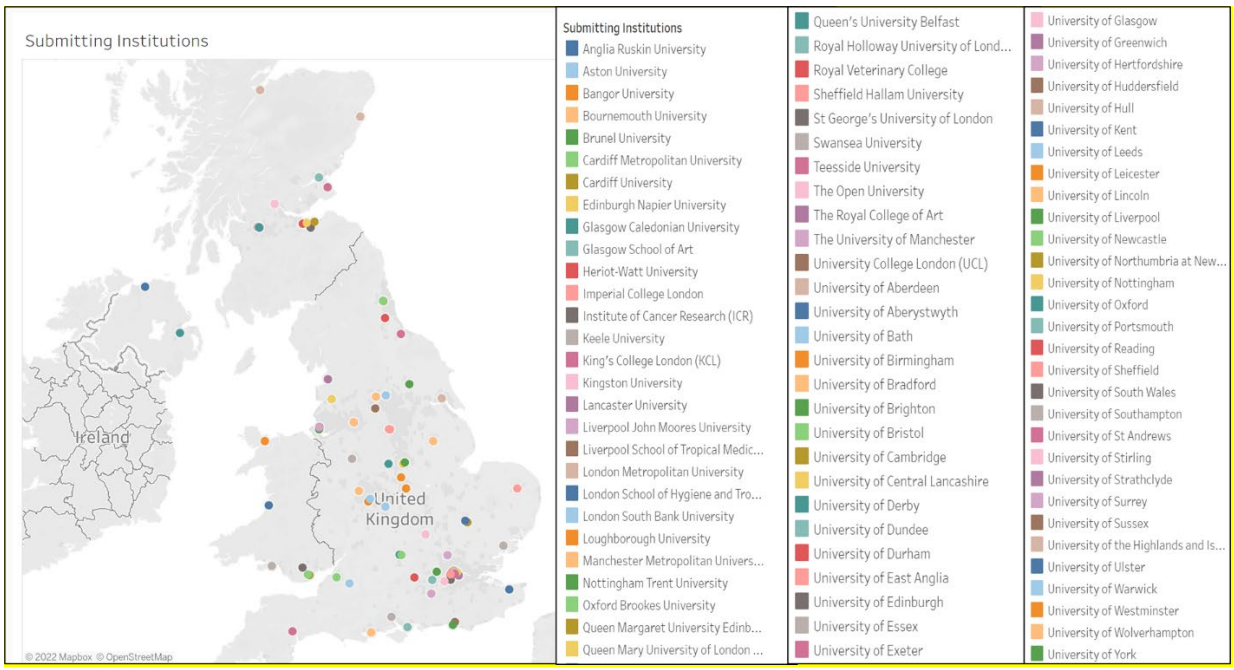


***Figure 2**: Map of submitting Institutions showing distribution of HEI submitting MRC-ICS across the UK*

Identification of collaborators and networks involved in the impact

We found MRC funding was instrumental in the collaborative process of creating impact as many grants were held between different institutions. The level of collaborations involved in each MRC-ICS can be seen in Figure 3, and although this is not always immediately evident in the text of the REF2021 ICS, the chart shows the complexity of interactions and networks needed to deliver these non-academic impacts. In this study, there were 484 research organisations, involved in 60 MRC-ICS with over 6000 co-author links and clusters of collaboration in Greater South East, Edinburgh, Newcastle and Cardiff as shown in Figure 3.

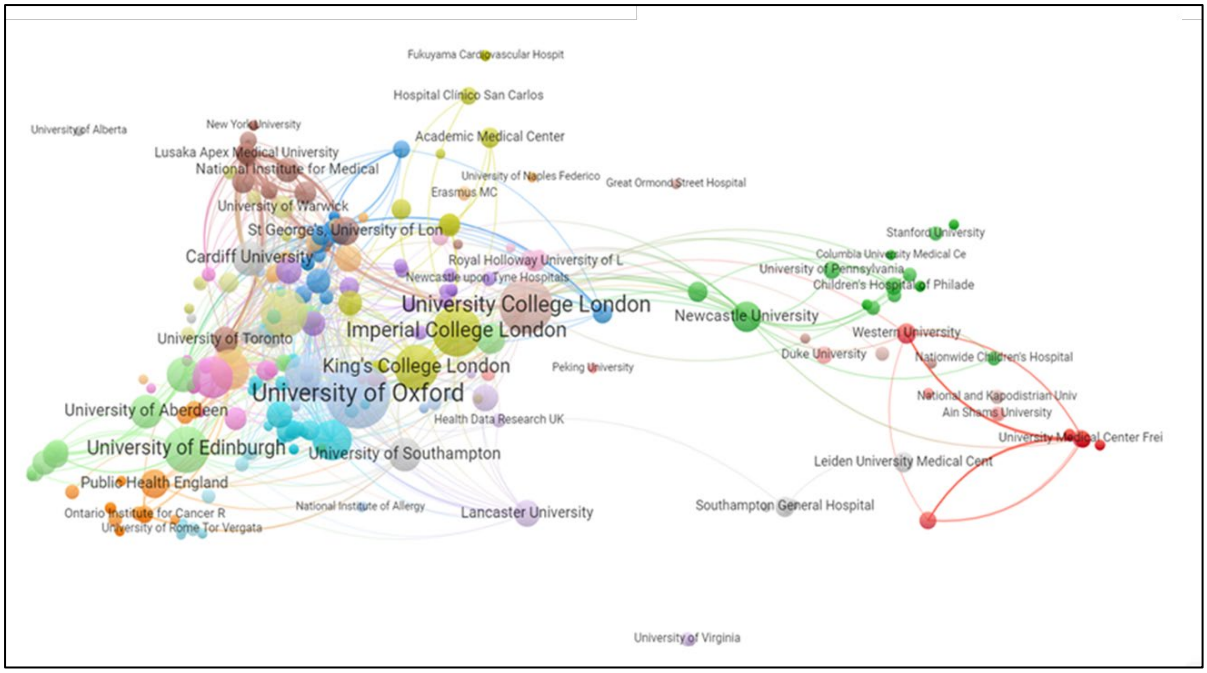


***Figure 3**: Vos viewer map showing the networks involved in the underpinning research from the 60 Exemplar MRC-ICS detailed in this report.*

Impacts in specific disease areas

The records (569 MRC-ICS) were tagged to identify specific disease areas (Figure 4) types of impact and MRC themes (Figure 5).

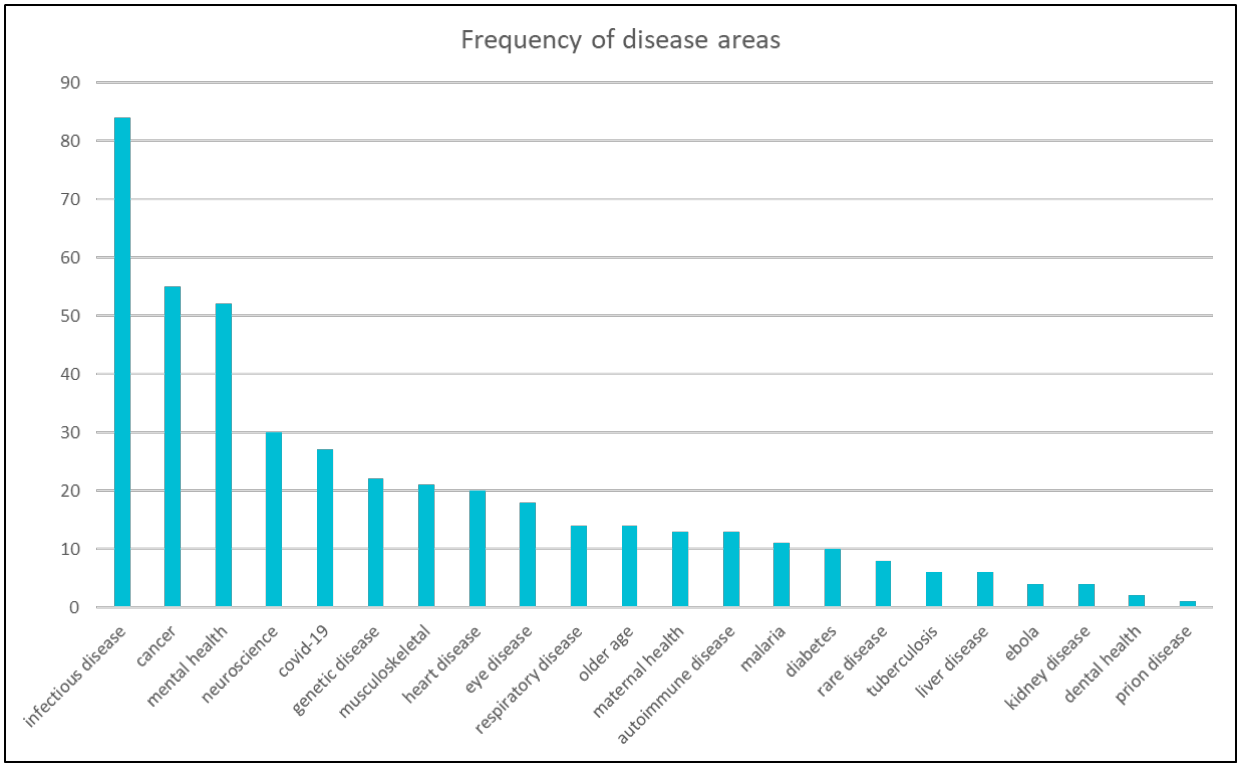


***Figure 4**: Disease Areas impacted by MRC research*

The most common disease area, infectious disease, covered all infectious diseases including COVID-19. There were also notable levels of impact reporting in areas such as cancer, mental

health, neuroscience, and heart disease. A selection of case studies in these disease areas is described below:

Infectious disease (including Covid-19)

Several MRC-ICS were relevant to the COVID-19 pandemic such as the RECOVERY trial and the development of the Oxford-AstraZeneca COVID-19 vaccine. The work on infectious diseases at MRC Units and Centres such as the MRC Unit The Gambia and the MRC Centre for Global Infectious Disease Analysis (GIDA) highlight research institutions that have delivered life-saving research impacts in tackling infectious disease.

9. Vaccination to reduce the global burden of invasive pneumococcal disease and pneumonia in communities

Clinical trials and modelling studies led by researchers at LSHTM, MRC Unit The Gambia (MRCG), and University of Edinburgh have established the safety and effectiveness of pneumococcal conjugate vaccines (PCVs). PCVs prevent pneumonia, one of the leading causes of death in children under 5 years of age. The research led to PCVs being licensed and introduced worldwide, with approximately 225 million children vaccinated by the end of 2019. The expansion of global PCV coverage from 19% in 2013 to 48% in 2020 resulted in 1,000,000 fewer child pneumonia deaths between 2013 and 2020 than would have occurred had 2013 mortality rates applied.

Research from MRCG has been vital for the introduction and expansion of PCVs. In 2005, the Gambian Pneumococcal Vaccine Trial Group led by MRCG researchers showed for the first time that in a rural African setting a PCV could substantially reduce hospital admissions and improve child survival. Research supported by MRC in 2007 provided background information around the incidence of pneumococcal pneumonia and helped identify the pathogens responsible for severe pneumonia in Gambian children. Following the introduction of a licensed PCV in The Gambia in 2009, funding in 2011 allowed MRCG researchers to monitor the impact and evaluate the efficacy of PCVs through clinical trials, providing the evidence needed for expanding global PCV coverage.

10. RECOVERY Trial: Global adoption of effective COVID-19 treatments to save lives

University of Oxford researchers initiated and led the earliest, fastest, and largest randomised clinical trial of treatments for COVID-19 in 2020: RECOVERY (Randomised Evaluation of COVID-19 Therapy). Results from three arms of RECOVERY announced in June 2020 showed dexamethasone reduces death rates among seriously unwell patients, whereas hydroxychloroquine and lopinavir-ritonavir are ineffective. These findings immediately transformed global clinical guidelines and practice. Dexamethasone usage rapidly increased worldwide on the basis of the RECOVERY results, leading to an estimated 650,000 lives saved by the end of 2020.

MRC funding supported the RECOVERY trial directly through the COVID-19 Rapid Response Initiative in 2020. Long-term MRC funding has underpinned development of the clinical trials methodologies that enabled the successes of the RECOVERY trial, with the establishment of the Methodology Research Programme in 2008 and the formation of the MRC Hubs for Trials Methodology Research Network in 2009. Statisticians funded through these programmes and others developed a large corpus of fundamental research into the design of early and late phase clinical trials, especially in adaptive trial designs, where the allocation of patients to treatments in later stages of the trial depends on the outcomes of earlier patients in the trial. These methods allowed quicker, more accurate decision-making, leading to faster development of treatments.

11. The Oxford-AstraZeneca COVID-19 vaccine

Researchers at the University of Oxford developed ChAdOx1 nCoV-19/AZD1222, an efficacious vaccine to protect against SARS-CoV-2 infection. Over 11,000 participants in the Oxford COVID-19 vaccine clinical trials from the UK, Brazil, and South Africa, and 20,000 in the US, received the vaccine; these individuals showed 70% reduced risk of COVID-19 and 100% reduction in risk of hospitalisation or death. The vaccine has contributed to saving 6.3 million lives around the world in the first year of rollout. The underlying vaccine platform, ChAdOx1, has been licensed to companies worldwide and resulted in significant investment and business growth in the UK.

While MRC funding also supported the making of Oxford AstraZeneca COVID-19 vaccine, the success of this vaccine is underpinned by decades of MRC funded research that supported the development of the ChAdOx1 adenovirus vector. Funding in 2010 for the pre-clinical development of the ChAdOx1 vector for a universal influenza vaccine was the first clinical use of any ChAdOx1-vectored vaccine. It showed safe and statistically significant boosting of memory T cells in young adults. The ChAdOx1 vector was then used in a phase I clinical trial against the Middle East Respiratory Syndrome (MERS) coronavirus in 2019 via MRC/BBSRC as part of the UK Vaccine Network and showed the safety and effectiveness of the ChAdOx1 platform. This underpinning research was vital for the rapid development and subsequent testing of the Oxford-AstraZeneca COVID-19 vaccine in 2020.

12. Optimising Treatment Regimes to prevent deaths caused by Cryptococcal Meningitis in Developing Countries

Cryptococcal Meningitis is a major cause of HIV-related deaths in developing countries and sub-Saharan Africa, accounting for 15-20% of all HIV-related deaths and more than 180,000 deaths per year. Previous treatment regimens involved costly intravenous medications and regular toxicity monitoring in hospitals. Researchers at the University of Oxford, Liverpool School of Tropical Medicine, London School of Hygiene and Tropical Medicine and St. Georges, University of London conducted clinical trials demonstrating the efficacy of an antifungal drug, flucytosine, limiting hospital admissions. These findings stimulated investment in a generic version of flucytosine to increase access for low-resource settings and also catalysed a $20 million investment from the global health organisation, UNITAID, enabling seven African countries to benefit. The WHO implemented the findings into their guidelines which reduced costs, improved access, and led to reductions in mortality in areas such as Tanzania, Nigeria, South Africa, Botswana, Malawi, Lesotho, and Uganda.

MRC funded research into cryptococcal meningitis has supported key clinical trials to determine the optimum combinations of fluconazole in 2003, flucytosine in 2012, and amphotericin B in 2016, providing the evidence needed for implementing these guidelines. The MRC Tropical Epidemiology Group, based at LSHTM, has received funding, since 1975, to study interventions against diseases of major public health importance in Africa and other parts of the developing world including cryptococcal meningitis.

13. Better protection against influenza through national childhood vaccination programmes

Reverse genetics technology invented by University of Oxford researchers has been used to generate influenza vaccine strains for the production of vaccines used worldwide. MedImmune (now part of AstraZeneca) used the patented technology to generate FluMist Quadrivalent, an intranasal live attenuated vaccine protective against four influenza virus strains, for use in children. In the UK, annual outbreaks of seasonal flu affect 5 to 20% of the population, with hospital costs for influenza-related admissions at approximately £100 million per season, with the 65+ year group associated with the highest costs and proportion of in-hospital deaths. By providing protection to approximately 20 million children and vulnerable members of the population by reducing community transmission, the vaccine programme has significantly reduced the incidence of influenza in primary care and influenza hospital admissions in children and has led to a reduction in the excess respiratory mortality.

MRC funding has been crucial for supporting the underpinning reverse genetics technology since 1998 and 1999 where the Oxford team devised this method for producing a wide range of influenza viruses within the laboratory. The method was powerful because it enabled any desired mutation to be introduced into any of the eight individual RNA segments that comprise the influenza RNA genome. This has facilitated the fast commercial production of flu vaccines every year in anticipation of the circulating strains of flu virus across the seasons.

14. Real-time pathogen genome sequencing to inform outbreak response

Researchers at the University of Birmingham have utilised rapid whole genomic sequencing methods, including portable sequencing tools, to transform the management of infectious disease around the world. This has improved the understanding of pathogen evolution and sites of persistence, and the identification of transmission pathways. Deployed during the 2014 Ebola epidemic in West Africa, rapid genome sequencing shortened the length of the epidemic reducing mortality, morbidity, and economic loss. The approach was then applied to other diseases such as Zika in 2016 and the SARS-CoV-2 pandemic in 2020. The benefits led to changes in policy and practice within the World Health Organization to improve rapid sharing of sequence data.

MRC funding since 2012 has supported the University of Birmingham team to apply rapid genome sequencing (including nanopore sequencing via the first field-use of the portable MinION platform) to microbial pathogens such as Ebola in 2014 and Zika in 2016. MRC funded discovery science at the University of Oxford was also crucial for the development of nanopore sequencing utilised in this project, with funding in 2005 that led to the spin-out company Oxford Nanopore Technologies.

15. Understanding the transmission and control of COVID-19

Research from Imperial College London and Oxford University informed control strategies during the COVID-19 pandemic. This work provided key data underpinning school closure policy and social gatherings and contributed to the recommendation of interventions to protect those living in large households. The research has transformed our understanding of the epidemiology of COVID-19 and the measures required to protect public health. This includes the Real-time Assessment of Community Transmission (REACT) programme which has been estimating prevalence of SARS-CoV-2 infection and antibodies since May 2020.

Since 2020, MRC Centre for Global Infectious Disease Analysis (GIDA) scientists have tailored their research focus to SARS-CoV-2 to provide rapid, open access, real-time modelling and assessment analysis targeted at the needs of policy makers. Scientists at Imperial College London at the MRC Centre for Environment and Health have utilized their epidemiological expertise to develop the REACT studies in 2020 which have improved our understanding of COVID-19 disease mechanisms and susceptibility at the population level. Since its establishment in 2008, GIDA scientists provided insight into previous outbreaks of Ebola and zika and worked with public health agencies and policy makers to improve preparedness and responses to disease outbreaks.

Cancer

Our analysis identified 55 case studies relevant to cancer. There was significant evidence of impactful research in prostate cancer, with two summaries below covering progress in treating both localized and advanced prostate cancer which were evidenced in eight ICS. These summaries recognise the contribution of MRC funding towards clinical trial design and methodology through the MRC Clinical Trials Unit. The treatments identified through these trials have been translated into new healthcare guidelines and changes in policy. The inclusion of monoclonal antibodies in REF21 ICS demonstrate the far-reaching impact of long-term investment by the MRC; these were discovered and developed by MRC LMB scientists over several decades and mentioned as a key achievement in the 2014-2019 MRC Strategic Plan.

16. Establishing new worldwide standards of care for patients with advanced prostate cancer

Blue Ribbon Symbol for Prostate Cancer Beside a Syringe on White Surface Research from UCL and the MRC Clinical Trials Unit, together with academic, charity, and pharmaceutical partners has delivered life-saving treatments to prostate cancer patients. The STAMPEDE trial has established new worldwide standards of care since its launch in 2005 and has reported practice-changing results that show adding docetaxel or abiraterone improve disease control and life-expectancy. Abiraterone has transformed the care of prostate cancer, with more than 500,000 men worldwide receiving treatment gaining an estimated 300,000 extra life years. Similarly, docetaxel treatment led to an overall survival benefit of 15 months, and by 2019 it was estimated that 36% of UK patients were being treated using this approach gaining an estimated 31,250 extra life years. By employing a new and efficient clinical trial design, STAMPEDE has rapidly delivered findings that would have taken decades using a traditional trials approach.

MRC has supported STAMPEDE primarily through the MRC Clinical Trials Unit, by funding the development of novel adaptive trials methodology since 1998 and the subsequent coordination of the trial since its launch in 2005. MRC has funded or coordinated a range of clinical trials such as PR04, PR05, PR06, PR07, and PROMIS investigating different treatments for prostate cancer, which provided the evidence needed to subsequently inform and design STAMPEDE. MRC funding has also provided underpinning evidence for the treatment approaches used in STAMPEDE, for example, in 2008, the development of MRI based on hypoxia for targeted radiotherapy planning.

17. Evidence-based treatments for clinically localised prostate cancer: policy, practice, and health impacts of the ProtecT trial

Research led by the University of Oxford has changed the way that men with early-stage prostate cancer are diagnosed are treated. The ProtecT trial published the first and only robust randomised evidence about clinical and patient-reported outcomes following surgery, radiotherapy, and active monitoring treatments for clinically localised prostate cancer. The trial evidence demonstrated that a prostate cancer screening programme using a single PSA (prostate-specific antigen) blood test offers no survival benefits but causes over-detection of indolent cancers and potential harm due to over-treatment. ProtecT trial evidence has changed health policy and clinical practice through updated guidelines and optimised treatment. It continues to improve patient health and care by enabling informed and evidence-based treatment decision-making.

MRC funding has supported the underpinning work carried out at the University of Bristol through the MRC ConDuCT-II Hub in 2014. This project explored high-quality, cutting-edge methodological research of relevance to randomised controlled trials with a particular focus on surgical methods. The research led to the development of an intervention that optimized recruitment and informed consent during the ProtecT trial, addressing recruitment difficulties that were considered “impossible” before the intervention.

18. Delivering clinical and commercial impact through novel monoclonal antibody cancer treatments

University of Southampton research has underpinned the clinical development of several key anti-cancer monoclonal antibodies (mAb). The most advanced are two anti-CD20 mAb: ofatumumab and obinutuzumab, used to treat leukaemias such as chronic lymphocytic leukemia (CLL) and follicular lymphoma (FL). Approvals of ofatumumab for CLL has grown from 27 countries to more than 60 while obinutuzumab has been approved for use as a treatment for FL and CLL. The patented anti-FcγRIIB (Fc gamma receptor II B) research was collaboratively developed and licensed to a Swedish biotech firm, resulting in a clinical trial programme that led to a £73 million commercial agreement.

MRC funding in 2009 to University of Southampton supported the characterization of Fc gamma receptors leading to novel insights how antibodies are activated, and how antibody therapies can be improved, particularly to overcome the development of drug resistance. MRC funding has supported this field of research since the 1970s when scientists at the MRC LMB discovered monoclonal antibodies and later developed humanized monoclonal antibodies in the 1990s for which they won Nobel prizes.

Mental health

A total of 52 case studies out of the 569 MRC-ICS were identified by our analysis as relating to mental health. Several case studies describe research in low- and middle-income countries (LMICs), highlighting the global health challenges in this area. MRC funds were used to address unmet need in mental health awareness, diagnosis, and treatment.

19. The Friendship Bench for common mental health problems

Researchers at KCL, LSHTM, and the University of Zimbabwe have developed a low-cost intervention for treating depression and anxiety in Zimbabwe. Known as the 'Friendship Bench', the intervention was developed and delivered through primary health care in community settings with extremely positive results. The intervention is now rolled out in Kenya, Malawi, Zanzibar, and the US. To date at least 63,000 people are documented as having received the intervention, leading to improved mental health for individuals and communities globally.

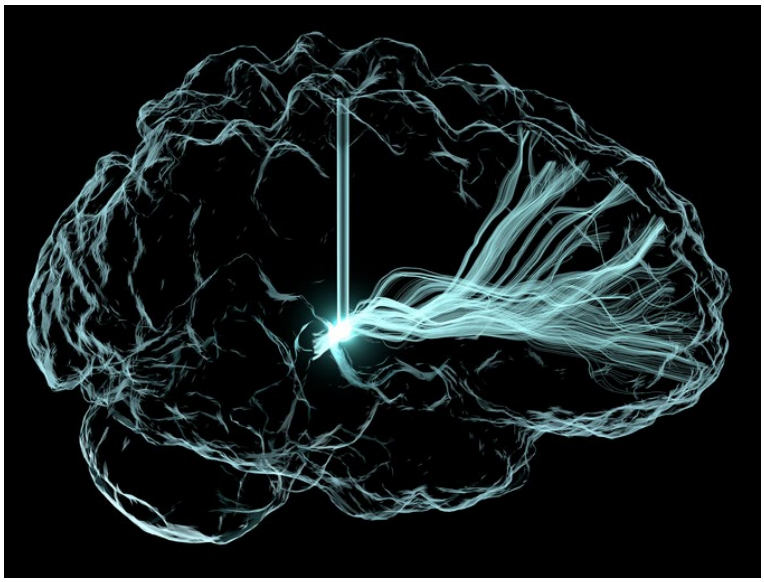
Since 2008, the MRC Tropical Epidemiology Group expanded their work to mental health, with trials of interventions against common mental disorders including the Friendship Bench in 2009. In 2017 MRC funded the expansion of this approach for treating adolescents in Zimbabwe aged 16-19 years old. The MRC Tropical Epidemiology Group, based at LSHTM, has received funding since 1975 to study interventions against diseases of major public health importance in Africa and other parts of the developing world.

20. Take-home Naloxone: developing a nasal spray and making it widely available in the community to prevent deaths from heroin and other opioid overdose

Researchers at Kings College London have developed a naloxone nasal spray for reversing the effects of opioid overdose. The team recognised that overdoses of heroin/opioids are most life-threatening in community settings where medical staff are absent, and pioneered the concept of pre-providing naloxone to laypeople, known as Take-Home Naloxone (THN). The research led to the development of a medically approved naloxone nasal spray as a safer, easier mode of administration than injection. The team provided evidence to support the United Nations and World Health Organisation endorsements of THN, resulting in over 23 countries now implementing THN programmes.

MRC has funded research into substance abuse in vulnerable populations since 2000 when MRC Biostatistics Unit researchers first quantified the high risk of drugs-related deaths soon after prison release. This finding subsequently led to the launch of the N-ALIVE clinical trial in 2008 by the MRC Clinical Trials Unit, which looked at whether naloxone can help to stop fatal opioid overdoses in former prisoners within 12 weeks of release from prison. The positive results from THN led to the development of the nasal spray delivery method for THN, creating a step-change in the wider provision of naloxone.

Neuroscience



ICS submitted to UoA 4 contain neuroscience research, which includes research on stroke and motor neuron disease (MND). Many ICS highlight improvements in healthcare by advances in technology, as well as describing changes to national guidelines which were also adopted internationally. For example, MRC funded research has highlighted the importance of preventative measures and early diagnosis strategies for stroke and MND that have led to increases in life expectancy and cost-savings for the NHS. New drug treatments were developed by MRC funded researchers for epilepsy, while improvements in imaging techniques used the magnetic fields generated by neurons to provide an indication of relative brain health. Collaborations with other funders such as Wellcome and EPSRC have translated and commercialised initial MRC funded discovery science into technologies that are practical and cost-effective for the clinic (for example, development of Magnetoencephalography (MEG) head scanner). Long-term MRC funding for brain banks has also aided research to detect changes in brain structures such as white matter regions that are indicative of MND as described below.

21. Urgent secondary prevention after transient ischaemic attacks and minor stroke, and the identification of cost-effective imaging strategies to diagnose acute stroke

Research from the University of Oxford and Edinburgh has radically changed how stroke is diagnosed and managed, leading to significant patient benefit, stroke prevention, and cost savings for the NHS. Researchers in Edinburgh have showed that immediate computerised tomography (CT) is the most cost-effective way to use brain imaging to diagnose acute stroke. Similarly, researchers in Oxford showed that transient ischaemic attacks (TIAs) and minor strokes should be rebranded as a medical emergency in all clinical guidelines, mandating the rapid implementation of urgent treatment. The team also found that early use of antiplatelet drugs led to substantial patient benefits and changes in clinical guidelines. This research has led to approximately 70,000 strokes being prevented since 2013 in the UK, saving the NHS £200 million per year in costs. Similarly, the impact of immediate CT scanning in the UK has been 42,000 more quality adjusted life years.

MRC has funded this research since 2005 by supporting the International Stroke Trial, which looked at whether patients with stroke could benefit from clot-busting antiplatelet drugs. The trial results provided evidence that treatment within 6h improved patient benefits, including for elderly patients. MRC also provided funding in 2006 to support the development of simple prognostic tools to improve the effectiveness of stroke prevention. This led to the finding that that the risk of a major stroke in days after a minor stroke/TIA was found to be much higher than thought. In 2007, MRC funding further contributed to the research by identifying genes associated with blood clotting, which could serve as prognostic markers to assist in stroke prevention.

22. Standardised cognitive screening tools to underpin personalised care for people with cognitive impairments worldwide

Neuroscientists at the Universities of Edinburgh and Cambridge have developed and validated bespoke assessment tools to address neurological conditions such as motor neurone disease, Alzheimer's disease, and delirium. The ECAS tool characterises a specific profile of cognitive and behavioural changes in patients with motor neurone disease. Similarly, cognitive research software known as CANTAB can detect mild cognitive impairment as a precursor to Alzheimer's disease, and enable earlier treatment with potential pharmaceutical treatments for dementia, thereby optimizing their impact. The 4AT tool can detect delirium, and is now the most-used clinical tool for delirium assessment in 80% of NHS acute hospital trusts in the UK. Collectively, these tools have been standardised across different languages, embedded in clinical guidelines across the world, and used as outcome measures in international clinical trials testing effective treatments for these conditions. The cost-savings impacts are also wide-ranging, for example improved detection of delirium using 4AT results in a conservatively estimated cost saving of £100 per patient, which can translate to NHS savings of £56 million every year.

MRC, BBSRC, EPSRC, and ESRC funding has contributed to this research through the Centre for Cognitive Ageing & Cognitive Epidemiology in 2008 and 2013 by supporting the underpinning research for the ECAS tool. MRC funding in 2010 for the Behavioural and Clinical Neuroscience Institute in Cambridge directly contributed to the development of CANTAB. Similarly MRC funding in 2005 led to deeper mechanistic insights into delirium, with further funding in 2014 to develop the 4AT tool. MRC support for brain banks in 2011, 2013, and 2018 has also underpinned the analysis of donated brain tissue from patients with cognitive impairments to detect changes in white matter.

23. Optimising diagnosis of treatable autoimmune disorders of the central nervous system

Researchers at the University of Oxford have identified four new autoantibody targets and developed diagnostic tests for autoimmune disorders of the nervous system. These autoantibodies produced by the immune system can erroneously target host cells, leading to autoimmune diseases. Autoantibodies targeting the nervous system can cause conditions such as encephalitis. Accurate diagnostic tests using these autoantibodies have improved the early treatment of patients. Many of the diagnostic tests have been evaluated in large multinational studies (for example the use of aquaporin-4-IgG autoantibody to diagnose neuromyelitis optica) leading to changes in laboratory practices across multiple international testing centres.

The team have been supported by MRC funding since 2005 which allowed the identification of pathogenic antibodies from neuronal cultures derived from patient samples, subsequently developed into a new diagnostic test. Further funding in 2007 led the team to identify several of these autoantibody targets such as LGI1 and CASPR2 in limbic encephalitis. In 2021 the team received further MRC funding to identify autoantigen-specific human B cells, to better study the underlying disease pathology for these nervous system autoantibody diseases.

24. Post-hypoxic cooling reduces mortality and improves long-term outcomes in infants

Researchers at the University of Bristol and Imperial College London have pioneered therapeutic hypothermia (cooling) to improve survival and limit brain damage in babies after oxygen-deprivation at birth. This cooling protocol has reduced mortality and severe disability from 66% to 51% at both 2 and 7 years of age, as well as reducing the risk of cerebral palsy by 15% and improving motor function scores. As well as the significant saving of lives, therapeutic hypothermia might save the NHS over £500 million every year given the substantial life-long care needs of individuals with cerebral palsy and the loss of income for their carers.

MRC funded research in 2002 led to the pivotal TOBY clinical trial, which showed that moderate whole-body cooling is an effective treatment to reduce long term severe neurological damage following oxygen-deprivation at birth. Further funding in 2010 supported a follow-up study on the outcomes at school age following the treatment and confirmed the long-term neurological benefits.

Heart disease

20 MRC-ICS report impacts for heart disease including safer and more accurate methods of detecting inherited blood and heart diseases. Several ICS submitted by UCL included genetic tests for Familial Hypercholesterolaemia (FH), safer diagnostic tests for Transthyretin amyloidosis (ATTR) and the use of mathematical modelling to predict the risk of hypertrophic cardiomyopathy (HCM). The diagnosis of chest pain leading to diagnosis of coronary artery disease has become more accurate and cost-effective due to research from the University of Edinburgh. Researchers used CT scans at MRC funded imaging centres to replace a previous diagnostic method, preventing over 600 myocardial infarctions per year since it was introduced into NICE clinical guidelines in 2016.

25. Accelerating the identification and treatment of patients with familial hypercholesterolaemia (FH) through the establishment of a DNA diagnostic service: a paradigm example of Personalised Genomic Medicine

Scientists at UCL have developed genetic tests for Familial Hypercholesterolaemia (FH), leading to an increase in the number of patients with FH being identified and treated for high cholesterol. This has significantly reduced the incidence of avoidable cardiovascular disease. The research led to specific recommendations in national and international guidelines for diagnosis and treatment of adults and children with FH. The diagnostic programme has identified over 9000 patients since 2013 and has led NHS England and Public Health England to set a target in the NHS Long Term Plan to identify at least a quarter of the expected 200,000 FH patients in the UK by 2024.

MRC funding has supported the underpinning discovery science for this research since 2010, through investigation of the genetic mutations and disease pathways involved in FH. Collaborators at the London School of Hygiene and Tropical Medicine conducted genetic association studies to identify the disease pathways, utilizing genomic data from a BHF cohort of 50k individuals, to predict disease risk.

26. Big data to improve care and outcomes for millions of people with cardiovascular disease

Researchers at UCL have used large-scale patient data to shape national and international clinical guidelines for the prevention, diagnosis, and treatment of a range of cardiovascular diseases. This has benefited care and improved outcomes for millions of patients worldwide. Evidence from the research has informed new blood pressure thresholds for more accurate diagnosis of

hypertension, and for more accurate early diagnosis of stable coronary disease, preventing 1,100 heart attacks and strokes per year.

MRC funding has contributed to this research since 2012 to develop and systematically apply concepts and methods across cardiovascular disease to enhance the translational impact of prognosis research. This includes investigating genetics, biomarkers, wellbeing, exploitation of health records, population-based data, and translational research. MRC funding in 2013 also identified associations of high blood pressure with 12 different presentations of cardiovascular disease in a cohort of 1.25 million people, underpinning the changes to clinical guidelines.

27. Transforming the diagnosis and treatment of ATTR amyloidosis: from a rare untreatable disease to a common remediable disorder

Research at UCL's National Amyloidosis Centre (NAC) has revolutionised diagnosis and clinical staging of Transthyretin (ATTR) amyloidosis, a fatal cardiomyopathy, previously diagnosed using invasive and risky heart biopsies. The UCL team has repurposed a widely available scintigraphic imaging technique, developed new cardiac MRI technologies, and created clinical management algorithms that uniquely allow non-invasive diagnosis, staging and quantitative monitoring of ATTR amyloidosis. These tools have been adopted worldwide in clinical guidelines and have facilitated clinical trials and development of new treatments. In the UK alone, approximately 500 people/year are now correctly diagnosed with ATTR amyloidosis using these safe, widely available clinical tests.

MRC funding has made significant contributions to amyloidosis research; for example, in 2010, generating pre-clinical data needed to demonstrate the efficacy of therapeutic antibodies against a key protein. This enabled subsequent investment into the approach by GSK. Funding for UCL research in this area has led to the development of a NHS Amyloidosis Centre of Excellence, contributing to improvements in drug development and treatments to treat amyloidosis (submitted to a previous REF2014 exercise). MRC funding has supported the underpinning research into amyloidosis disease mechanisms since 1979, leading to the identification of significant proteins involved in the disease.

Breadth of impacts occurring from MRC research

Analysis was performed to determine the type and range of impacts claimed in the MRC-ICS (569), as shown in Figure 5.

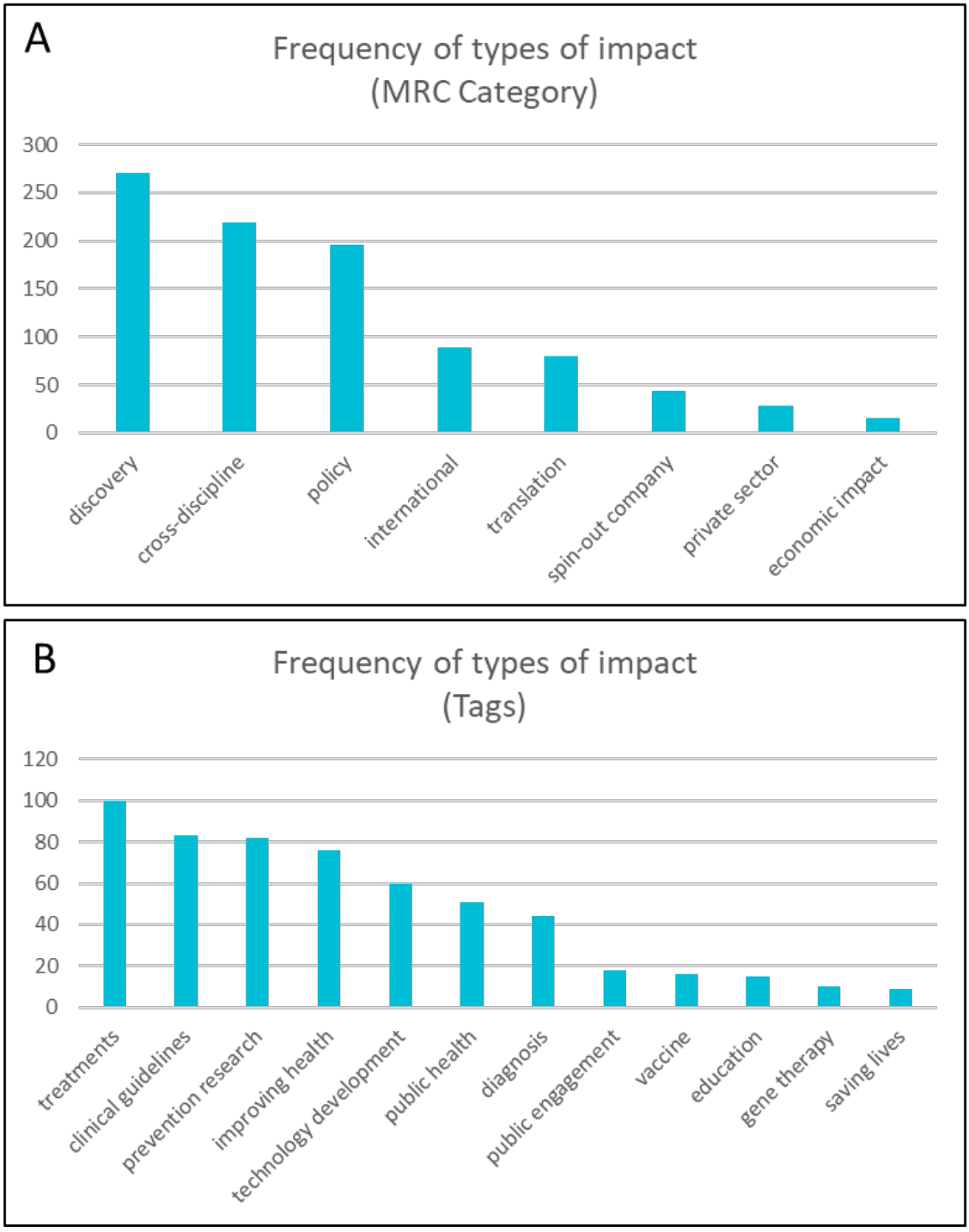


Figure 5: *Analysis of the types of impact occurring from MRC research*

Nearly a half (47%) of all MRC-ICS led to impacts in discovery science (Figure 5A). This reflects MRC's consistent mission to "advance the frontiers of knowledge" and for "strengthening the translation of discovery science and experimental medicine". Significant examples include the "Real-time pathogen genome sequencing to inform outbreak response" at University of Birmingham, "Development and validation of the first treatments for Duchenne Muscular Dystrophy

and Spinal Muscular Atrophy" at UCL and "The Oxford-AstraZeneca COVID-19 vaccine". Cross-discipline research has delivered impacts beyond traditional subject categories as detailed in Cross-discipline impacts above. A third (33%) of MRC-ICS show impacts and influence on policy. Around 1 in 5 of these policy impacts were delivered in the area of infectious diseases and highlight the vast policy changes, evidenced by MRC research, that occurred during the COVID-19 pandemic, as detailed in section Infectious disease (including Covid-19). Spin out companies, private sector and economic impact were generated in 73 impact case studies (e.g., "Development of novel therapies for inborn errors of immunity in children and adults via a spin-out company and an NHS England commissioning policy").

The analysis of REF2021 ICS highlights the contribution of MRC funded research to developing treatments, improving clinical guidelines, targeting prevention strategies, and improving health, as shown in Figure 5B. Other significant impacts were technological developments (10%) (e.g., "Smartphone technology for innovative targeted treatment of poor vision and blindness") and improvements in public health (9%), (e.g., "Development of the 'Stoptober' smoking cessation campaign and evaluation to influence commissioning decisions worldwide").

For more than 50 years, MRC has funded a diverse range of population cohorts that have provided important insights into the determinants of health, wellbeing, and disease, with approximately 2·2 million people in the UK taking part in these large population cohort studies in 2014. Several (19) studies make use of this cohort data to underpin discoveries in areas such as motor neuron disease, ADHD, cardiovascular disease, covid-19, liver disease, sexual health, mental health of military personnel and genomic research.

Environmental/Pollution

Health related impact due to environmental factors has been a focus of MRC funded research for over a century. For example, in 1917 Dame Hariette Chick showed that children who were either given cod liver oil or allowed to play outside in the sunshine could be cured of rickets, caused by a lack of vitamin D. Similarly, the REF2021 submission contained ten MRC-ICS linked to air pollution, highlighting this as a current area of interest for MRC. Research on air and noise pollution

at the MRC Centre for Environment and Health, Imperial College London, contributed to policy informing in the expansion of Heathrow airport and the creation of the London Ultra-Low Emission zone. The research evidenced the link between noise pollution and the risk of heart disease, leading to restrictions around aircraft noise, particularly at night. These national schemes have also led target setting of fine particulate matter that has a detrimental effect on health and are being utilized by European and global agencies, for example, the European Commission and WHO.

28. Air pollution research leads to local, national, and international policies and actions that reduce air pollution impacts

Pioneering research on the extent and impact of air pollution from researchers at the University of Cambridge and Imperial College London have informed policies and guidelines for reducing human exposure to air pollution in the UK, Europe and beyond, potentially benefiting billions of people worldwide. The data has informed international agreements and cost-effective national

strategies to reduce emissions, while incorporating previously overlooked dimensions, including local processes and entrenched human behaviours.

The underpinning methods used by the team for estimating travel patterns and traffic volume using image data, working with both Google Street View and satellite data was developed with MRC support in 2017. Additionally, the Integrated Transport and Health Impact Modelling Tool (ITHIM) developed by researchers at the MRC Centre for Diet and Activity Research in 2013 was essential for performing integrated assessment of the health effects of transport scenarios and policies at the urban and national level. The health effects of transport policies identified in this case study were modelled using ITHIM, which includes using data such as changes in physical activity, road traffic injury risk, and exposure to fine particulate matter (PM2.5) air pollution.

29. Evidence-based traffic schemes cut toxic emissions and improve air quality in London and beyond

Researchers at King College London have provided the scientific foundation for a series of environmental policies to improve air quality in London. This included the Congestion Charging scheme and the Low Emission Zone (LEZ), which were in force throughout the assessment period, and the Ultra-Low Emission Zone (ULEZ) from 2019 onwards. The research also quantified the health impacts of air pollution, helping to drive public support for more ambitious policies.

Collaborators at Imperial College London at the MRC Centre for Environment and Health contributed to this research in 2014. They developed the London Hybrid Exposure Model dataset, which calculates exposure of the Greater London population to outdoor air pollution sources, in-buildings, in-vehicles, and outdoors, using survey data of when and where people spend their time. Funding in 2011 for the MRC-Asthma UK Centre in Allergic Mechanisms of Asthma has also supported this research by highlighting the link between nitrogen dioxide and the increased risk for childhood asthma.

30. Revolutionising the understanding of childhood food allergy to halt the epidemic

King’s College London and St. George's Hospital Medical School researchers have shown that childhood peanut allergy is a largely preventable disease, and that early introduction of peanut in the diets of high-risk infants can prevent children from developing peanut allergy. This breakthrough research has reversed global public health strategy and led to new international guidelines on infant weaning. The research paves the way for exploring similar approaches to preventing other food allergies and will have a lasting impact on generations to come.

MRC has supported this research since 2008 via the Enquiring About Tolerance (EAT) Study which demonstrated that the early introduction of allergenic foods into an infant's diet reduced the likelihood of developing food allergies. MRC funding in 2011 to the MRC-Asthma UK Centre in Allergic Mechanisms of Asthma also supported this work through involvement in the Learning Early About Peanut allergy (LEAP) study which demonstrated for the first time that early exposure to peanuts is an effective strategy in preventing allergy from developing in children. Further funding in 2010 and 2015 allowed the researchers to investigate mechanisms of allergy and tolerance, and develop new diagnostic tests for peanut, cow's milk and egg allergies.

Research Methodology

MRC funding has supported methodology research for decades through the MRC Biostatistics Unit and the MRC Hubs for Trials Methodology Research Network. The impacts of this research ranges from designing adaptive clinical trials to developing software to improve the statistical analysis used in clinical trials. These have had a wide-ranging impact on population health, leading to

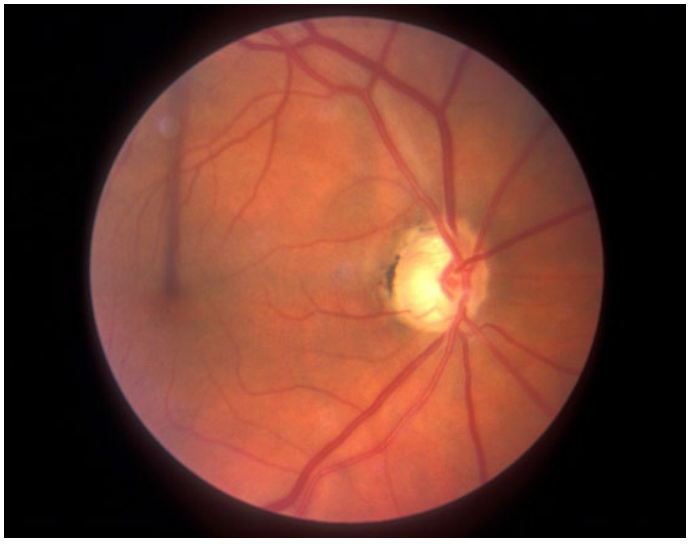
improved healthcare delivery and patient benefit as evidenced below with WinBUGS software development.

31. Evidence synthesis methods yield benefits to patients, organisations issuing healthcare policy and guidance, and commercial companies

Software and methodology developed by researchers at Imperial College London and University of Bristol has transformed how the National Institute for Health and Care Excellence (NICE) evaluates the cost-effectiveness of medicines and treatments for the NHS. Patients around the world are more likely to receive the most effective healthcare at affordable cost from these methods used to develop national recommendations. WinBUGS software and the methods developed using it has brought flexible Bayesian data analysis to non-statisticians and created significant societal benefits and economic value.

WinBUGS was originally developed by researchers at the MRC Biostatistics Unit (BSU) in 2000. Funding in 2004 allowed the development of statistical methods for evidence synthesis including refinements to WinBUGS. MRC funding to the University of Bristol in 2006 allowed them to collaborate with BSU to improve methods for conducting meta-analysis using WinBUGS. Further funding in 2008 led to a tool for assessing the risk of bias in the results of clinical trials included in systematic reviews, leading to improved evidence for medicine. Funding in 2015 and 2017 then led to improved methods for summarising treatment effects on multiple outcomes and the calibration of multiple treatment comparisons using individual patient data, all contributing to improved clinical care.

32. EAGLE transforms the evidence base for primary angle-closure glaucoma, changing guidance and practice



Research at Queen's University Belfast is transforming glaucoma treatment across the world, leading to changes in practice and national and international guidelines. Glaucoma is the leading cause of irreversible blindness in the world, but a type of surgery known as clear lens extraction (CLE) has shown measurable benefits in reducing the burden of this disease. The surgical method was evaluated in the Effectiveness, in Angle-closure Glaucoma, of Lens Extraction (EAGLE) trial, which provided robust evidence for the treatment, supporting a change in practice. The EAGLE trial showed that CLE surgery offers a cost-effective approach to treating glaucoma compared to standard care, with a 67-89% chance of being cost-effective at 3 years and be cost saving by 10 years.

MRC funded the EAGLE trial in 2008 with a unique design which included several innovative methodological aspects and novel features such as the use of a patient-reported general health utility measure as primary outcome. MRC funding in 2008 also supported the evaluation of screening tests for use in EAGLE recruitment.

Gene Therapy

Setbacks in gene therapy clinical studies in the late 1990s highlighted daunting technical challenges to the approach, but fueled MRC funding for discovery research that has now led to

safer and more efficient gene transfer vectors being developed. Recently the first gene therapies have received regulatory approval in the US and Europe. The following REF2021 submissions detail exemplar case studies highlighting advances made by MRC funded researchers to bring these novel treatments into the clinic while creating new spin-out companies generating economic benefit.

33. Development, and validation and delivery of the first gene therapies for haemophilia, and creation of the biopharmaceutical spin-out company Freeline Therapeutics

Researchers at UCL are transforming the lives of people with haemophilia by pioneering single-dose gene therapy that restores blood-clotting and can be delivered at 1% the cost of conventional treatment. Haemophilia is an inherited blood clotting disorder that causes internal bleeding and significantly affects quality of life for the 800,000 affected males, worldwide. The team successfully trialed novel therapies which deliver a functional gene to patients' cells allowing them to produce the clotting factor proteins they are missing. The therapies have treated over 300 patients in clinical studies to-date and a spinout company, Freeline Therapeutics, was launched in 2015 to develop the approach.

In 2007 and in 2011, MRC funding supported the UCL team launching a dose escalation gene therapy study for haemophilia B and generating the clinical data needed for a Phase I/II gene therapy trial for haemophilia A. In 2015, a dose escalation study of a gene therapy for haemophilia A demonstrated the safety and efficacy of this approach, supporting subsequent commercialization through Freeline Therapeutics and the translation of treatments into the clinic. MRC funding has supported the underpinning research for haemophilia for over 60 years, including the identification of the enzyme cascade process of blood coagulation in 1964 at the MRC Blood Coagulation Research Unit in Oxford.

34. Nightstar: Improving vision and creating the world's largest retinal gene therapy company

Research at Imperial College London and the University of Oxford has pioneered the first clinical trials of gene therapy for two inherited diseases leading to blindness, choroideremia and X-linked retinal pigmentosa. The research discovered the biochemical basis for choroideremia and developed a gene therapy vector, leading to the first treatment trial which evidenced significant improvement in vision for some of the patients treated. The results led to the formation of a spinout company, Nightstar, in 2014. Licensing of subsequent research at Oxford, extending the approach to other kinds of retinal pigmentosa, created the world's largest retinal gene therapy company.

MRC funding in 2008 led to the development of a gene therapy vector patented in 2012. A Phase I/II trial in collaboration with Oxford in 2014 validated this approach, supporting subsequent commercialization by Nightstar. Gene therapy for retinal disease has been underpinned by MRC

funded research since 1998, which supported the development of mouse models, allowing the researchers to learn where the disease starts in the retina, thereby identifying the most important target for therapeutic correction.

35. Development and validation of the first treatments for Duchenne Muscular Dystrophy and Spinal Muscular Atrophy

Researchers from UCL and Royal Holloway and Bedford New College have developed treatments that are transforming the lives of children with neuromuscular diseases that affect over 2 million children worldwide. It has led to approval of the first effective treatments for Duchene Muscular Dystrophy (DMD) and Spinal Muscular Atrophy (SMA). Two medicines for DMD - Exondys 51 and Vyondys 53 – which improve quality of life and life expectancy for at least 20% of DMD patients have been approved by the FDA and have already benefitted more than 1500 patients. Spinraza, for treating SMA is available via NHS since June 2019, with 300 patients already gaining access. These medicines have together generated sales of more than $5.5B.

MRC has supported research into neuromuscular disease in 2006 through the MRC Centre for Neuromuscular Diseases in Children and Adults at UCL. MRC also funded a Phase I study in 2006 followed by a Phase II clinical trial in 2013 into the exon skipping drug Exondys 51. Similarly, MRC funding in 2014 supported the development of Vyondys 53 drug. Additionally, MRC funding to researchers in Oxford since 2006 has supported the underpinning research into developing antisense oligonucleotide therapies such as Spinraza for treating SMA, with a Phase I study in 2013. MRC has supported the underpinning discovery science for over four decades; for example, work at the MRC Functional Genetics Unit led to the discovery of the utrophin gene with similar properties to the dystrophin gene, mutated in children with DMD. Research is still on-going to identify drugs that can provide a sustained increase in the levels of utrophin, to compensate for the missing dytrophin gene in patients with DMD.

References

Table 1: Details of the case study summaries featured in this report and links to the source REF2021 ICS database in accordance with the creative commons license for this material.

No.	Title	Section	Units of Assessment (UoAs)	REF ICS(s)	Submitting Institutions
1	Development of effective communication tools has Improving mental healthcare	Cross-discipline impacts	UoA11: Computer Science and Informatics	1a	Queen Mary University of London
2	Creating Step Changes in Cycling Policy and Infrastructure Planning across the UK	Cross-discipline impacts	UoA13: Architecture, Built Environment and Planning	2a	The University of Westminster
3	Protecting human health from infectious diseases in low-resource settings	Cross-discipline impacts	UoA14: Geography and Environmental Studies	3a	University of Brighton
4	Development of applied cell engineering in knee joints: from the bench to a NICE-approved treatment for early osteoarthritis	Cross-discipline impacts	UoA12: Engineering	4a	University of Keele
5	Instantaneous Wave-free Ratio (iFR) for the Diagnosis of Coronary Heart Disease	Cross-discipline impacts	UoA1: Clinical Medicine UoA12: Engineering	5a 5b	Imperial College London
6	Harnessing the draw of professional sports clubs to deliver improvements in health and wellbeing among at-risk groups	Cross-discipline impacts	UoA2: Public Health, Health Services and Primary Care UoA20: Social Work and Social Policy, UoA24: Sport and Exercise Sciences, Leisure and Tourism	6a 6b 6c	University of Glasgow University of Edinburgh

7	HIV policy formulation and prevention: driving the decision for and implementation of publicly-funded pre-exposure prophylaxis in Scotland	Cross-discipline impacts	UoA2: Public Health, Health Services and Primary Care UoA20: Social Work and Social Policy	7a 7b 7c	University of Glasgow University College London
8	The impact of user centred design on health, wealth and innovation culture	Cross-discipline impacts	UoA32: Art and Design: History, Practice and Theory	8a	Cardiff Metropolitan University
9	Vaccination to reduce the global burden of invasive pneumococcal disease and pneumonia in communities	Infectious disease (including Covid-19)	UoA1: Clinical Medicine	9a	London School of Hygiene and Tropical Medicine
10	RECOVERY Trial: Global adoption of effective COVID-19 treatments to save lives	Infectious disease (including Covid-19)	UoA1: Clinical Medicine UoA2: Public Health, Health Services and Primary Care UoA10: Mathematical Sciences	10a 10b 10c	University of Oxford University of Lancaster
11	The Oxford-AstraZeneca COVID-19 vaccine	Infectious disease (including Covid-19)	UoA1: Clinical Medicine	11a	University of Oxford
12	Optimising Treatment Regimes to prevent deaths caused by Cryptococcal Meningitis in Developing Countries	Infectious disease (including Covid-19)	UoA1: Clinical Medicine	12a 12b	St. George's Hospital Medical School Liverpool School of Tropical Medicine
13	Better protection against influenza through national childhood vaccination programmes	Infectious disease (including Covid-19)	UoA5: Biological Sciences	13a	University of Oxford
14	Real-time pathogen genome sequencing to inform outbreak response	Infectious disease (including Covid-19)	UoA5: Biological Sciences UoA8: Chemistry	14a 14b	University of Birmingham University of Oxford

15	Understanding the transmission and control of COVID-19	Infectious disease (including Covid-19)	UoA2: Public Health, Health Services and Primary Care UoA10: Mathematical Sciences	15a 15b	University of Oxford Imperial College London
16	Establishing new worldwide standards of care for patients with advanced prostate cancer	Cancer	UoA1: Clinical Medicine UoA2: Public Health, Health Services and Primary Care	16a 16b 16c 16d	Institute of Cancer Research University of Birmingham University College London Cardiff University
17	Evidence-based treatments for clinically localised prostate cancer: policy, practice, and health impacts of the ProtecT trial	Cancer	UoA1: Clinical Medicine UoA2: Public Health, Health Services and Primary Care	17a 17b 17c 17d	University of Oxford University of Sheffield University of Bristol
18	Delivering clinical and commercial impact through novel monoclonal antibody cancer treatments	Cancer	UoA1: Clinical Medicine	18a	University of Southampton
19	The Friendship Bench for common mental health problems	Mental Health	UoA2: Public Health, Health Services and Primary Care UoA4: Psychology, Psychiatry and Neuroscience	19a 19b	King's College London London School of Hygiene and Tropical Medicine
20	Take-home Naloxone: developing a nasal spray and making it widely available in the community to prevent deaths from heroin and other opioid overdose	Mental Health	UoA4: Psychology, Psychiatry and Neuroscience	20a	King's College London

21	Urgent secondary prevention after transient ischaemic attacks and minor stroke, and the identification of cost-effective imaging strategies to diagnose acute stroke	Neuroscience	UoA4: Psychology, Psychiatry and Neuroscience	21a 21b	University of Edinburgh University of Oxford
22	Standardised cognitive screening tools to underpin personalised care for people with cognitive impairments worldwide	Neuroscience	UoA4: Psychology, Psychiatry and Neuroscience	22a 22b 22c	University of Edinburgh University of Cambridge
23	Optimising diagnosis of treatable autoimmune disorders of the central nervous system	Neuroscience	UoA4: Psychology, Psychiatry and Neuroscience	23a	University of Oxford
24	Post-hypoxic cooling reduces mortality and improves long-term outcomes in infants	Neuroscience	UoA4: Psychology, Psychiatry and Neuroscience	24a	University of Bristol
25	Accelerating the identification and treatment of patients with familial hypercholesterolaemia (FH) through the establishment of a DNA diagnostic service: a paradigm example of Personalised Genomic Medicine	Heart disease	UoA1: Clinical Medicine	25a	University College London
26	Big data to improve care and outcomes for millions of people with cardiovascular disease	Heart disease	UoA2: Public Health, Health Services and Primary Care	26a	University College London
27	Transforming the diagnosis and treatment of ATTR amyloidosis: from a rare untreatable disease to a common remediable disorder	Heart disease	UoA1: Clinical Medicine	27a	University College London

28	Air pollution research leads to local, national and international policies and actions that reduce air pollution impacts	Environmental/Pollution	UoA14: Geography and Environmental Studies	28a	Imperial College of Science, Technology and Medicine
29	Evidence-based traffic schemes cut toxic emissions and improve air quality in London and beyond	Environmental/Pollution	UoA2: Public Health, Health Services and Primary Care	29a	King's College London
30	Revolutionising the understanding of childhood food allergy to halt the epidemic	Environmental/Pollution	UoA1: Clinical Medicine UoA2: Public Health, Health Services and Primary Care UoA3: Allied Health Professions, Dentistry, Nursing and Pharmacy	30a 30b 30c	King's College London St. George's Hospital Medical School
31	Evidence synthesis methods yield benefits to patients, organisations issuing healthcare policy and guidance, and commercial companies	Methodology	UoA2: Public Health, Health Services and Primary Care UoA10: Mathematical Sciences	31a 31b	University of Bristol Imperial College of Science, Technology and Medicine
32	EAGLE transforms the evidence base for primary angle-closure glaucoma, changing guidance and practice	Methodology	UoA2: Public Health, Health Services and Primary Care	32a	Queen's University of Belfast
33	Development, and validation and delivery of the first gene therapies for haemophilia, and creation of the biopharmaceutical spin-out company Freeline Therapeutics	Gene Therapy	UoA1: Clinical Medicine	33a	University College London

34	Nightstar: Improving vision and creating the world's largest retinal gene therapy company	Gene Therapy	UoA4: Psychology, Psychiatry and Neuroscience	34a 34b	Imperial College of Science, Technology and Medicine University of Oxford
35	Development and validation of the first treatments for Duchenne Muscular Dystrophy and Spinal Muscular Atrophy	Gene Therapy	UoA1: Clinical Medicine UoA5: Biological Sciences	35a 35b	University College London Royal Holloway and Bedford New College