MRC Medical Research Council

MRC Translational Research 2008-2018

Evaluation Report

2nd edition

Ipsos MORI

technopolis |group|

Foreword

Professor Dame Anna Dominiczak (DBE, MD, FRCP, FRSE, FMedSci) is Regius Professor of Medicine, Vice Principal and Head of College of Medical, Veterinary and Life Sciences at the University of Glasgow as well as honorary consultant physician and non-executive member of the NHS Greater Glasgow and Clyde Health Board.

My role as the new Health Innovation Champion for MRC and Chair of the Translational Research Group means that I have taken a keen interest in the strength of MRC translational research. The MRC has a distinguished record of supporting discoveries that translate into new products with global impact. From the humanisation of monoclonal antibodies to the invention of MRI, and the application of rational structure-based drug design to GPCR proteins - all three discoveries leading to the creation of new global markets.

The last decade has seen the successful development of a dynamic and unique UK landscape made up of public, private and philanthropic support providing a continuum of funding to enable effective translation of excellent UK discovery science into health and economic benefit. MRC has played a leading and catalytic role in the evolution of this translational ecosystem. Since 2008, MRC has committed to providing directed translational funding schemes open to all, rising to the challenges laid down in a Treasury review of health research to bridge the translation Valley of Death[i]. As you will see from these initial 10-year outputs, the impact of this funding has been significant, not only in terms of economic benefit to the UK, which chimes with the Industrial Strategy, but in fostering a positive change in UK research culture, catalysing innovative partnerships between the public and private sector and realising benefits for patients.

There is more work to be done and the MRC, through UKRI will continue to drive the innovation of translation creating the conditions for the UK to continue to grow and prosper.

Professor Dame Anna Dominiczak

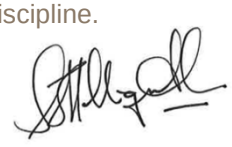
Professor Simon J. Hollingsworth (PhD, FRCPath, FRSB) is Vice President and Global Medicine Leader at AstraZeneca, and Visiting Professor at Kings College London, Division of Cancer Studies.

My remit in taking on the position of Chair of the Expert Advisory Group was to ensure a rigorous, independent assessment of the role the MRC has played in the UK translational landscape. Furthermore, to challenge how the MRC, moving forward, foresees it will continue to be relevant in this area. With this report, readers should have no doubt that the MRC has been pivotal to establishing and evolving this landscape.

From the start of this evaluation I was clear that for it to have any real merit, it would need to be scrutinised independently with the highest possible rigor, so had to be based on detailed analysis and aimed at answering key, specific questions. The findings of this work are underpinned by evidence not anecdote. The evaluation, conducted in partnership with Ipsos Mori and Technopolis has taken a year to come to fruition, which gives some indication as to scale and complexity of the task undertaken. My fellow advisory group members, drawn from clinical, academic and industry sectors, have collectively challenged the MRC and consultants at every step of the process to ensure that the right questions were being asked, the right analyses being undertaken, and the right interpretation made – all robust to the most detailed scrutiny.

The impact of sustained MRC funding over this 10-year period is evidenced and clear to see. However, we have only just scratched the surface and many of the potential impacts on clinical practice will take longer to be fully realised. There is however the counter to this that attrition is and remains a central feature of translational research, and not every translational project will result in the clinical impact it was designed to have. Translational research is not easy, it doesn't follow a linear path and it almost always requires iteration. The path from discovery to the clinic and / or commercialisation is long and challenging – this has been well documented in industry, but we now have the evidence base to show this is equally so in the academic arena too.

Through this evaluation, the MRC now has the evidence upon which to shape the case for, and design of, future funding mechanisms to ensure the UK remains at the forefront of this essential scientific discipline.



Professor Simon J. Hollingsworth

Executive Summary

In 2008 the MRC introduced a programme of initiatives directed toward supporting early phase, academic-led, translational research projects. Since then over £530 million of new funding has been allocated to this programme and 900 projects supported (in addition 625 Confidence in Concept (CiC) projects have completed since 2012).

In supporting high quality translational research, the MRC set out to deliver more innovation into health care, across therapies, diagnostics, devices and other areas, and to strengthen the return on investment from fundamental research. The MRC's role is to support the development of opportunities to the point where early translational public funding is no longer needed and these opportunities can then be taken forward by other investors / organisations. The MRC has steadily adapted its approach, learning from early results and incorporating this into the design of subsequent rounds of funding or the launch of new initiatives. The pathway from discovery science to health intervention is challenging and often long-term process. For researchers to navigate the translational process requires perseverance, the likelihood that projects will fail to deliver discoveries that can be taken into practice is high and increases as projects progress along the translational pathway toward implementation.

This evaluation has examined the outcomes of completed translational projects, comparing different elements of the programme and contrasting them with output from the rest of MRC's research portfolio. Central to the work was a detailed analysis of 250 interviews with principal investigators leading MRC translational research projects to determine in detail the progress that had been made.

We found strong, positive evidence of translational progress. The majority (60 percent) of directed translational projects examined via these interviews were found to have advanced to a later stage of translational development during MRC support. A third of projects across the whole MRC directed portfolio had secured funding to support work beyond MRC's remit e.g. to start later phase clinical studies, or industry sponsored research. Furthermore, projects were found to have delivered a diverse range of outcomes ranging from new tools for research, to new devices and drug treatments now being tested in later phase studies.

The ongoing CiC and DPFS initiatives, which account for almost half of MRC's directed investment in translation over the decade were found to be a major driver of commercialisation outcomes and a noteworthy UK success in expanding the pipeline of products in development. Spin-out companies established to take forward the development of research supported by CiC and DPFS projects established since 2008, secured over 40 percent of all equity investment in UK start-ups in the biotechnology and medical technology sector in 2018, and were valued in total at £2.7 billion.

In addition to engaging with researchers funded by the MRC, the evaluation was an opportunity to seek views from a broad range of stakeholders with influence in UK and international translational research. Feedback was consistently positive about the contribution that MRC funding had made to changing the culture in UK academia toward translational research and supporting its expansion. The conclusion is that the UK is now better equipped to support translational research than it was 10 years ago following additional investment by the UK government through the MRC, NIHR and Innovate UK, and by the charity sector.

Through this evaluation we show that it is possible to compile evidence of progress from biomedical research investments within a ten-year timeframe. Importantly we detail key aspects for researchers to consider in planning and conducting a translational project.

Looking to the future the MRC will plan to build on this maturing landscape and further enable innovative development. Learning from this evaluation, robust and agile support for successful programmes, tied to clear mechanisms to quickly identify and terminate failing projects will be important, alongside continued openness to emerging areas of scientific opportunity.

Acknowledgements

This study was commissioned by the MRC Translational Research Group and conducted by the MRC Evaluation and Analysis Team, Ipsos MORI and Technopolis Group. The work was overseen by an independent expert advisory group chaired by Professor Simon Hollingsworth.

The study team is extremely grateful for the time taken by 250 researchers and over 100 other key stakeholders to explain in detail the progress of their MRC funded projects and offer their views on the rapidly changing translational research landscape.

The study team included Ian Viney, Louise Jones, Emily Gale, Kevin Dolby, James Carter, Buddhini Samarasinghe, Emily Stevens, and Louise Leong from the MRC, Chris Hale, Michelle Mackie, Jan Franke, and Reuben Balfour from Ipsos MORI, Peter Varnai, Maike Rentel, Anoushka Dave and Emma Pottinger from Technopolis Group, as well as many contributions from other colleagues in all three organisations.

The senior responsible officers for the project were Dr Declan Mulkeen and Professor Anna Dominiczak.

This report published on 9/10/2019 is a first update to the version published on 12/9/2019. This edition corrects some typographical errors, makes some minor changes to charts and acknowledges additional members of the study team.

Contents

1. Introduction

This report looks at MRC's support for translational research and the progress made since the MRC increased its commitment to translation in 2008/9 following the Cooksey review[1]. The evaluation explored what MRC translational research had delivered, the national and international context for translational research, and issues to address in future funding.

The work examined completed projects from MRC's directed funding initiatives in detail, contrasted this with selected completed projects from the rest of the MRC portfolio, but excluded MRC's investments in later translational work (post Phase IIb)[2]. The projects examined were initiated and completed within the ten financial years 2008/09 to 2017/18, wherever possible outcomes were examined using the most recent data available, in one case utilising data that was refreshed in August 2019.

Ipsos MORI and Technopolis brought independent expertise to the compilation and analysis of results, and an independent expert advisory group[3] oversaw the project and agreed the main conclusions and recommendations.

The report is split into **7 sections** which cover the following:

1. **Introduction** – MRC funding for translational research
2. **Analysing translational progress and outcomes** – how we assessed a diverse portfolio of projects
3. **Effects in the private sector** – an analysis of commercialisation outcomes
4. **Impact of MRC focused translational research** – a summary of how schemes, such as DPFS that are predominantly focused on the development of new products, have delivered impact
5. **Other MRC support for translational research** – a summary of how the rest of MRC's translational research initiatives have delivered
6. **Changes in the translational research landscape over the last ten years**
7. **Findings** – a summary of the key points from the evaluation and discussion of the areas that will shape MRC's approach to supporting translational research in future

The MRC can draw on feedback provided by researchers via Researchfish®[4] against most projects it has supported since 2008. However, the use of interviews with a sample of 250 researchers allowed in-depth discussion about specific aspects of translation and identification of evidence to substantiate outcomes. Information about project outputs were where possible validated using external data sources. The large dataset created will continue to be analysed by the MRC as it seeks to better understand how research leads to impact. A brief summary of the methods used in this evaluation is at Annex A1, and a fuller description of the methods, supporting information, summary of stakeholder interviews (excerpts from which are inserted throughout the report) and the literature review can be found online via Annex A2.3.

[1] A review of UK health research funding (2006) https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/228984/0118404881.pdf

[2] Later phase translational work supported by the MRC includes funding for late-phase UK clinical trials (the Efficacy and Mechanism Evaluation (EME) programme in partnership with NIHR), global health trials and health systems research (total £334 million). The NIHR has recently initiated an evaluation of the EME programme.

[3] Expert advisory group members: Simon Hollingsworth (Chair, AstraZeneca), Gilllian Burgess (Vertex), Ruth Plummer (Newcastle University), John Brown (MRC Council), Roberto Solari (Imperial College), Wendy Tindale (Sheffield Teaching Hospital), Dario Alessi (University of Dundee)

[4] Researchfish® is an online platform for researchers to record brief details of research outputs, link these to relevant grant funding, and provide this structured data to funding agencies https://www.ukri.org/funding/information-for-award-holders/research-outcomes/. Information about research outputs collected via Researchfish® and linked to UKRI awards are made openly accessible on the UKRI online grant portfolio database Gateway to Research https://gtr.ukri.org/resources/about.html

1.1. Translational Research

Translation is the innovative process of turning fundamental discoveries into improvements in human health and economic benefit[ii]. At every step in this process there are opportunities for discovery science to deliver improvements in speed, efficiency and effectiveness. In addition, results from clinical studies have the potential to inform the design of further early-stage studies into the cellular and molecular basis of disease. Although the pathway for research ideas from bench to bedside is often simplified to a linear process emphasising forward translation, in practice it will involve a complex series of iterations and cycles between new knowledge and product development throughout, and frequent changes of direction or fresh starts. Effective projects often involve work on separate stages of innovation proceeding in parallel.

The MRC has a distinguished record of supporting discoveries that lead to new products with global impact[iii]. Successes include the humanisation of monoclonal antibodies, the invention of Magnetic Resonance Imaging, and the application of rational structure-based drug design to GPCR proteins (all three discoveries leading to the creation of new global markets). The MRC has been actively working to address bottlenecks and challenges in translation for more than three decades[iv]. MRC initially focused only on its intramural programme, by supporting MRC Technology (now LifeArc[v]) to develop and commercialise MRC-owned intellectual property, through Development Gap Funding and provision of facilities. Since 2008, MRC has committed to providing directed translational funding schemes open to all.

1.2. UK Strategy for Translational Research

UK government support for translational biomedical research was strongly influenced by the review of health research, chaired by David Cooksey in 2006. This HM Treasury sponsored review highlighted the UK's strength in basic biomedical research and emphasised the need to co-ordinate activities across agencies supporting the entire spectrum of health research[vi]. The review stated a concern that "the pharmaceutical, devices, diagnostics and biotech companies often found it easier to develop products outside the UK", and that action should be taken to retain current and attract future private sector R&D investment. Recommendations included a clear delineation of responsibilities between the MRC and National Institute for Health Research (NIHR) with the Office for Strategic Co-ordination of Health Research (OSCHR) established to oversee work to accelerate translation of biomedical research into patient benefit. Following the 2007 spending review the MRC committed an additional £130 million to grow funding for translational research via a series of directed initiatives while sustaining funding levels for discovery research and training. New funding mechanisms were launched to accelerate translation, build translational research capacity and overcome specific bottlenecks in translational medicine.

Despite a difficult funding climate following the economic crisis, the 2010 spending review[vii] (2011/12 to 2014/15) protected MRC funding in real terms. The settlement was intended to complement additional funding in the Department of Health research budget via NIHR to "support the translation of research into practical applications" but limited the growth in new strategic MRC commitment to this area. In 2011 the coalition government published the first industry sector strategy focused on life sciences. The strategy stated the importance of creating an environment conducive to translational research, by encouraging innovation through the translational funding gap. While growth returned to science funding in the 2015 spending review (2016/17 – 2019/20)[viii] this was largely ring-fenced for challenges.

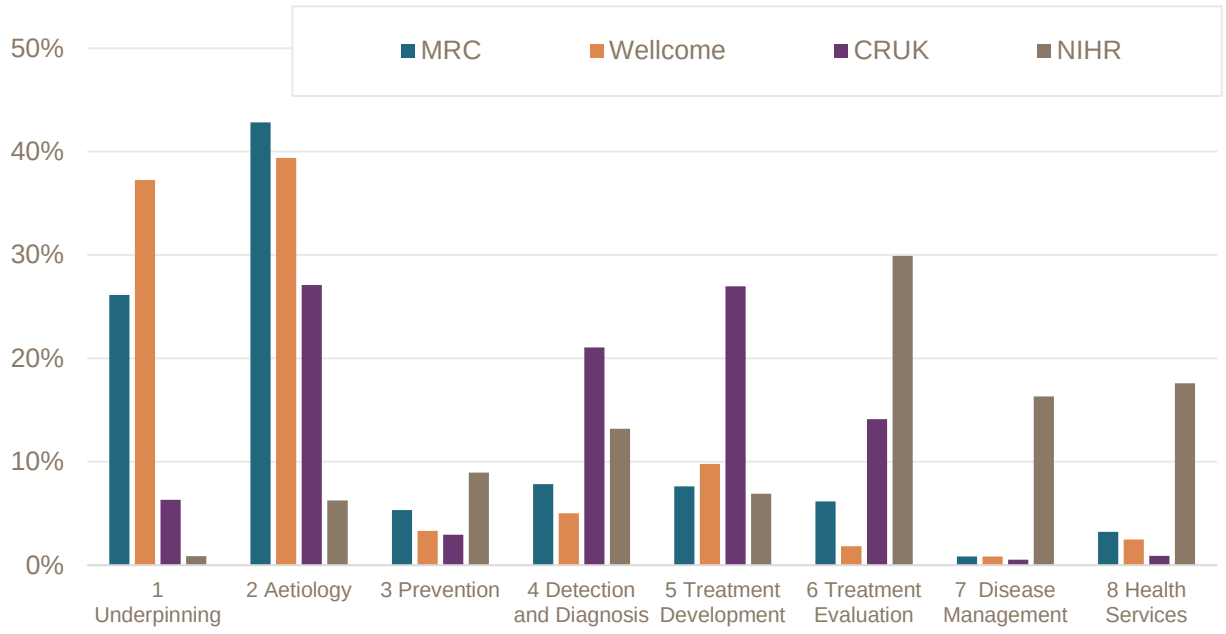
1.3. Translation within the UK Health Research Funding Landscape

Health research in the UK is supported by private, public and charity sector funders. A little under half of the £8.6 billion per year support for research and development flows from the public and charity sectors. In the most recent UK Health Research Analysis (2018)[ix], detailed funding data was collated from charity and public sector organisations

that fund health research in the UK and awards coded using the Health Research Classification System (HRCS). This analysis encompasses all research relevant to health, so includes directed translational projects that are focused on development of a specific product or method (often funded / overseen by a specialist committee), projects which combine discovery science with some work aimed at a specific application (often funded through response mode), as well as discovery science projects with no immediate translational intent. However, HRCS Research activities four to six roughly correspond to early through to late phase translation, with some research activity three (prevention) also including early translational work. This provides us with an approximation of changes in translational focus for UK health research over the decade.

In 2018, funding for specific research projects that can be coded using the HRCS totalled roughly £2.5 billion; funding for health-relevant infrastructure[5] (which cannot be coded using the HRCS) totalled £1.5 billion. 70 percent of the project funding and 72 percent of the infrastructure funding is accounted for by MRC, NIHR, Wellcome and Cancer Research UK (CRUK). The distribution of UK health-relevant project funding coded by HRCS research activity, for these four funders in 2018 is shown in Figure 1.1 below. Across all public and charity funders, the proportion of project spend allocated to HRCS research activities four, five, and six grew from 27 percent in 2009 to 32 percent in 2018.

Figure 1.1 Distribution of **project** funding for MRC, NIHR, Wellcome and CRUK, as a proportion of combined total expenditure in 2018



Source: UKCRC Health Research Analysis (2018)

The role of NIHR funding since it was established in 2006 in the translational landscape has been crucial, and not properly reflected in the analysis of project funding in Figure 1.1. NIHR has made significant investments via its Biomedical Research Centres and Units, the Clinical Research Networks and support for NIHR faculty to improve the infrastructure, capacity and skills in England for conducting experimental medicine studies and later Phase trials, strengthening the relationship between the NHS and academia, and pulling through discovery science to patient benefit[x]. Analogous initiatives are also supported in Scotland, Wales and Northern Ireland[xi].

[5] A large proportion of this funding is the support provided by NIHR for Biomedical Research Centres and Units.

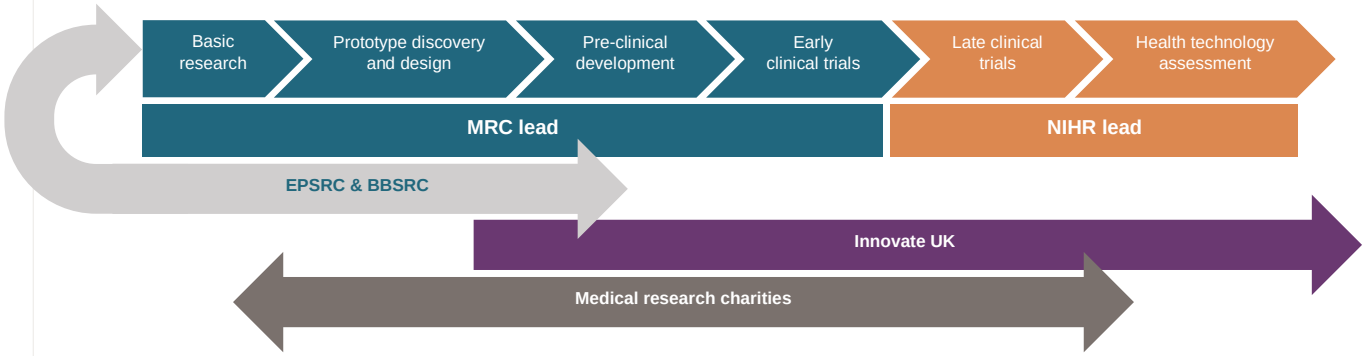
In parallel to the changes in government funding policy since the Cooksey review, many charities (including the Wellcome and CRUK) have also developed and / or refined their own schemes for supporting translational projects, improving industry partnerships, or supporting preclinical and clinical infrastructure and skills.

The Technology Strategy Board (TSB), which was renamed Innovate UK in 2014, was established in 2004, and became an independent body in 2007. TSB's strategy included support for expanding health and life science innovation in industry, and TSB funding for translational medical research (through industry-led projects and collaborations) also grew over the decade. Innovate UK (formerly TSB) funding for health relevant research was £81.9 million expenditure on projects (plus £103.8 million on infrastructure) in 2018.

1.4. MRC Strategy and Funding for Research with Translational Aims

The MRC's role in supporting translational research was developed in discussion with the Office for Strategic Coordination of Health Research (OSCHR) and NIHR, and subsequently Innovate UK and reflects government strategies such as the *UK Strategy for Life Sciences*[xii]. A simplified overview of MRC's remit alongside other UK funders is shown in Figure 1.2. below, reflecting the models envisaged immediately after the Cooksey Review.

Figure 1.2 Summary of funder remits along the translational pathway



The MRC strategic aims published in December 2007[xiii] included:

- A new funding initiative, the Developmental Pathway Funding Scheme (DPFS) for focused translational projects
- Increased earmarking of funding for collaboration with industry, and ambitions for joint calls for proposals with the Technology Strategy Board (TSB)
- Strategically directed initiatives in areas such as patient cohorts / collections, biomarkers, new non-human model systems
- A new joint MRC-NIHR Methodology Programme (MRP)
- Expansion of relevant clinical and non-clinical training and support for leadership
- Continuation of strategic programmes for regenerative medicine and stem cell research

Major programmes such as Confidence in Concept for small-scale rapid investments; large scale Stratified Medicine Consortium funding (now Precision Medicine Consortia); and the Biomedical Catalyst (BMC) partnership with TSB (later Innovate UK) came later. Two examples of how MRC's strategy evolved over time are in Box 1.

MRC delivery plans after 2008 emphasised that the aim was ultimately to deliver more innovation into health care, across therapies, diagnostics, devices and other areas, and that the MRC's role was to develop opportunities to the point where early translational public funding, or MRC funding, was no longer needed, and other investors or organisations took the opportunity forward. Progress towards this stage and towards application was, for DPFS, the dominant goal. In designing the focused initiatives MRC did not anticipate significant high-profile publication output.

By 2014, the MRC was describing its strategy as "to drive innovation, facilitate the transfer of the best ideas into new interventions, and improve the return on investment in fundamental research[xiv]". It emphasised directed initiatives to de-risk approaches and build evidence and confidence to the point where the private sector or other parties will invest in the later stages of translation; and MRC supports pre-clinical to early clinical development across all health areas and technologies.

"[On the broader translational funding landscape] the UK is now better equipped for translational research than it was 10 years ago in terms of both people and facilities, and [..]public funders such as the MRC, NIHR, Innovate UK and the Wellcome have significantly contributed to this outcome."

Statement from summary of key stakeholder interviews

Box 1 Changes to MRC directed translational initiatives

The journey of Stem Cell research – from TSCRC to RMRC

The Translational Stem Cell Research Committee (TSCRC) was established in 2008, when stem cell research was in its infancy, as a specialist funding panel to support high quality research aiming to apply stem cell technology to improve human health.

In 2012, the MRC on behalf of the Research Councils and Innovate UK (TSB at the time) published *A Strategy for Regenerative Medicine*[xv] aimed at delivering the significant promise of regenerative medicine. In line with the strategic recommendations, the UK Regenerative Medicine Platform (UKRMP) was launched. Initially a £25 million joint investment by MRC, Engineering and Physical Sciences Research Council (EPSRC) and Biotechnology and Biological Sciences Research Council (BBSRC) to address key early knowledge gaps and bottlenecks to develop generic tools and approaches.

As the regenerative field advanced beyond pure stem cells research, the TSCRC scheme evolved into the Regenerative Medicine Research Committee (RMRC) to offer optimum alignment to the progressing landscape. The RMRC remit was expanded to encompass all translational approaches towards cellular and tissue regeneration and focused its scope on therapeutic interventions, with the MRC Research Boards providing a complementary responsibility for supporting pre-development, discovery science programmes.

In response to the needs of the community, the remit of RMRC was refreshed in 2016 to focus on the early translation space, de-risking the early steps towards leveraging larger scale translational investment to bring the therapeutic towards human applications. In 2018, it was agreed that the UK regenerative medicine research field had sufficiently matured that the MRC research boards and the DPFS panel were well-placed to manage funding requests in this area without the need for separate dedicated funding and the RMRC panel was disbanded.

Towards the continuum of funding for translational research

Between 2009 and 2011, MRC piloted a devolved portfolio approach for the DPFS with five universities; University of Dundee, University of Edinburgh, King's College London, University of Nottingham and a partnership between the Universities of Bristol and Cardiff. Each institution was awarded £2 million over this period to support a portfolio of translational research projects, with the funding decisions delegated to the host institutions. This pilot highlighted that there was a clear local appetite and demand to support early translational projects, with a quarter of the projects supported classed as seed projects. In addition, the pilot demonstrated that this had an enabling effect on the institutional translational activities; institutions with devolved portfolios had an increased volume of submission of proposals to DPFS and reporting enhanced translational activities beyond downstream funding.

Recognising the opportunity to capitalise on portfolios of early translational projects within the university setting and the need to better bridge the gap between discovery research and viable translational projects, Confidence in Concept (CiC) was launched in 2012. The purpose of CiC was to de-risk concepts to a stage where they are competitive for more substantial translation funding, from DPFS, industry or other sources. The annual CiC competition is open to all research institutions and awards of up to £1 million are allocated to institutions on a competitive basis. While CiC is focused on providing rapid and flexible funding for early translation, institutions with CiC have reported wider benefits, such as leveraging resources within the universities (e.g. project support and support staff), increased interactions with industries, and a stronger local translational culture and awareness of development pipeline. We are now seeing pull through of ideas supported through CiC securing further funding through DPFS and Innovate UK (for spin-outs), highlighting the continuum of funding that has been created.

1.5. Scale and type of MRC funding

Two approaches were used to reach an estimate of MRC's funding for translation over the last ten years. Firstly, expenditure via schemes directed specifically to translation were counted fully, and then an estimate was made of the proportion of all other projects that were relevant, based on any stated intent to translate.

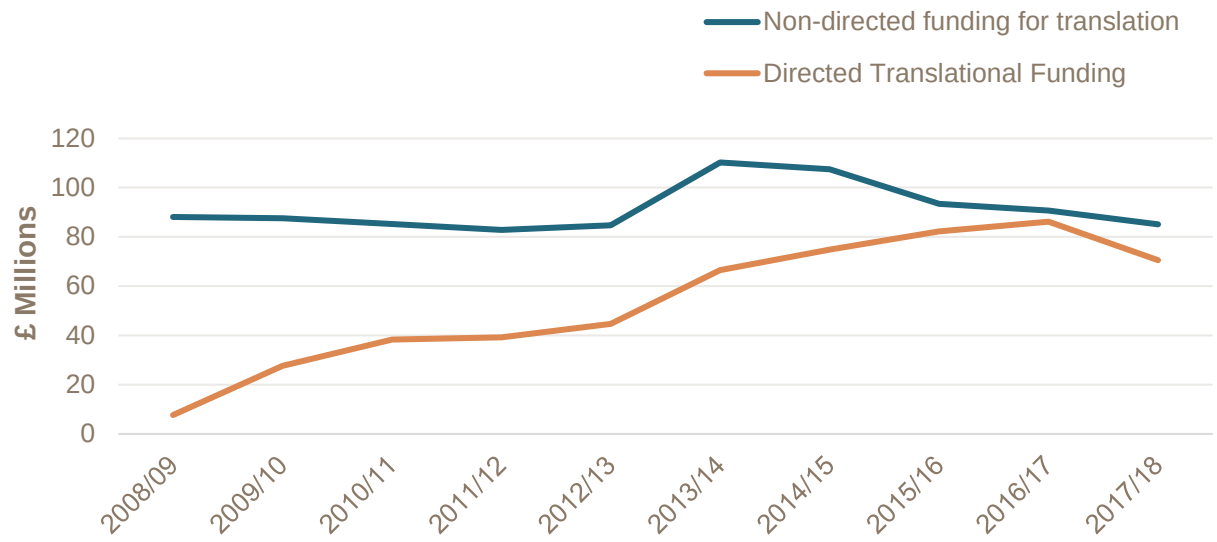
- **Directed funding**. Expenditure via schemes focused wholly or mainly on translational aims, and reviewed and often monitored from this perspective, have grown from zero to 14 percent of MRC's total expenditure over the period 2008/09 – 2017/18 (total expenditure £538 million, the orange line in Figure 1.3 below)

- **Estimates of projects with translational intent**. Using HRCS coding to provide consistent estimates of the fraction of MRC investigator-developed awards with more translational or applied aims, this wider effort is estimated to total roughly 20 percent of MRC's overall spend over the last ten years (approximate expenditure £989 million between 2008/09 – 2017/18, the blue line in Figure 1.3 below) and was found to have been stable year on year.

Combining both figures, approximately 30 percent of MRC funding over the last ten years has been at least partially directed at new treatments or diagnostics (£1.5 billion out of a total MRC expenditure of £5.3 billion over the last ten years).

This figure excludes funding for late phase clinical trials or related applied projects in the UK or internationally.

Figure 1.3 *MRC support for translational research 2008 - 2018*



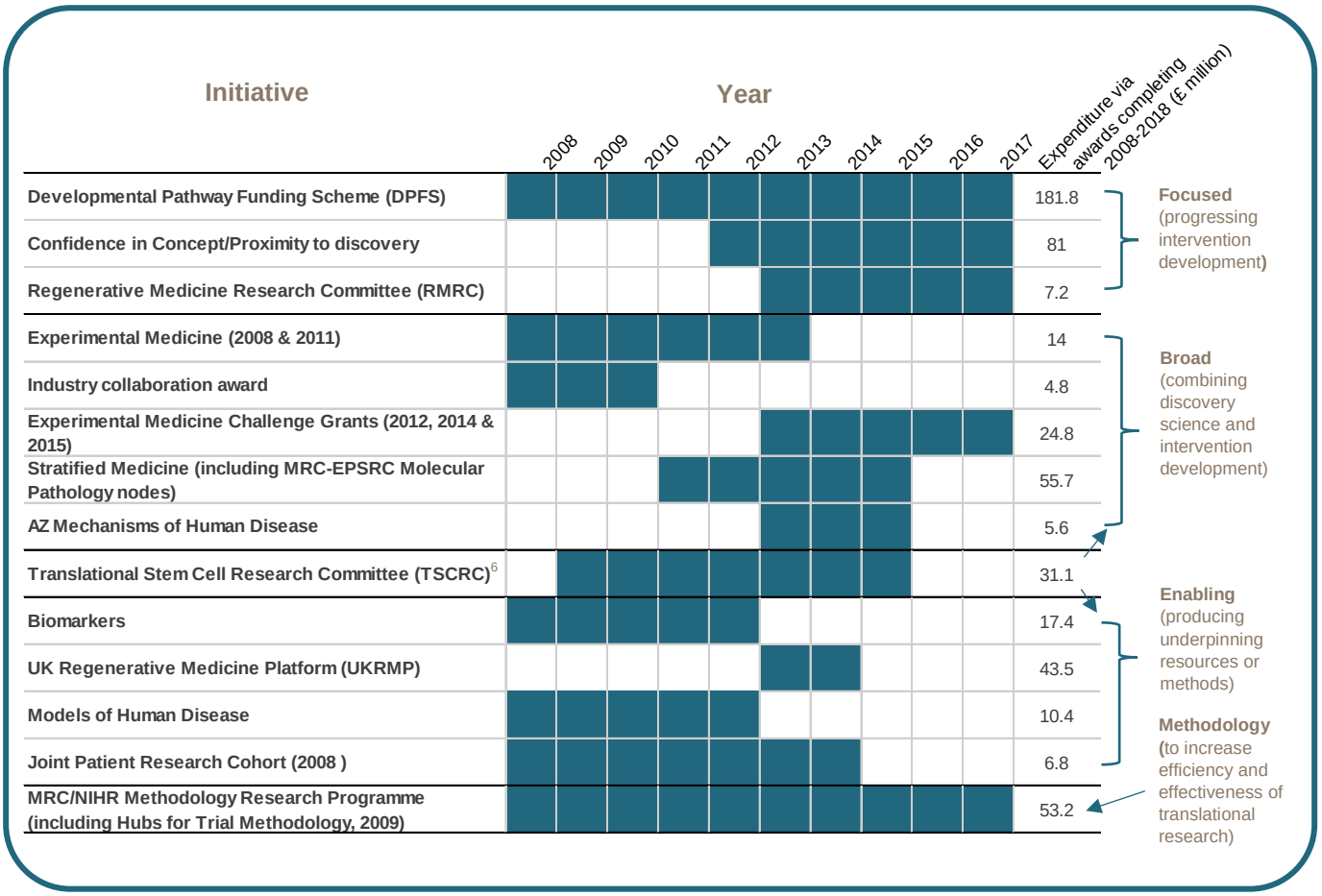
Source: MRC monitoring information

Within the directed portfolio there have been 14 different funding schemes launched. We can categorise these into four groupings, a breakdown and timing of these are set out in Box 2.

"[On the catalytic role in translational research funding] … the MRC is a global leader in supporting translational research and establishing innovative partnerships with industry (often ahead of other UK research councils), which in turn has driven changes in the level and nature of translational research activity and research culture in the UK."

Statement from summary of key stakeholder interviews

Box 2 Timeline of MRC translational initiatives across the decade

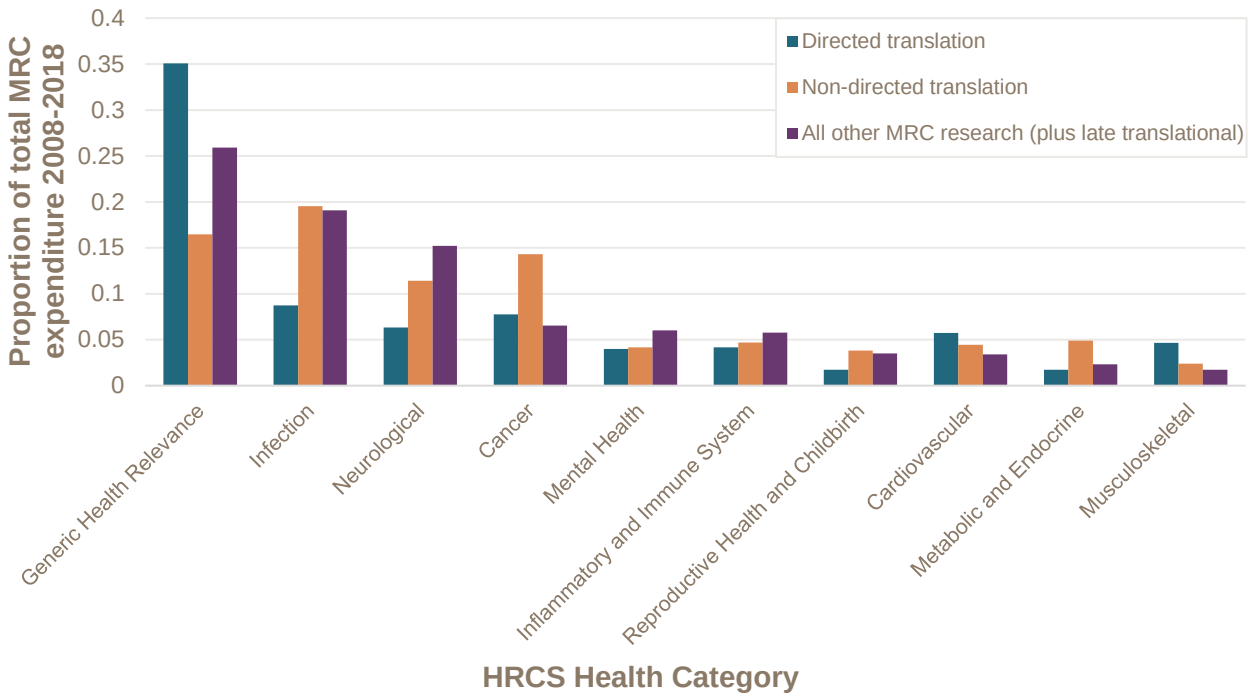


Analysis of the health objectives of MRC projects shows that there are small differences in the directed translational, non-directed translational and overall MRC portfolio (see Figure 1.4). The directed translational funding has a higher proportion of expenditure with generic health relevance[7], cardiovascular and musculoskeletal disease relevance, but lower expenditure on projects relevant to infection research. Looking at directed and non-directed support for translation, there is also a lower proportion of expenditure on translation relevant to neurological conditions than in the rest of the MRC portfolio.

There has not been much change in the balance between health categories over time. Comparing directed translational expenditure at the start and end of the decade, there has been a slight increase in the proportion of inflammation and immune system relevant research, as well as research relevant to mental health.

[6] Interviewed projects funded by the TSCRC were split between the broad and enabling portfolios
[7] The higher proportion of generic health relevance for directed translational awards is due to UKRMP and methodology initiative awards being relevant to a wide range of health categories

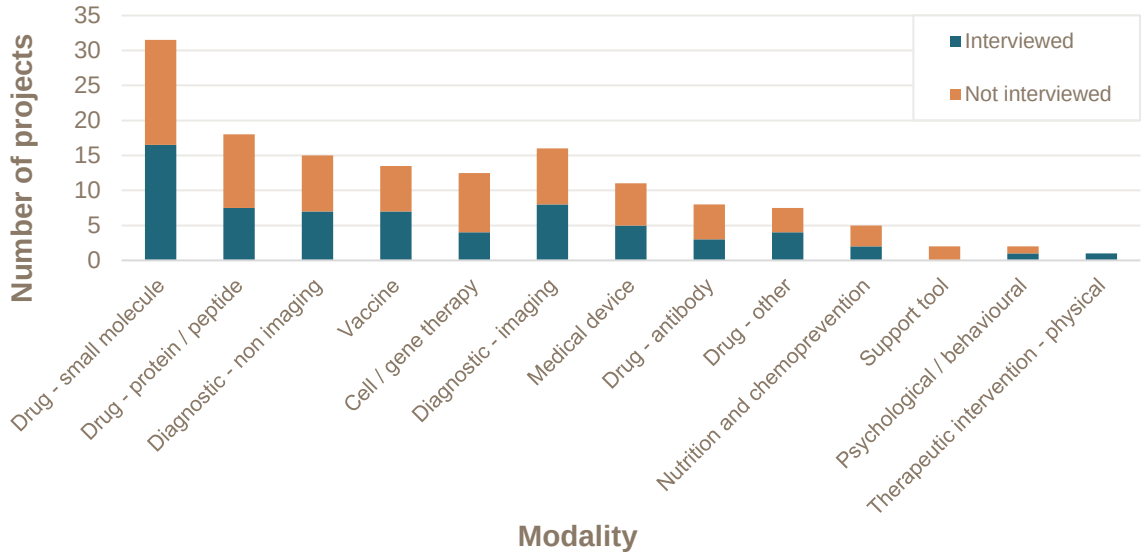
Figure 1.4 Expenditure across top 10 health categories via directed/non-directed/ other mechanisms as a proportion of the total expenditure via each mechanism



Source: MRC monitoring information

Figure 1.5 shows the spectrum of technologies used in DPFS projects, projects to develop small molecule or protein drugs are most prevalent in the directed portfolio, but the full spectrum of technologies including diagnostics, devices and psychological / behavioural interventions are represented.

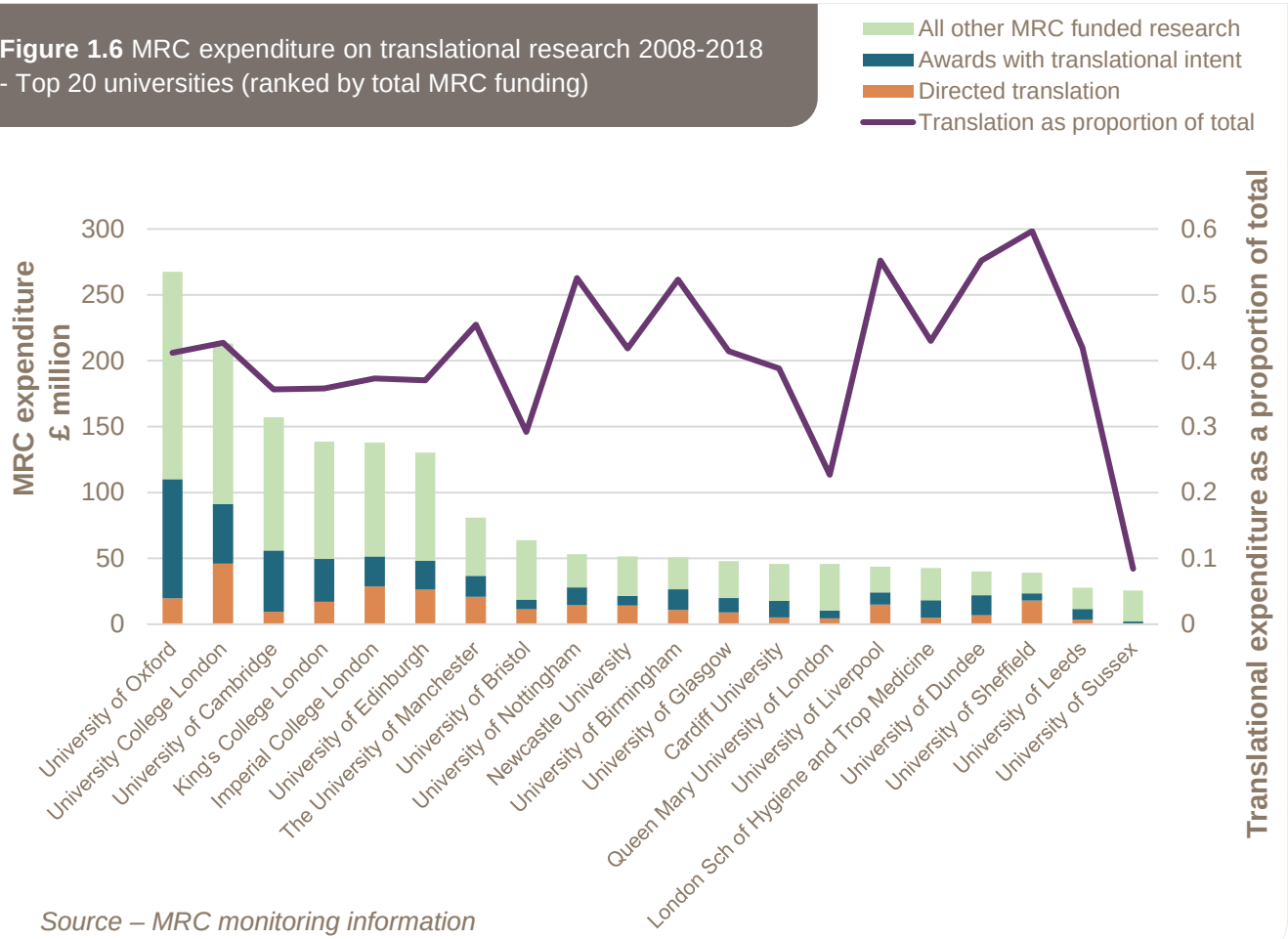
Figure 1.5 Distribution of "modalities" for DPFS projects



Source: MRC monitoring information

The graph in Figure 1.6 shows MRC directed (orange) and non-directed translational (blue) expenditure (ranked by directed expenditure) for the 20 universities receiving most MRC funding between 2008 – 2018[xvi]. Adjustment is not made for MRC Units transferring to university ownership in this period.

Figure 1.6 MRC expenditure on translational research 2008-2018 - Top 20 universities (ranked by total MRC funding)



Source – MRC monitoring information

While the proportion of total MRC funding that is translational (the total of directed and non-directed translational expenditure as a proportion of all MRC funding) is similar in the top six institutions (shown by the purple line in Figure 1.6), the share of MRC funding each university has secured from directed support for translation (orange bar) does vary significantly. The MRC's directed translational funding has a different geographical distribution to other MRC support. Edinburgh, Manchester, Nottingham, Newcastle, and Sheffield all are in the top ten recipients of MRC directed translational funding by awarded value. However, examining DPFS application and award rates, both Oxford and Cambridge apply less frequently than other institutions and receive less awards. Both application and success rates drive the overall funding secured by institutions, and the result is that 65 percent of MRC's directed translational funding is spent outside of London and the South East, in contrast to 48 percent of total MRC funding.

There is also a regional difference in the modality of DPFS projects funded, with institutions in London and the South East having a higher proportion of projects focused on cell / gene therapy and vaccine development, and institutions outside of the South East having a higher proportion of projects focused on developing medical devices.

1.6. Section summary

- MRC has over the last decade introduced a series of directed translational initiatives, in part supported by new government funding, rising to 14 percent of total MRC spend. Support for basic research has been maintained, and the emphasis on translation or applied goals in general funding has not changed over the decade.
- MRC's funding emphasises very early phase, academic-led, translational research.
- MRC directed funding is more geographically diverse than other MRC funding with a majority (65 percent) being spent in institutions outside of London and the South East.
- Institutions and regions show some tendency to specialise; with differences in the topics and modalities funded within and outside the South East.

2. Analysing translational research progress and outcomes

This section describes how the evaluation approached the challenge of assessing a diverse translational portfolio and includes overall data on some general characteristics of the portfolio.

The points the evaluation and Expert Advisory Group aimed to address can be summarised as:

- What has resulted from the directed translation portfolio in contrast to the broader portfolio of translational research supported by the research boards?
- Can we understand the translational research landscape and MRC's place in it over the decade, and position MRC for future translational success?
- Can analysis of the progress of projects identify determinants of performance?

The evaluation only examined MRC awards that had completed MRC funding before 2018, resulting in awards that started in the early part of the decade being more prevalent. This sampling meant that there was an average of four years post completion of projects allowing the importance of the outcomes and their later development to become clearer.

Table 2.1 Number and value of completed awards by translational grouping

MRC portfolio translational research groupings	All awards started 2008 - 2018		All awards finished 2008 - 2018	
	#awards	Spend 2008-2018 £ million	#awards	Spend 2008-2018 £ million
Directed translational research	907	538	608	337
Non-directed translational research	1350	989	964	713
Late translational research	275	334	218	294
Other MRC research	3646	3380	2624	2199
Total	**6178**	**5241**	**4411**	**3543**

To assess outcomes, the evaluation drew on Researchfish® data, and supplemented this with:

- In depth interviews with investigators, gathering more precise information on subsequent progress of a potential product, the status of further investment etc.
- Independent data on spin-out companies and investment
- Bibliometric data

A comprehensive literature search was undertaken to support comparisons between MRC's programmes and others, and to inform evaluation methods. This is published separately (see Annex A2.3), but in brief, while there have been numerous translational initiatives worldwide over the last two decades, no evaluations were found that offered useful benchmark quantitative data on issues such as project progression rate or number and value of impacts. Some bibliometric data is available (see below) and a little data is available on focused and uniform programmes (e.g. success rates from academic / industry drug screening collaborations) but these are not comparable to MRC's diverse programmes. Some major schemes are still too new, and so better quantitative evidence might emerge over the next few years. Box 3 illustrates some of the more diverse translational projects MRC supported.

Box 3 Examples of outcomes from MRC translational research projects

Pressure sensors to help prevent pain for amputees[xvii]

A DPFS-supported project[xviii] at the University of Southampton collected data using a novel sensor for measuring rubbing against lower limb prosthetics. The project captured crucial data wirelessly from amputees walking in real world situations and subsequently secured Innovate UK funding with industry partner Chas A Blatchford and Sons Ltd. a manufacturer of prosthetic limbs, to take the device to market. The project combined expertise from medical engineering and physics and has potential application to the design of insoles, mattresses, special seating, assistive rehabilitation robotics, and orthotics.

Hydrogels – a unique solution for stem cell storage and transport[xix]

Researchers at the University of Reading were supported via an award[xx] from the TSCRC to investigate the use of hydrogels to package and deliver stem cells for repair of the cornea. Encapsulation in alginate was unexpectedly found to keep cells in a low respiring dormant state. Although this meant that hydrogels were not suitable as a stem cell delivery system, encapsulation was found to be ideal for room temperature transport and long-term storage of a range of cell types. The team, now at Newcastle University, has extended the approach to storage of cultured tissue and established a spin-out company Atelerix[xxi] to further develop and market the product.

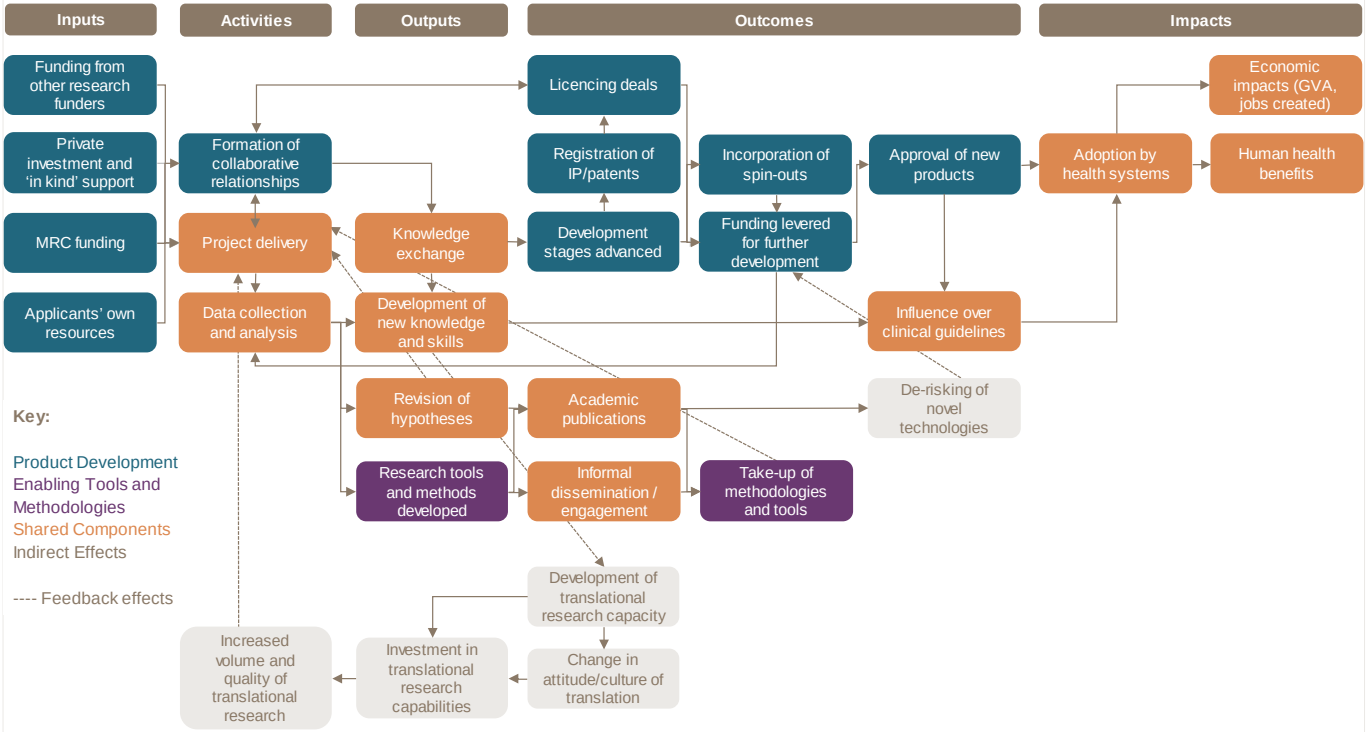
Development and validation of cardiovascular MR imaging and spectroscopy at 7 Tesla.

This £1.4 million 2011 non-directed research grant sought to develop tools and methodology for clinical cardiac MRI at 7 Tesla, from building the hardware right through to running studies with clinical researchers. One of the studies exploiting this infrastructure studied liver fibrosis, and during the work a novel liver inflammation and fibrosis (LIF) score was calculated which overcame the confounding effect of iron storage in the liver. This score was found to closely match the accuracy of liver biopsy and to be particularly good at spotting early signs of disease. Earlier diagnosis may allow patients to make lifestyle alterations before they progress to potentially irreversible cirrhosis. The project outcomes supported the creation of the Oxford University spin-out, Perspectum Diagnostics to commercialise the diagnostic test as LiverMultiScan™. The company has achieved CE and FDA certification for the test, and an Innovate UK funded study showed that use of the test could halve the number of liver biopsies needed in the UK. The company has secured support from Galectin Therapeutics which will use the test to conduct a Phase II trial of a potential treatment for liver fibrosis in the USA. The company now employs more than 70 people.

2.1. Theory of change

To guide the evaluation, a theory of change was developed, which set out the full set of expected causal processes from MRC funded research to eventual impact that might be seen across the whole portfolio, while recognising that within single funding schemes a smaller set of pathways and processes might be relevant (see Figure 2.1 for a summary of the theory of change and full details of this work is in Annex A2.1). This framework highlighted likely differences in emphasis between the focused and enabling mechanisms within the directed translational portfolio.

Figure 2.1 A theory of change for translational research



Source: Ipsos MORI and Technopolis

2.2. Categorising progress along the translational pathway

Full details of the approach used to sample projects for interview is at Annex A2.2. In brief we identified all MRC research projects that had completed between 2008 and 2018 and categorised these by funding initiative. We sampled purposefully from this list with a preference for those projects that had started, and therefore completed, earlier in the decade (thereby biasing the sample toward projects that had longer to develop outcomes). However, we sought to ensure a mix of projects that had reported translational outputs[8] via Researchfish® and projects that had reported no output via Researchfish® in the same proportion as was found across the whole portfolio, thereby seeking to ensure that we had a mix of projects that had and had not progressed successfully.

[8] Translational outputs included private sector funding, products in development, spin-outs, patents etc.

Detailed interviews with over 250 researchers that had led MRC funded projects (190 from the directed portfolio and 60 from the non-directed portfolio) allowed us to assess the progress achieved over the course of the project and subsequent translational development of the core asset. We defined a set of developmental stages to subdivide the translational pathway[xxii] and during interviews collected evidence for assigning a stage to the project at its outset, at the end of the project and at the time of the interview[9]. This approach allowed us to provide evidence of progression in a semi-quantitative way although the developmental stages are not equal in terms of the complexity, resources, or time required to progress from one stage to another. Stages are also not equivalent for projects with different modalities (e.g. the development of drugs *vs* the development of digital health interventions).

Of 151 interviewed projects to which developmental stages could be assigned (excluding CiC), 60 percent made progress within the tenure of the award[10] (although for most projects this was just to the next developmental stage). The proportion of projects that had progressed rose to 70 percent by the time of the interview. This measure, by itself, was not enough to form an evaluative judgement regarding the success of projects but was used in combination with other indicators. Box 4 includes selected examples of projects that were judged to have advanced along the developmental pathway.

***Box 4** Examples of MRC translational research project progression*

Monitoring wound status using multi-parameter optical fibre sensors (MR/R025266/1[xxiii])

MRC funding to the University of Nottingham allowed a device employing hyperspectral imaging to monitor wound healing to be tested in a study of 43 patients in a diabetic foot ulcer clinic. A prototype of the device had been developed with support from an NIHR i4i award (£70k). On the strength of this study the research team then partnered with a company, Footfalls and Heartbeats, funded by Innovate UK (£175k), to look at the feasibility of integrating optical fibres into textiles and measuring blood flow under the foot in a sock. EPSRC impact accelerator support (£150k) supported improvements to the monitoring equipment. Now with real world data and a steadily improving prototype, the team secured an MRC DPFS award in 2018 (£900k) to develop a wound dressing that incorporates optical fibre sensors to monitor key parameters associated with healing.

Development of a Novel Liver Dialysis Device (G0902211[xxiv])

MRC DPFS funding (£950k) in 2010 led to advancement of a prototype liver dialysis device, initially developed via NIHR funding, to extend the life of patients with acute-on-chronic liver failure (ACLF). ACLF patients typically have short life expectancy, with the only treatment being liver transplant. The clinic-ready dialysis device is being commercialised through UCL, with the formation of the spin-out company Yaqrit and a multi-centre Phase IIb clinical trial is nearing completion funded by a €6.4 million European Union Horizon 2020 award in 2017.

Development of a smartphone application for measurement of attentional deficits in delirium (MR/L023210/1[xxv])

Initially supported via the cross-research council Life Long Health and Wellbeing initiative, researchers in Edinburgh developed a new neuropsychological test for the objective measurement of inattention in delirium. Delirium affects at least 1 in 8 acute hospital patients, it has multiple severe consequences but is grossly under-detected. The test was originally implemented on a purpose-built computerised device (Delbox)[xxvi], but with further support via the DPFS the team developed a prototype software application (DelApp) for smartphones. DPFS funding supported the use of DelApp with more than 500 patients recruited from elderly care and acute orthopaedic hospital wards[xxvii]. This validation completed in 2018 is essential for the test to be developed further and gain wider use.

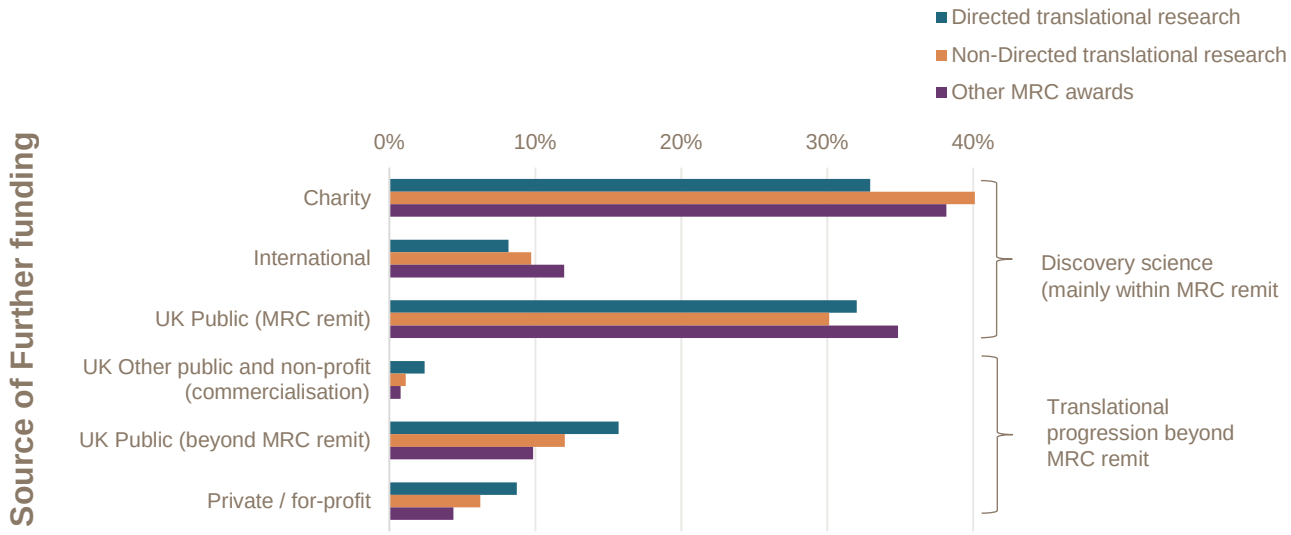
[9] Projects were interviewed on average 4 years post project completion
[10] The average duration of awards was 3 years

2.3 Securing further investment

MRC's largest and most novel scheme (DPFS) emphasised the aim of progressing opportunities to the point where the private sector or others would invest to take them towards clinical use and patient benefit. Independent investment in an opportunity also provides important, and presumably rigorous, confirmation of the potential importance of the product or method, and its feasibility, cost effectiveness etc. For these reasons the evaluation concentrated on whether projects progressed to further funding, and the nature and aims of that funding.

A critical distinction had to be drawn between those that were funded to conduct work at a later translational stage and those that were funded to do further discovery research or return to early translational work of the sort MRC itself might fund. We used the source of further funding (e.g. industry investment, funding from NIHR schemes aimed at later stage translational development) as an indicator across the portfolio of whether these projects were likely to have progressed to a point at which the work was substantively closer to market. For those projects interviewed we had the opportunity to refine this further by confirming the purpose of the subsequent grant in detail. Two thirds of projects across the MRC portfolio have reported details of further funding, and while the level of reporting is similar across the directed, non-directed and other award portfolios (64 to 66 percent), there is a marked difference between the progression of projects across the three translational groupings, as measured by the source of further funding (Figure 2.2 below).

Figure 2.2 Proportion of awards reporting further funding, by funding sector and MRC translational grouping



Source – Researchfish® data (16,000 reports across 2,700 awards active 2008-2018), note totals exceed 100 percent as projects may report funding from a variety of sources

Most UK charity funding (as can be seen in Section 1, Figure 1.1) supports work within a similar part of the translational pathway to the MRC (MRC remit), although a small proportion supports late phase trials. Similarly, international funding (e.g. funding from the European Commission) largely focusses on work that the MRC could support. In contrast it was possible to split UK public funding awarded by organisations into the following groups:

- **UK Public (MRC remit) funders -** also share the MRC's remit (academic / university, UK funding councils, learned societies and other research councils, included here is NIHR support for biomedical research centres and units)
- **UK Public and other non-profit (commercialisation) funders -** are focused on the commercialisation of research (Innovate UK, LifeArc, devolved nation innovation schemes (e.g. Scottish Enterprise) and commercialisation arms of universities (e.g. Oxford Innovation)), clearly beyond MRC's remit.
- **UK Public (beyond MRC's remit) funders -** primarily support research beyond of MRC's remit (NIHR or Department of Health and Social Care and devolved nation health department awards, also Public Health England and NHS Trusts)

Lastly awards that secured further funding from the private sector (Private / for-profit) were assumed to have progressed out of MRC's remit. We found that 32 percent of MRC's directed translational projects had secured further funding to support work beyond MRC's remit, 27 percent of non-directed projects with translational intent had done the same, whereas just 19 percent of other MRC awards had secured similar further funding. These overall proportions were supported by the more rigorously validated sample that were interviewed, where we could examine the purpose of further funding as well as its source.

2.4 Academic impact

An important output of research is new codified, publicly accessible, scientific knowledge, this allows others to build upon progress made, avoid repeating work and opens results up to scrutiny and peer review.

In the USA the Clinical Translational Science Awards (CTSA) is NIH's most significant directed investment in translational research[xxviii]. This programme has received $4.5 billion (£3 billion) NIH support since 2006. A recent bibliometric analysis[11] of the publication output of the CTSA programme found a higher level of productivity and citation impact than was realised from NIH awards overall. The CTSA was found to have produced 66,000 publications over a ten-year period (2006 – 2016), and on average these papers were cited twice as often as expected for articles of their publication years and disciplines.

Using bibliometric analysis of publication output from the MRC translational research programme, we found that MRC translational programme publication output compares favourably with the results from the rest of the MRC portfolio, and against output from similar NIH and Wellcome research portfolios (see Table 2.2 below). Contrary to earlier expectations, research from translational projects generally gave rise to high impact publications.

Table 2.2 Normalised citation score of papers from MRC/NIH/Wellcome research (2008 – 2015)

	MRC	NIH	Wellcome
Full portfolio	**2.03**	**1.71**	**2.08**
Exclusively papers linked to translational grants	1.98	1.73	2.09
Exclusively papers linked to non-translational grants	1.87	1.70	2.05
Papers linked to both translational & non-translational grants	2.70	2.18	2.77

Source: computed by Science-Metrix using data from WoS (Clarivate analytics), NIH RePORTER, Europe PubMed Central, and UKRI Gateway to Research

[11] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6028299/

2.5 Publications cited in guidelines, patents and clinical trials

We explored whether MRC papers are cited in clinical guidelines, patents or clinical trial protocols, as a proxy for uptake of MRC funded knowledge into clinical practice, intellectual property or new clinical studies. This measure was of interest especially where schemes aimed to develop biomarkers, measures, data sets, or methods to enable or support other translational research and development.

Analysis of the publication output of MRC awards suggests that the uptake of these papers in NICE guidelines, patents, and clinical trials is in line with the citation of NIH and Wellcome associated papers. Table 2.3 below shows that, e.g. 2.7 percent of MRC associated papers in the health sciences, published between 2008 and 2015, are cited by clinical trials indexed in ClinicalTrials.gov. This compares well with rates of 2.4 percent of NIH associated papers and 2.0 percent of Wellcome associated papers. Normalising by year against all health sciences papers indexed in the Web of Science for that period, gives the MRC a score of 1.66, where 1.0 is the world average and the NIH and Wellcome scores were 1.49 and 1.27 respectively. Across four categories of policy document citation, it is only in US patents where the MRC supported publications underperform those of the other two funders, and even here the MRC papers score well above world averages.

Table 2.3 Direct uptake of papers into clinical guidelines, patents and clinical trials, comparison across funders

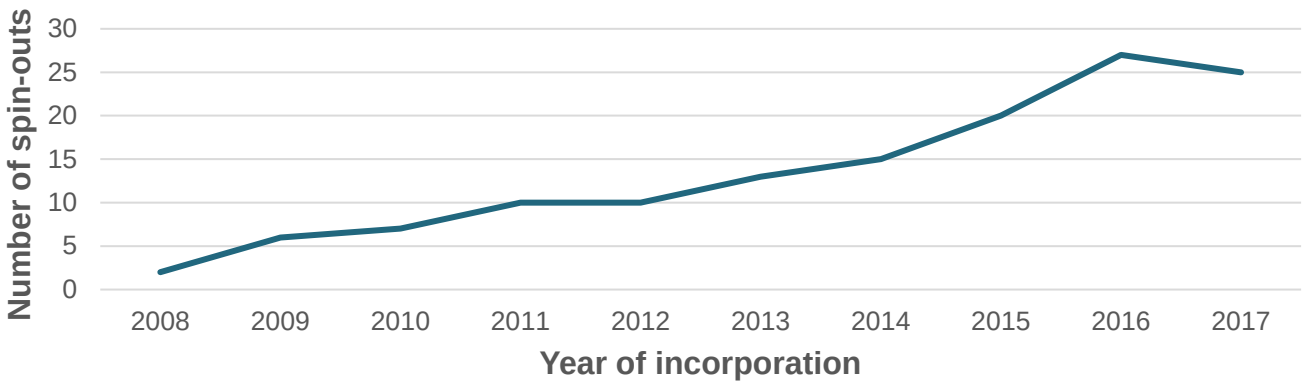
	Share of papers cited (percent)			Normalised (by year) share of papers cited		
	MRC	NIH	Wellcome	**MRC**	NIH	Wellcome
NICE guidelines (2008-2013)	**0.6**	0.3	0.4	**1.44**	0.69	0.84
USPTO patents (2008-2011)	**5.8**	9.5	6.6	**1.68**	2.76	1.95
EPO patents (2008-2011)	**3.2**	3.0	2.7	**2.60**	2.46	2.19
Clinical trials indexed in ClinicalTrials.gov (2008-2015)	**2.7**	2.4	2.0	**1.66**	1.49	1.27

Source: Computed by Science-Metrix using data from MRC, UKRI Gateway to Research, EPMC, NIH RePORTER, PlumX, PatStat and the WoS (Clarivate Analytics). All data represent papers indexed in the Health Sciences

2.6 Evidence of commercialisation

Finally, we can connect MRC funded projects to the establishment of new spin-out companies. The establishment of spin-out companies can be an important step toward taking new products to market, and we can discover a lot about the further development of these ideas by how the spin-out company performs and attracts further investment. Researchers report links between their work and new spin-outs via Researchfish®, and the MRC has maintained a dataset of these, supplemented with desk research to validate the links between MRC projects and companies[xxix]. Between 2008 and 2017, a total of 134 spin-outs were attributed to MRC projects (up to March 2018). Figure 2.3 below plots the incorporation of these companies over time. 124 of these companies remained active in 2018 with 92 percent incorporated in the UK. Putting this in context, data from the Office for Life Science (OLS) Bioscience and Health Technology Database indicate that 1,982 companies active in the biotechnology and medical technology sectors were incorporated over the same period (55[12] of these were spin-outs attributed to MRC translational research funding). On an illustrative basis, this indicates that 3 to 6 percent of new enterprises formed in the sector since 2008 have emerged from MRC funding.

Figure 2.3 Number of spin-outs attributed to MRC funded science since 2008, by year of incorporation



Source: MRC spin-out database, Companies House. The data excludes spin-outs established in 2018 as these were not yet fully captured in the monitoring information owing to reporting lags (15 were reported in the data available at the time of writing, though based on past patterns of reporting this is broadly consistent with figures for 2017 available in March 2018).

Section 3 provides detail concerning the breakdown of spin-out companies arising from the directed and non-directed portfolios and an estimate of the value of these companies.

[12] While the OLS Bioscience and Health Technology Database is the best available register of firms active in the life science industries, it is not complete and not all spin-outs from MRC funded research are captured in the database.

2.7 Section summary

- The MRC set out to increase the number of innovative projects developing new products and interventions. Almost a third (32 percent) of MRC's directed translational projects have progressed to secure funding to support work beyond MRC's remit and this was suggested to be the most useful proxy measure (from the point of view of the MRC) of successful translation.

- Approximately 60 percent of MRC funded translational projects had advanced to a later stage of translational development during the tenure of their MRC support. These results demonstrate that a majority of MRC funded projects are moving along the translational pathway.

- MRC translational research publication output compares favourably with the results from the rest of the MRC portfolio and output from similar NIH and Wellcome research portfolios. This indicates that the academic impact of MRC funded translational research is internationally competitive.

- Since 2008, a total of 134 spin-outs were attributed to MRC projects, a substantial effect on the UK private sector equivalent to between 3 to 6 percent of new life science companies formed since 2008.

- The MRC has regularly adapted its approach to translational research, learning from the early results of directed initiatives and incorporating this into the design of subsequent rounds of funding or the launch of new initiatives.

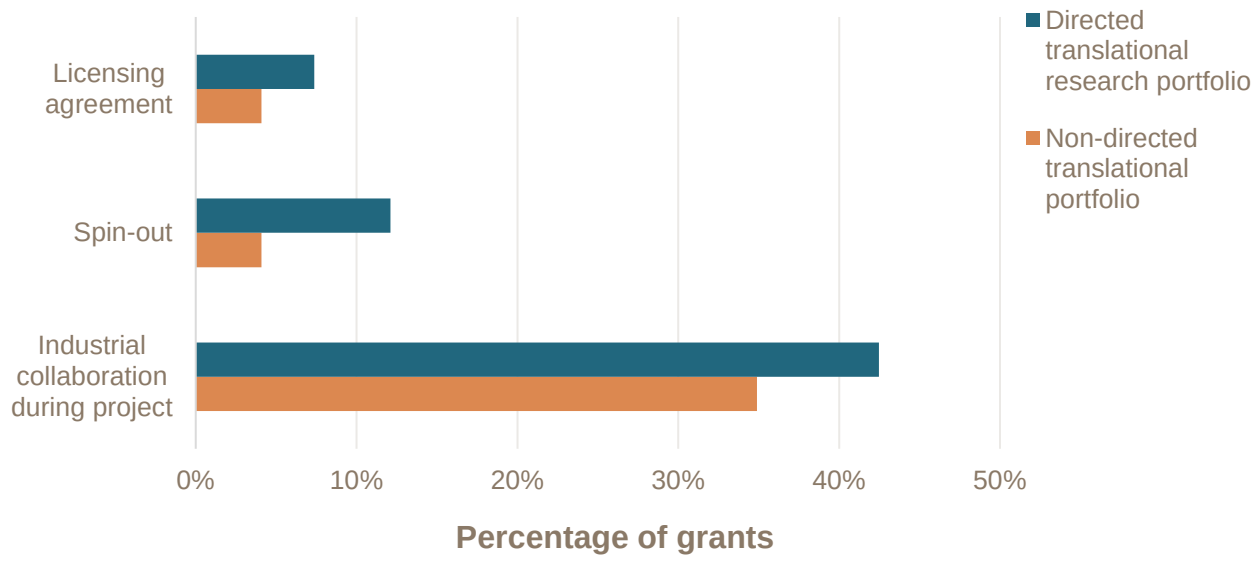
3. Effects in the private sector

This section explores the impact of the totality of the MRC directed translational research initiatives in the private sector and contrasts this with the impact from other funding.

3.1. Interactions with the private sector

Researchers funded through the directed translational research initiatives have interacted with the private sector in a variety of ways. This has included efforts to commercialise the technologies under development by establishing an external commercial vehicle (a spin-out) or reaching a licensing agreement with a commercial partner. However, investigators have also worked collaboratively with industrial partners in formal and informal ways to facilitate knowledge exchange and co-develop intellectual property assets. Figure 3.1 below illustrates the prevalence of these outcomes relative to the non-directed translational portfolio, based on interviews with principal investigators.

Figure 3.1 Interactions with the private sector, directed and non-directed translational research portfolio



Source: Interviews with principal investigators

"The MRC's funding schemes, such as the DPFS, CiC and the AZ/UCB schemes, had helped to improve this mutual understanding and openness to collaboration, and provided funding to drive the development of partnerships. Representatives from TTOs agreed that a culture change was evident in academics' views of industry collaborations, which were suspicious and standoffish in the past and are now warmer."

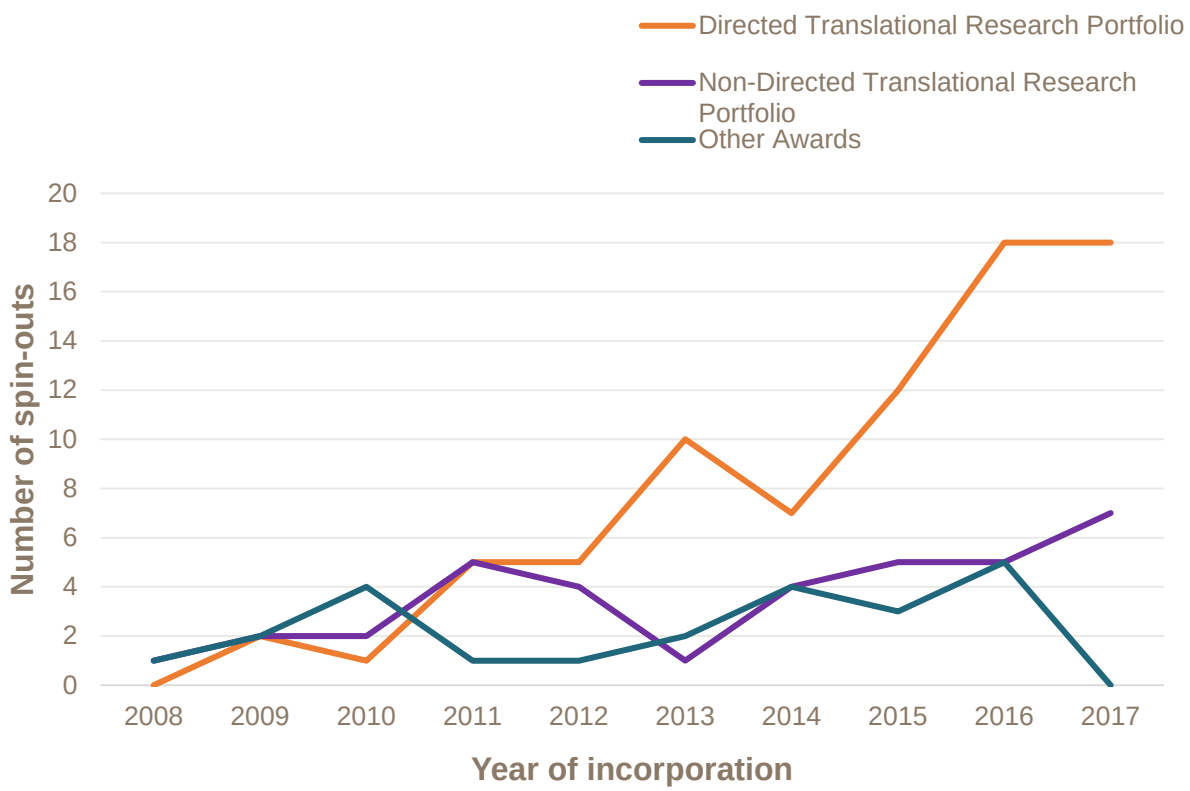
Statement from summary of key stakeholder interviews

3.2. Spin-outs

The most significant impact of the MRC directed translational research portfolio in the private sector has arisen from spin-outs established to continue the onward development of the assets supported by MRC funding. As set out in Section 2, a total of 134 spin-outs were incorporated between 2008 and 2017, linked to MRC research projects. The majority, a total of 78 spin-outs, emerged specifically from research funded through the directed translational research portfolio by the end of the 2017 (of which 72 were incorporated in the UK). As illustrated in Figure 3.2, the directed translational research portfolio has been more productive in this respect than the non-directed translational research portfolio and other awards made by the MRC. The profile of these spin-outs differed from other start-ups established in the sector since 2008[13]:

- Almost half of the spin-outs emerging from MRC funding were operating in the biopharma sector[14], relative to 17 percent in the wider sector. Advanced therapy developers were particularly overrepresented (14 percent of spin-outs versus three percent in the industry more widely).
- Most other subsectors were underrepresented, most significantly digital health (one percent of spin-outs versus 13 percent in the industry more widely).

Figure 3.2 No. of spin-outs incorporated each year, directed and non-directed translation research



Source: Researchfish®. Spin-outs from research funded through both directed translation research initiatives and other funding mechanisms are counted in multiple series.

[13] Based on analysis of the Office for Life Science's Biopharma and Medical Technology Database.
[14] Defined as manufacturers and developers of advanced therapies, antibodies, blood and tissue products, small molecules, therapeutic proteins, and vaccines

Thirty-eight of the spin-outs (49 percent) emerging from research funded through the directed translational research portfolio attracted a total of £1.1 billion (95 percent in UK headquartered companies) in external equity investment by the end of August 2019[15]. Most of this funding was raised privately, although three leading spin-outs progressed to an Initial Public Offering in which they raised a total of £275 million from capital markets. The spin-outs were collectively valued at £2.7 billion based on their most recent valuation, substantially exceeding the MRC's investment (£286 million) in the portfolio. The data gathered on these spin-outs provided some indication of the underlying patterns:

- **Advanced therapies:** The most successful companies emerging from the portfolio were developers of advanced therapies, and of the top 20 largest funding rounds over the decade, three were launched by spin-outs arising from the MRC directed translational research. The three spin-out companies attaining the highest valuations were focused on developing gene therapies for a variety of disorders (Orchard Therapeutics, NightstaRx and MeiraGTx) – see Box 5 and accounted for £2.1 billion of the £2.7 billion in economic value attained. There were signals that these firms are executing ambitions to develop vertically integrated operations (e.g. by making investments in manufacturing capabilities to support larger trial activities) which could mitigate against the possible future hazard that the long-term economic impacts are lost to overseas investors from acquisition deals.

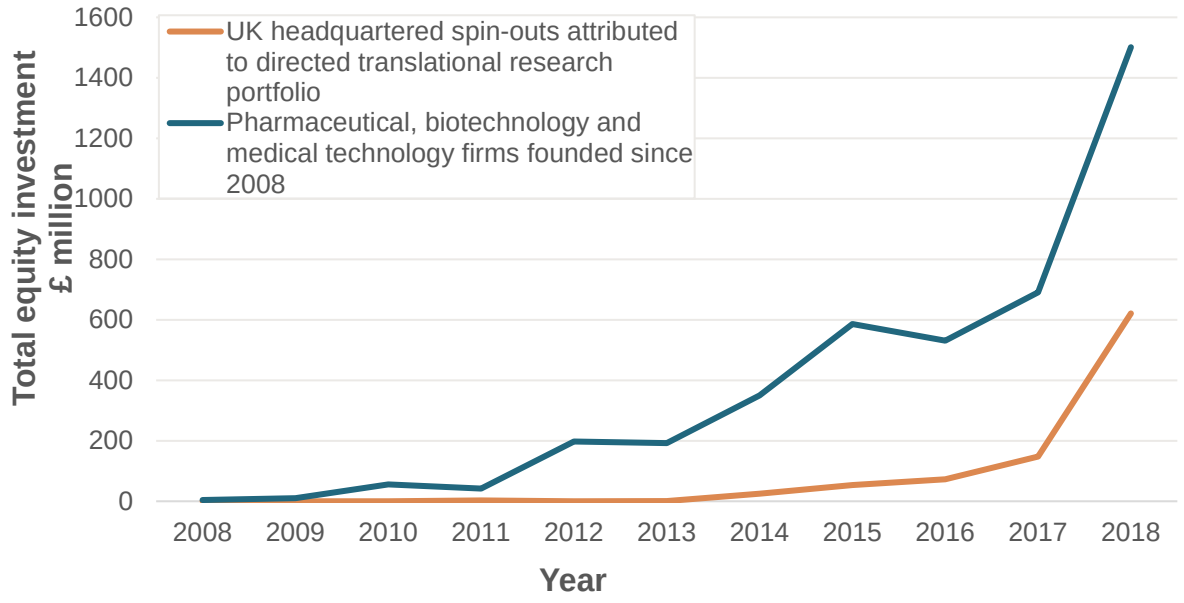
- **Nature of investors:** The spin-outs attracted capital from 205 different investors over 212 funding rounds. A third of these investors were headquartered overseas (largely in North America). University Venture Capital (VC) and investment funds, or funds targeting university spin-outs, played a significant role in capitalising spin-outs during earlier funding rounds. There was relatively little participation by generalist VC funds.

- **Regional distribution of investment:** Fundraising was overwhelmingly concentrated amongst spin-outs established in London, Cambridge and Oxford (mirroring wider patterns of VC investment in the UK). This will partly reflect differences in the characteristics of the underlying science being completed in these regions, where much of the research into advanced therapies was being completed. There are questions, however, as to whether the depth of the capital resources and investor networks outside of these hubs is enough to maximise the potential commercialisation impacts of translational research.

The spin-outs emerging from the MRC directed translational research portfolio were more likely to attract external funding – and attract funding in larger amounts – than those emerging from the non-directed translational research portfolio. This preference for the directed portfolio spin-outs is also evident when compared to other start-ups in the biopharma sector. Around 23 percent of the 36 spin-outs emerging from the non-directed translational research portfolio attracted external funding over the same period, raising £2 million on average (relative to £13.6 million). The spin-outs emerging from the directed translational research portfolio have also been significant in the recent biotechnology and medical technology start-up landscape, accounting for 21 percent of total equity investment in new entrants to the UK pharmaceutical, biotechnology and medical technology sectors in 2017 and 41 percent in 2018 (see Figure 3.3).

[15] Source: Pitchbook, 2019

Figure 3.3 Total equity investment, spin-outs attributed to the MRC directed translational research portfolio and all firms in the pharmaceuticals, biotechnology, and medical technology sectors founded since 2008 in the UK



Source: Researchfish®, Pitchbook, OLS Biopharma and Medical Technology Database

3.3 Licensing

Licensing agreements were less frequent. Interviews with lead investigators in the MRC directed translational portfolio indicated just over seven percent of projects led to a licensing agreement with an industrial partner (excluding cases where the relevant intellectual property (IP) was licensed to a spin-out company) in contrast to 12 percent choosing to create spin-outs. Interviews highlighted several commonalities that explain the relatively infrequent nature of licensing agreements:

- **Networks:** In 9 of 11 cases where the researcher was able disclose the relevant details, the relationship with the commercial partner was formed through the investigator (through prior collaborative projects or via direct approaches being made by either partner). In the remaining two cases, MRC Technology (now LifeArc) had proactively exploited their networks in industry to generate interest in the technology.

- **Patent costs:** Interviews also highlighted that licensing was considered a low value outcome, making it difficult for university Technology Transfer Offices (TTOs) to justify the ongoing costs of maintaining intellectual property rights unless a licensing agreement could be reached relatively quickly. In some cases, this led to patents lapsing after completion of the project, bringing an end to active attempts to develop the technology.

- **Level of development:** There were also several cases where discussions took place with commercial partners, but the underlying data package was insufficiently developed to justify their investment in onward development.

- **Motivations of investigators:** The interviews with principal investigators also indicated a preference for a spin-out route which afforded them greater control over the onward development of the technology.

Most of these licensing agreements were made with SMEs (9 in 12 cases), with the remainder being reached with large pharmaceutical companies. The licensing agreement generally led to further investment in the development of the underlying technology, though investigators were generally unable to describe the details of the agreement and value it had (or would) generate. In two cases, the licensing agreement led to the technology being shelved due to unconnected changes in company strategy (e.g. withdrawal from a disease area), creating some challenges for TTOs in reclaiming control of the IP rights.

3.4 Industrial collaboration

Collaboration with industry during the project was more prevalent in the MRC directed translational research portfolio (42 percent of projects) than in the non-directed translational portfolio (35 percent of projects). There were no cases in which the investigator had sought the involvement of an industrial partner but had failed to bring one on board, and little evidence of principal investigators seeking token collaboration with industrial partners to raise their chances for funding. The elevated level of industrial collaboration was also visible in bibliometric data (see Annex A2.5), which showed that 9.5 percent of papers arising from the directed translational portfolio involved co-authorship with industry (relative to 7.6 percent of those from the non-directed portfolio[16]).

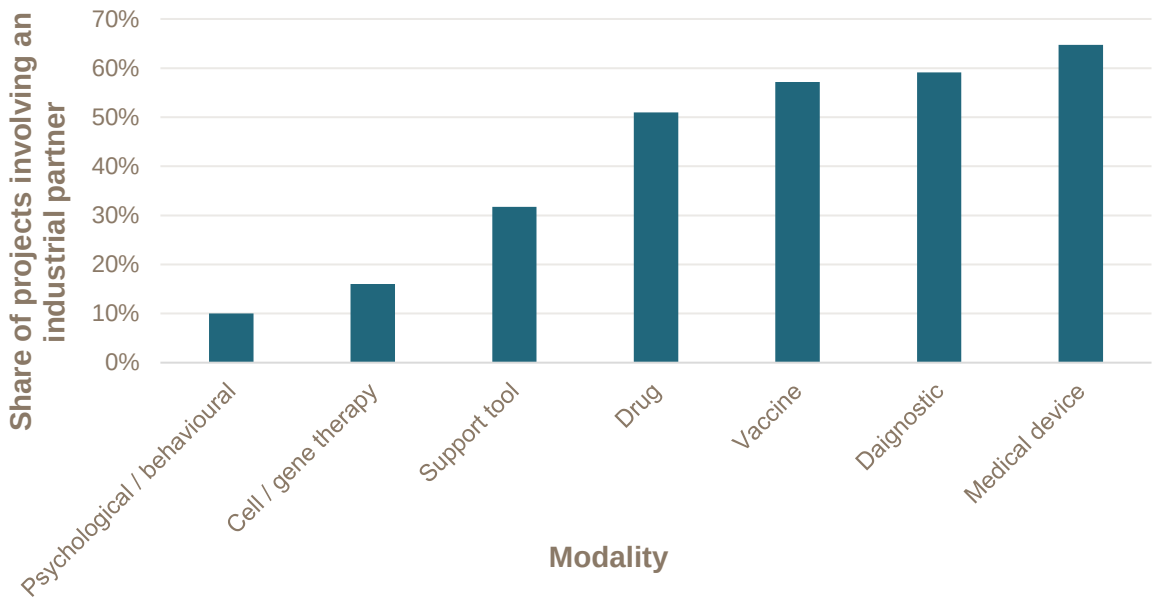
> "The boundary between industry and academia has become more 'porous', with better engagement from both sides and an enhanced understanding of the value each can bring to one the other. Academics now also have a better understanding of the importance of factors associated with commercialisation such as IP compared to 10 years ago. Academia can access some of the industrial R&D infrastructure, which was not the case 10 years ago."

Statement from summary of key stakeholder interviews

As can be seen in Figure 3.4, industrial collaboration was most prevalent for those projects involving a traditional product development pathway, and least prevalent for those projects aiming to produce translational outputs with public good properties (e.g. methodologies, tools, and psychological or behavioural interventions). Projects involving a focus on advanced therapies involved comparatively low levels of industrial collaboration, perhaps reflecting the comparative novelty of the technologies and the elevated level of commercial risk attached to their exploitation.

[16] This can also be benchmarked against Wellcome and NIH papers with translational intent.

Figure 3.4 Rates of industrial collaboration by modality



Source: Interviews with principal investigators

The range of industrial partners involved and motivations for collaboration was diverse:

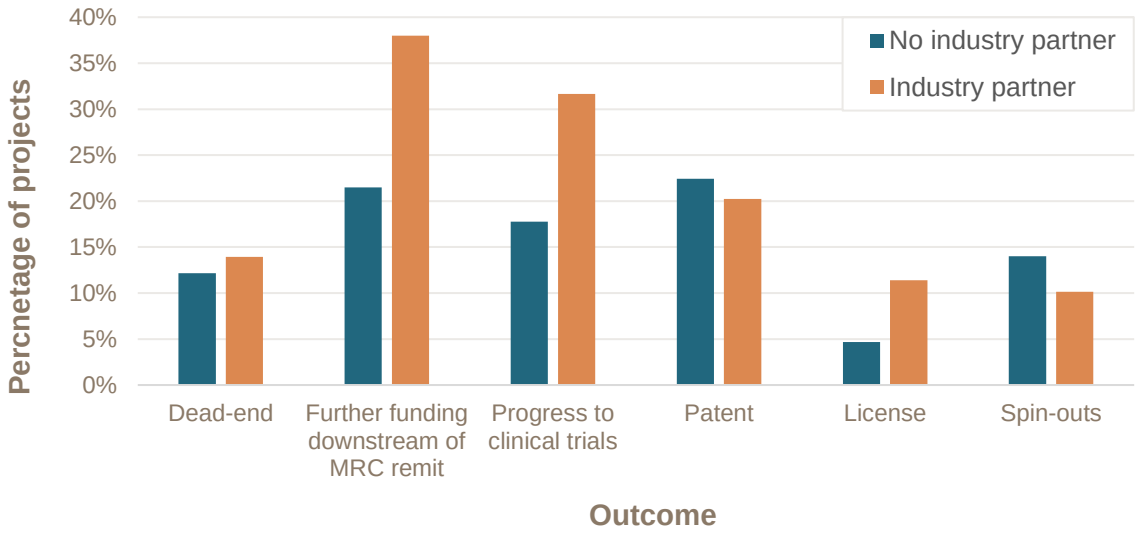
- **Collaboration with Small and Medium size Enterprises (SMEs):** In 22 percent of project relationships were formed with small biotechnology or medical technology companies. These were generally collaborative endeavours in which the academic team was working with the SME to develop a new product.

- **Large pharmaceutical firms:** Around 10 percent of projects involved a large pharmaceutical company. These relationships typically involved the academic research team reaching into the commercial sector on an informal basis to obtain inputs needed to progress the study. There were few examples of active co-development, possibly because the research was at too early a stage to attract industry interest.

- **Other large firms:** A further 10 percent of projects involved collaboration with multinational engineering companies or medical technology companies. In half of these cases, the investigator was working collaboratively with the company to develop a new device or application. In three further cases, the company was brought in to provide manufacturing capabilities to produce prototypes or because they produced the key inputs on which the project depended (e.g. MRI scanners).

Figure 3.5 below shows that if industrial partners were involved in projects, these projects were more likely to secure funding beyond MRC's remit, licensing and progress to clinical trials but less likely to secure patents or create spin-outs. Additionally, the involvement of a private sector partner slightly increased the likelihood that projects would be identified as not viable (dead-end). There was a variety of underlying patterns in the data.

Figure 3.5. Outcomes of directed translational portfolio with and without industry partners



Source: Interviews with principal investigators

- **Large and small firms**: Different patterns of collaboration were observed with large and small firms. Smaller firms often had a direct stake in the product or asset being developed as commercialisation partners, whereas larger firms were more often seen to engage in more long-term partnerships with discovery teams considered relevant to their strategic priorities.

- **Role of IP in collaborative projects:** The success of projects involving collaboration with industry in new product development appeared to be influenced by the background IP status of the project. Projects progressed more rapidly when the IP was held by the researcher or where there was no background IP.

- **Inherent risk of working with industry:** One issue emerging from the interviews was that the involvement of industrial collaborators did not always survive the duration of the project. In 20 percent of cases involving industrial collaboration, the collaborator disengaged with the project. Where large firms were involved, their withdrawal was connected to a change in strategic direction on the part of the company for reasons unconnected to the project (e.g. decisions to withdraw from the UK). SMEs withdrew for more diverse reasons including frictions with the academic team, because the investigator decided its involvement was no longer needed, or because it ceased trading. As the investigators were frequently dependent on the industrial partner to take the project forward, this created risks that were not present in projects that solely taken forward by academic research groups.

- **Creating new markets:** It should be noted that the most significant commercial successes have come in the field of advanced therapies where industrial collaboration has been least prevalent. These outlying successes indicate MRC funding for translational research may have its greatest direct economic impacts where resources are channelled into areas of novel science which are deemed too risky for the private sector and the commercialisation pathway is unclear.

3.5 Section Summary

- Projects supported under MRC's directed translational research initiatives have involved private sector collaborations, generated knowledge that has been commercialised via the establishment of spin-out companies, and licensed intellectual property to a greater extent than non-directed translational MRC projects. This provides evidence that the MRC's directed initiatives have encouraged expansion in productive academic / private sector interactions.

- Over half of all MRC attributed spin-out companies trace their origin to a project supported under a directed translational research initiative, and the situation as of 2018 was that these companies included the most highly valued companies. This demonstrates the significant success that directed schemes have had in generating results that are suited to a commercial development route.

- While most of the value of the portfolio of companies was concentrated in a small number of firms, MRC linked spin-out companies secured over 40 percent of investment in start-ups in the sector, established since 2008, a substantial slice of UK activity in 2018 and underlining the importance of these MRC linked companies in the current UK life science landscape.

- One third of the investors in these firms were based overseas. The remainder largely came from UK university raised funds, and the greatest availability of these funds is in the Oxford, Cambridge and London regions. This means that for university spin-out companies to grow, there is an advantage to locating in these regions, and at least one example of a company re-locating from the Midlands to the South East to enhance opportunities for investment was identified.

- Advanced therapies were particularly overrepresented in the MRC-linked spin-out companies (14 percent of spin-outs versus three percent in the industry more widely) this appears to be a result of the sustained long-term support MRC has provided to this field and pivotal set of contributions that these projects have made. Other subsectors were underrepresented, most significantly digital health (one percent of spin-outs versus 13 percent in the industry more widely) an emerging and fast-growing sector. This may highlight an opportunity for the MRC to encourage the translation of results from recent investments in data science and to increase partnership with the digital health sector.

- A diverse range of industry partners were involved with MRC supported projects and projects with private sector collaboration were more likely to secure funding for later phase translational work and progress to clinical trials. However, industry partnerships did not always survive the duration of the project

4. Impact of MRC focused translational research

This section provides an overview of the outcomes and impacts of the focused translational research portfolio. This portfolio includes the Development Pathway Funding Scheme (DPFS), the Confidence-In-Concept programme (CiC), and a share of the projects funded under the Regenerative Medicines Research Committee (RMRC). The results are largely based on in depth interviews with 91 principal investigators awarded funding through these programmes, triangulated with analysis of secondary data and wider stakeholder views where appropriate. The projects sampled under DPFS and the RMRC were broadly representative of the overall portfolio. While a very small proportion of the CiC portfolio projects were interviewed (20 out of 625 cases), an extensive output survey was completed for all 625 projects.

The DPFS is an open competition to support work in any disease area or therapeutic modality and is intentionally not restricted to ideas emerging from previous MRC grants. DPFS projects are required to set out up to four milestones plus expected project outcomes against which the MRC will assess progress to maximise the chances of success across the portfolio, enabling closure or re-direction of projects once active. In addition, the funding panel may suggest enhancements to proposals.

> "The DPFS review panel, which includes individuals with high-level industry, VC, basic research and clinical research expertise and in-depth knowledge of product development and translation processes, was viewed as the main enabler of DPFS's success."

Statement from summary of key stakeholder interviews

CiC awards are made to research organisations to support a portfolio of projects, the decision as to which specific projects are supported is devolved to those institutions. The institutions are expected to establish processes for the assessment of proposals, agreement of appropriate milestones and management of projects against these milestones.

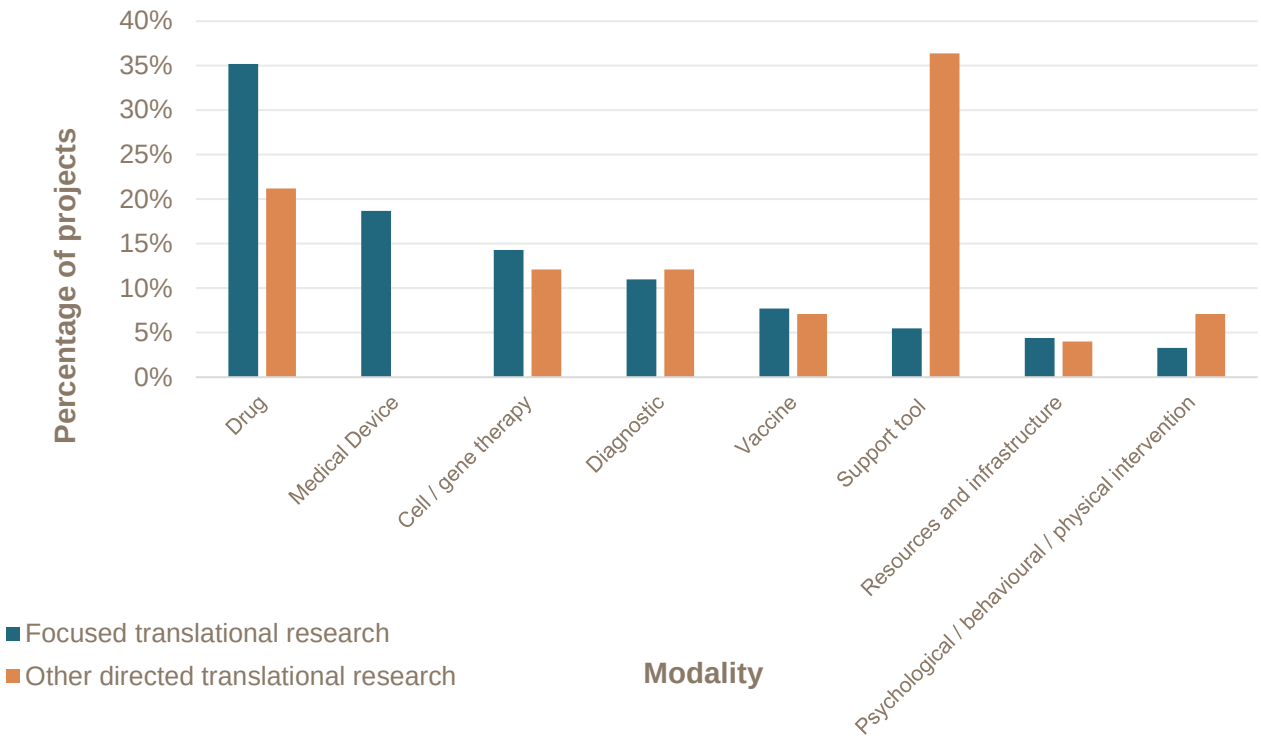
> [CiC was important in] Enabling testing of ideas emerging from discovery science, steering further efforts (with fast failure as a positive outcome) [and] Allowing universities to support multi-disciplinary and high-risk projects (for which there is often no clear route to funding)

Statement from summary of key stakeholder interviews

4.1. Characteristics of projects

The projects funded under this portfolio were predominantly on a product development pathway and unlike other directed mechanisms for supporting translational research, there were few projects that were focused on provisioning of public goods (e.g. knowledge-based outputs aiming to influence clinical guidelines or provide tools to enable more effective translational research). These patterns are clear in the Figure 4.1, which illustrates the distribution of projects by modality across the focused and other elements of the directed translational research portfolio (the high share of support tools in the latter is attributable to the large number of projects that have been funded through the Methodology Research Programme). Further distinctions between the directed translational sub-portfolios are detailed in section 5.

Figure 4.1 Share of projects by modality, focused translation and other MRC directed translational research



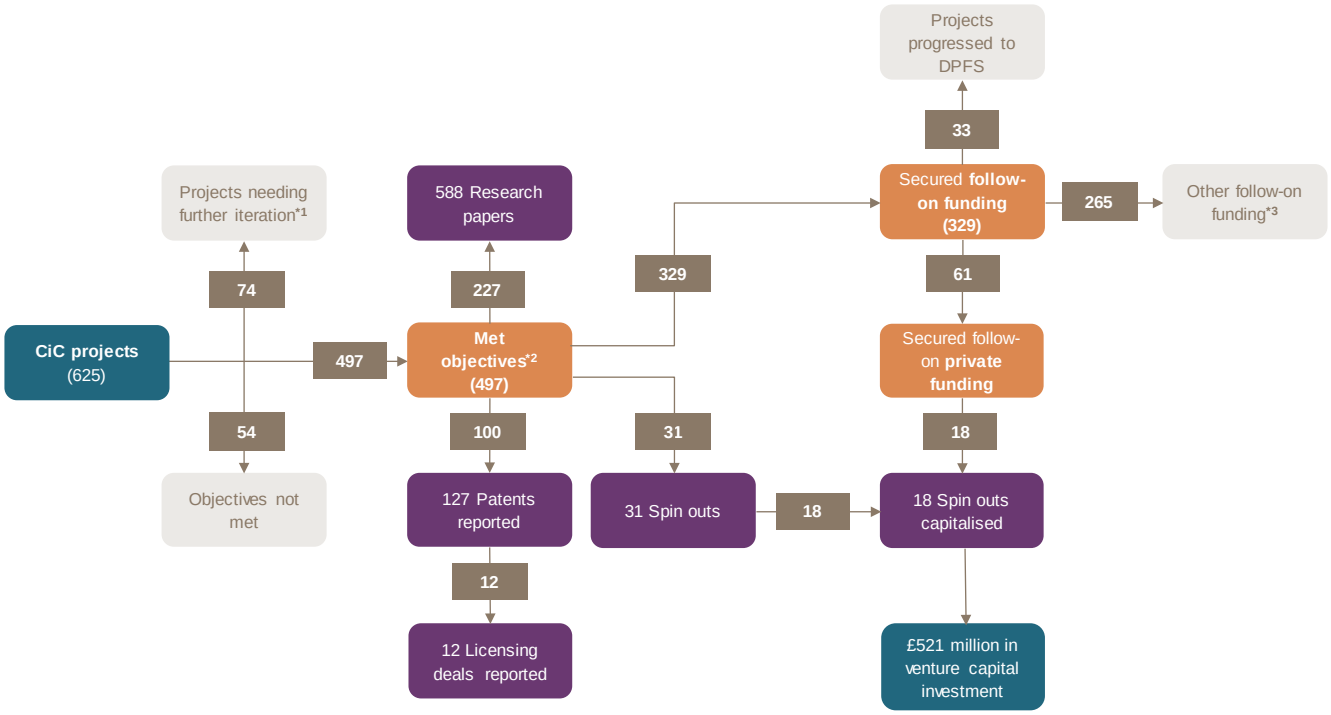
Source: Interviews with principal investigators. Analysis of the overall focused portfolio shows a similar distribution of projects by modality

Universities across the UK are represented in the focused portfolio, 62 percent of projects in the sample were led by researchers based outside of London, Cambridge, or Oxford. However, the 38 percent of projects carried out at institutions in the London, Cambridge and Oxford regions tended to begin at more advanced stages of initial development at the point of award than those from other universities. There was also a greater prevalence of projects focused on the development of advanced therapies (30 vs 8 percent), while projects at institutions outside of these regions were more likely to focus on small molecule or protein / peptide-based therapeutics and medical devices.

4.2. Overview of outcomes

The diagrams below provide an overview of the outcomes associated with the CiC (Figure 4.2) and the DPFS and RMRC programmes (Figure 4.3). The former draws on annual reports provided by institutions awarded CiC funding in which they provide comprehensive details of their outputs. The latter is based on the interviews with lead investigators. Illustrative case studies of individuals are provided to highlight differences in the types of the projects funded under CiC (Box 5) and DPFS (Box 6).

Figure 4.2. Outcomes associated with the Confidence-in-Concept programme



*1 Includes projects noted as "partially meeting objectives" or "requiring further iteration"
*2 Projects that met their objectives may have dismissed or provided confidence in the concept.
*3 Includes 67 projects that gained further MRC funding

Source: Annual Reports provided by recipient institutions

Box 5. MRC Confidence in Concept (CiC) scheme

Small (average £50k) short-term (6 to 12 month) milestone driven studies to provide confidence in a concept and thereby the foundation for a larger scale research project.

Example: To optimise the preparation of cancer immunotherapeutic T-cells. A CiC project (£82k) in 2014 enabled the development of a GMP protocol for the isolation and culture of gamma delta T cells, a rare type of T cell found to be involved in a wide range of immune responses. New immunotherapeutic approaches for cancer treatment, using genetically engineered T-cells (CAR-T cell therapy) have recently gained market authorisation and this has focused attention on the potential for gamma delta cells to offer improvements over the more common T-cell types. The positive results from the CiC project; that demonstrated for the first time that these cells could be isolated, cultured free of contaminating tissue and remained viable, strengthened the foundations for a spin-out company established by the Francis Crick Institute, Kings College and Cancer Research UK (GammaDelta Therapeutics). Abingworth and Takeda Pharmaceuticals have now invested $100 million in the company to utilise these cells in Phase I clinical trials.

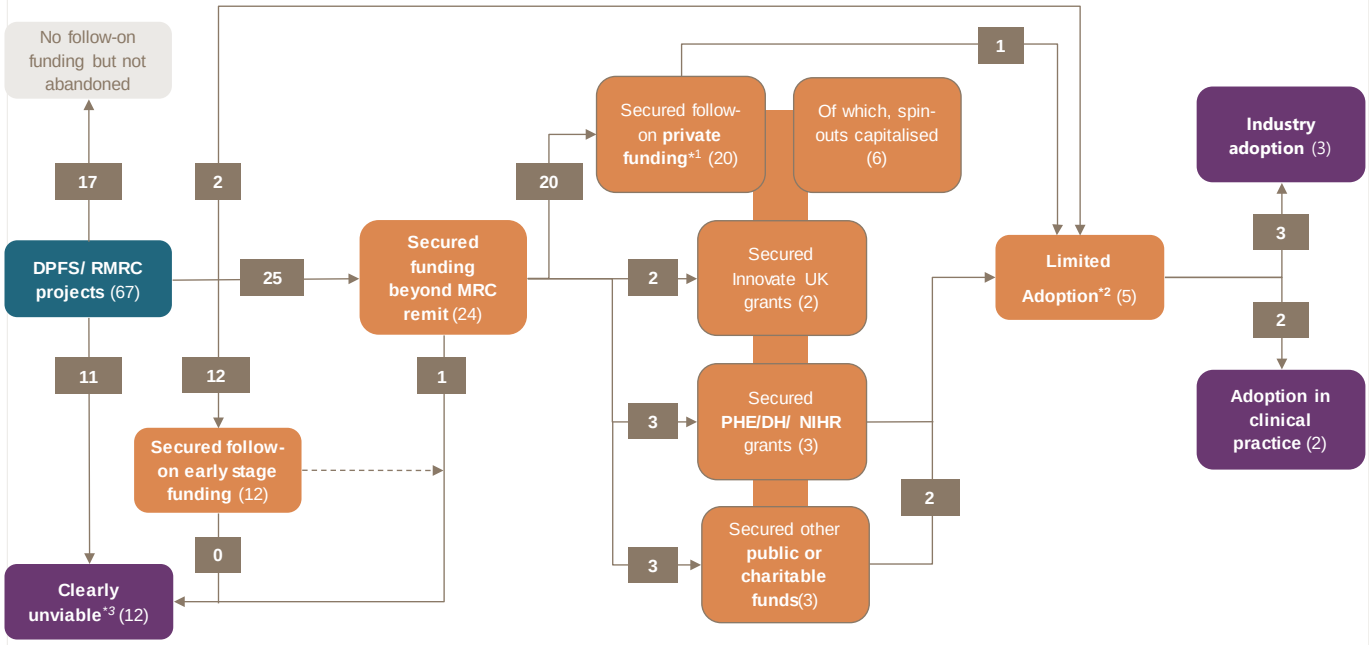
[On CiC driving culture change] “CiC is an important pump-priming scheme which is delivering significant outputs. As a knowledge exchange professional from an academic institution commented: I started with an institute with no translation, now, about 50% of the principal investigators engage in translation.”

Statement from summary of key stakeholder interviews

“The devolved nature of the scheme was particularly valued, allowing universities to identify and play to their strengths, as well as holding them responsible for engaging in TR. This incentivises institutions to enhance their translational capacity and skills, and to build connections to other players in the TR ecosystem, e.g. industry and investors. “

Statement from summary of key stakeholder interviews

Figure 4.3. Outcomes associated with the DPFS and Regenerative Medicine Platform



*1 *Includes follow-on funding from industry for further research, licensing outcomes where there is evidence that the licensee has invested resources in taking the project further, and spin-outs that have been capitalised by external investors.*

*2 *“limited adoption” refers to a mix of small-scale adoption (e.g. in a single / small number of centres outside the originating team) or interventions such as mobile apps at a national scale.*

*3 *“clearly unviable” refers to researchers reporting that the project has been abandoned.*

Source: Interviews with principal investigators

Box 6. MRC Developmental Pathway Funding Scheme (DPFS)

Average £1 million projects of 3 years duration to support the pre-clinical development and early clinical testing of novel therapeutics, devices and diagnostics, including "repurposing" of existing therapies.

Example: Development of an AAV vector for treatment of inherited retinal dystrophy caused by RPE65 deficiency

MRC DPFS funding (£300k) in 2011 supported critical work that enhanced viral vectors for delivering genes to the retina, with the aim of treating inherited blindness. DPFS funding at this pre-clinical stage supported several patentable modifications that improved the efficiency of transgene expression levels. The results were confirmed by *in vitro* and *in vivo* testing and then progressed to clinical trials, two of which were funded by the MRC (total £5 million). This line of gene therapy research had been funded by the MRC and others since 2004 (£10 million in total MRC support) and following the successful completion of this specific DPFS project in 2013, four programmes (two in Achromatopsia, two in Retinitis Pigmentosa) utilising the viral vector that had been developed were transferred to the UCL spin-out company MeiraGTx (now a publicly traded company valued at $450 million). The first patients enrolled in the clinical trials have benefitted from significant vision restoration.

"[DPFS] The scheme was seen as having assisted in improving collaboration between academia and industry, changing academic researchers' attitude towards translational research, and upskilling of academic researchers."

Statement from summary of key stakeholder interviews

4.3 Progression

The evaluation validated a wider body of research that shows translation is a long-term process. Projects funded in this portfolio were typically built on an underpinning platform of fundamental research and early stage laboratory work, and on completion, would almost always still require substantial further refinement before the underlying technologies could be adopted into health systems. The progression of projects along this continuum was understood by allocating each technology to a translational development stage as discussed in section 2. Stages were assigned to projects at the point at which MRC funding was awarded (from the project application details and interview), at the end of the grant, and at the time of the interview (capturing any follow-on development after the grant was complete). Analysis of the interviews indicated:

- **Progression through the development pathway:** Twenty-eight percent of projects continued to progress further along the development pathway after the MRC funded award was complete. The most rapid progression to clinical practice was observed amongst projects focused on developing of psychological, behavioural and physical interventions and support tools. Basic measures of progress appeared to show that projects carried out at all UK institutions progressed at a similar rate.

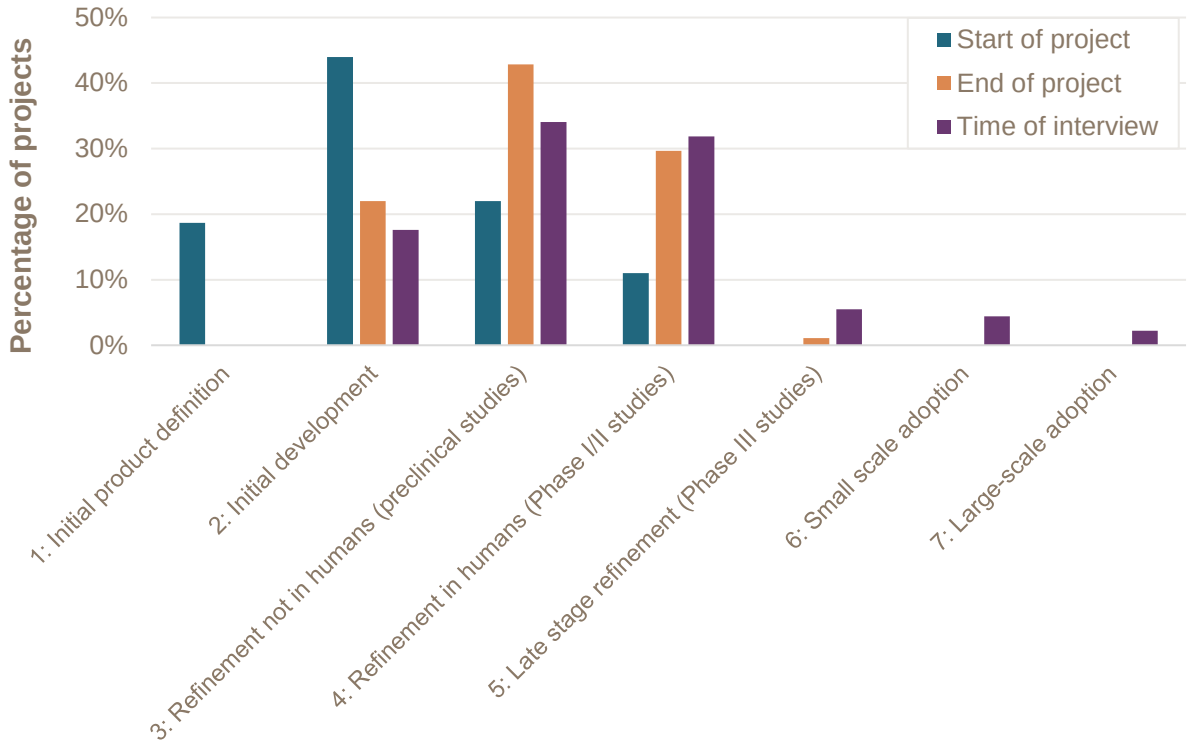
- **Clinical trials:** Ten percent of projects sampled (nine cases) progressed to Phase I or II clinical trials (excluding cases where the MRC funded early stage trials as part of the project itself). A further five percent of projects progressed to later stage (Phase IIb / III) trials (four cases). Two of these involved the development of digital applications to support remote data collection to support the management of health conditions, and there were two cases of small molecule pharmaceuticals reaching late stage trials. These follow on clinical studies were almost

exclusively funded by the private sector, and two of the projects interviewed progressed to NIHR funding.

- **Follow on funding:** Fifty-three percent of investigators (49 of 91 cases) attracted follow on funding to support further development of the asset. In 18 percent of cases (16 of 91 cases), this funding was attracted from public or charitable sources to continue research within the broad remit of MRC (i.e. preclinical and early stage clinical studies). However, 36 percent of projects (33 of 91 cases) attracted further funding from industry sources or public sources of funding that could be considered beyond the MRC remit. Projects focusing on the development of advanced therapies were the most likely to secure further funding from the private sector.

- **Attrition:** Fifteen percent of projects (14 of 91 cases) reached a dead end. In most cases (8 of 14 cases), this was due to scientific or technical problems; e.g. where the project involved a clinical trial failing to demonstrate show safety or efficacy. In 4 of these 14 cases, the product was shelved for commercial reasons (i.e. the commercial case for the product was insufficiently strong or a competing treatment had emerged). The progression of focused projects was constrained by similar economic issues in 10 out of the 91 cases overall.

Figure 4.4. Progression of projects through the development pathway



Source: Interviews with principal investigators

4.4 Commercialisation outcomes

The focused portfolio was the most significant driver of the commercialisation outcomes described in Section 3. In terms of commercialisation outputs (based on comprehensive data covering the portfolio overall), the focused portfolio led to:

- 68 spin-out companies incorporated to exploit the results of research funded through the focused portfolio (note that the underpinning research may also have been supported by other initiatives);
- 32 of these companies raised some investment, and a small number raised significant investment, with a total of £1.1 billion of external equity investment secured by these firms since being founded. Three companies progressed to an Initial Public Offering (IPO).
- These companies were valued in total at £2.7 billion and account for over 99 percent of the economic value arising from the directed translational research portfolio.
- Licensing agreements were comparatively infrequent, for reasons described in Section 3.

4.4.1 Attribution to MRC funding

Development from discovery to clinic is a long and involved process which requires support from many public, charity or private sources. DPFS provides an injection of funds at a critical point in the translation process and there is a question as to what outcomes would have occurred in the absence of this funding. More detailed statistical analysis[17] focused on comparing marginal applicants to the Development Pathway Funding Scheme (DPFS)[18] around the threshold for funding was completed to examine what may have occurred in its absence (using administrative data that supported coverage of all applicants for funding). The main findings of this analysis are illustrated in Figure 4.5 and summarised below:

- At the margin, the DPFS did not have a statistically significant effect on the overall likelihood an investigator founded a spin-out to progress development of the technology under investigation.

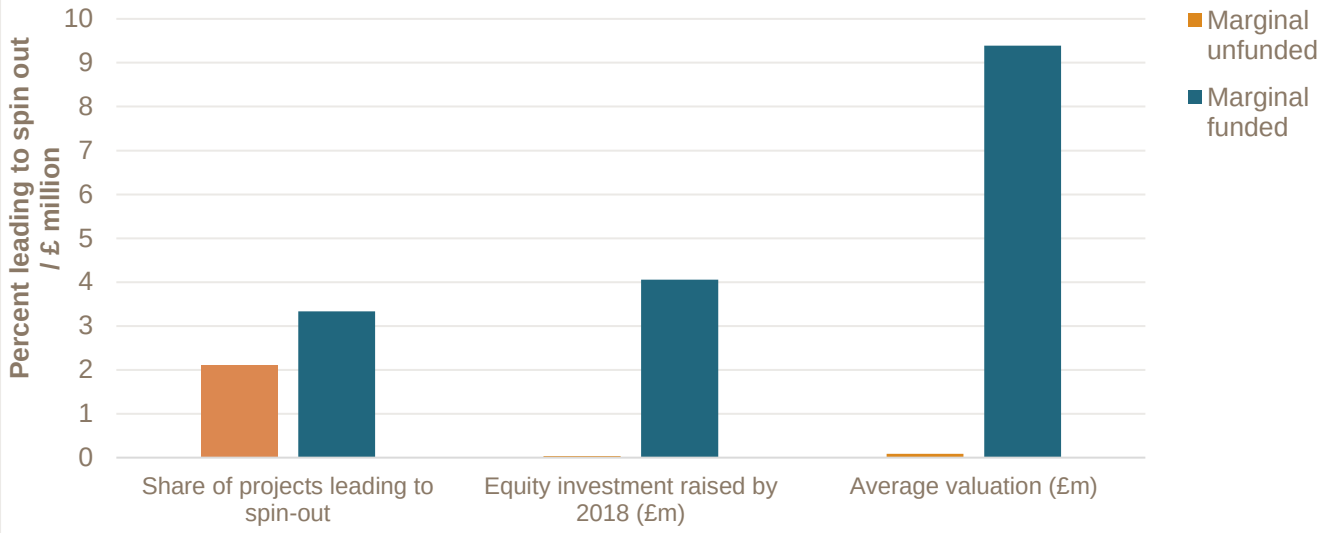
  The DPFS had a causal role in enabling spin-outs to secure equity investment and in raising the underlying value of the spin-out. At the margin, those investigators receiving an award from DPFS raised an average of £4.0 million in equity investment relative to just £40,000 amongst those who were declined funding. The average valuation of firms established by Investigators awarded funding was £9.4 million relative to £90,000 amongst those declined funding.

- The DPFS is a central driver of the commercialisation outcomes described in the preceding passages, and this suggests that a significant share of the overall economic outcomes associated with the MRC's investments in translational research would not have occurred in its absence.

- One possible explanation for this is that the de-risking of the technologies achieved with DPFS funding is critical in enabling spin-outs to leverage enough private funding to make significant further progress and attain higher valuations. If researchers cannot find equivalent alternative sources of funding in the academic sector, they may establish spin-outs before they are ready (for example, if the data package is insufficiently complete), and struggle to realise the potential value of their intellectual property assets.

[17] See Annex A2.7
[18] This analysis focuses on the DPFS as the data on declined applicants needed was not available for other initiatives.

Figure 4.5. Comparisons between marginal applicants to DPFS



Source: MRC monitoring records, Companies House, Ipsos MORI analysis

4.4.2 Commercialisation skills

If projects are on a commercialisation pathway, then their success will be predicated on the strength of the commercial case for the underlying product. However, the progression of projects was constrained by the economics underlying the projects in around one in ten projects. For example, one team developing a biosensor in collaboration with an industrial partner undertook a health economic analysis as the project ended. This study concluded that there was no business case for the biosensor and the industrial partner decided not to pursue it further. There were also other similar examples in the portfolio in which a greater amount of market validation ahead of the underlying research and development would have revealed concerns regarding the long-term commercial viability of the product. It should be noted, however, that the commercialisation pathway remains unclear for the advanced therapies that have driven much of the commercial value of focused translational portfolio.

4.5 Adoption and health outcomes

A small share of the projects sampled (6 of 91 projects) led to adoption by the NHS or by industry at the point of the interview and generally at a small scale. This reflects the long-term nature of the translation process described above, it was therefore not surprising that there were few examples of MRC projects leading to new interventions adopted into practice, and there is optimism that the pipeline of focused translational projects will continue to mature and yield further products with patient benefit.

4.5.1 Take-up by NHS

Three products had been adopted in the NHS (details in Box 7)

Box 7. Adoption of the results from MRC focused translational studies in the NHS

Changing Health: The research team received CiC funding to develop a digital health platform to provide personalised behaviour change programmes for Type 2 diabetes management accessible through a smartphone. The beta platform was commercialised via a spin-out (Changing Health) and has now been adopted nationwide by the NHS. An evaluation of Changing Health by Imperial College Health Partners in 2018 indicated that patients enrolled on the service saw reductions in HbA1c, BMI, and blood pressure.

Endovaginal coil: One DPFS funded project focused on refining an MRI probe to image early stage cervical cancer, with the aim of enabling fertility saving surgery. The prototype was validated during the project and is used in clinical practice at the NHS Trust associated with the principal investigator. A second device was manufactured for use in another NHS Trust. However, the device could not be commercialised, as the effectiveness of screening programmes reportedly limited the size of the potential market. No studies have been completed in terms of exploring the benefits of the device on clinical outcomes.

Affigo: MRC DPFS funding (£400k) in 2009 led to development of ClinTouch[xxx], the first mental health mobile smartphone app in the UK. The MRC funded project demonstrated that the app could promote self-management and improve outcomes for people living with schizophrenia. ClinTouch now has funding from the NHS and is implemented in the Greater Manchester area (covering 500,000 people), with global expansion to China and the US.

4.5.2 Take-up by industry

Three products had been adopted in by industry on a small-scale basis. This included two biomarker projects including a study to explore how far nerve excitability testing could be used as a translational biomarker for ion channel function, as a means of testing the action of drugs (the has since been used by large pharmaceutical companies) and second project focused on developing a methodology to simultaneously measure target proteins in a high number of samples to screen existing drugs for repurposing (which has found application in eight further academic projects). The final project involved the development of an assay to facilitate the development of a vaccine, which was reportedly planned for use in clinical trials (though there was a limit to what the researcher could disclose in this instance).

4.6 Section Summary

- The MRC focused translational portfolio mainly comprises the ongoing CiC and DPFS initiatives. 68 spin-out companies were incorporated to exploit the results of research funded through the focused portfolio (although it is important to note that underpinning research may also have been supported by other initiatives). 32 of these companies raised a total of £1.1 billion of external equity investment since being founded, with three progressing to an Initial Public Offering (IPO). These companies were valued at £2.7 billion and account for over 99 percent of the total economic value arising from the directed translational research portfolio. The conclusion is that CiC and DPFS have been a major driver of product development leading to successful commercialisation outcomes. There is also some evidence to suggest that the award of DPFS support significantly increased the value of underlying knowledge assets used to establish spin-out companies.

- The evaluation validated a wider body of research that shows translation is a long-term process. Projects funded in this portfolio were typically built on an underpinning platform of fundamental research, and early stage laboratory work, and on completion, would almost always still require substantial further refinement before the underlying technologies could be adopted into health systems. It was not therefore surprising that there were few examples of MRC projects leading to new interventions adopted into practice, and there is optimism that the pipeline of focused translational projects will continue to mature and yield further products with patient benefit.

- In the time covered by the evaluation and where this could be determined, a little under 20 percent of CiC projects progressed to secure follow on funding from the DPFS, industry or led to a spin-out. This reflects the fact that CiC projects are usually early stage, small scale and high risk. In contrast 38 percent of DPFS projects had moved along the translational pathway to a stage beyond the MRC remit. For both schemes this was considered a good rate of progression and sets a benchmark that can be revisited in future.

- Some modalities progressed more rapidly (e.g. those developing psychological, behavioural and physical interventions or support tools) due to less complex routes to adoption.

- The remainder of projects either led to further discovery science and so were still generating potentially useful insights or were reported as no longer being pursued. Reasons for projects reaching a dead end were in the main scientific or technical (e.g. failing to show efficacy in clinical studies), but a minority of projects were shelved due to it becoming clear that the economics of the approach were unlikely to be viable. These findings are important as there might be cases where the likely market for an intervention could be assessed in advance of taking a decision to fund a project. This also highlights a need for research teams to be able to access expertise to validate the market for products in preparing proposals.

5. Other MRC support for translation research

This section explores the impact of three components of MRC directed translational research portfolio: Broad, Enabling and Methodology. These mechanisms are discussed here:

- **Broad translation**: Projects designed to translate, investigate mechanisms of disease and address gaps in the underlying knowledge that is necessary to support translational research. For example, projects funded under the Experimental and Precision Medicine initiatives.

- **Enabling translation**: Projects designed to accelerate translational research focusing on new and improved tools, methods and techniques. For example, projects funded under the Biomarkers and Models of Disease initiatives.

- **MRC-NIHR Methodology Research Programme (MRP):** Projects designed to support and enable translational research by producing methods and tools as well as methodological knowledge. Including awards to establish Hubs for Trial Methodology.

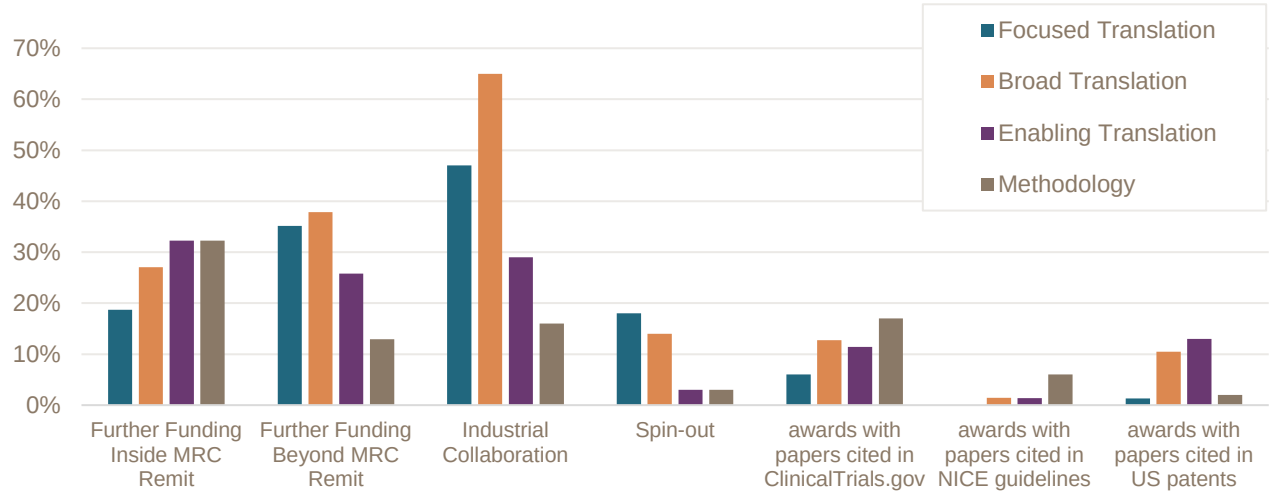
This section synthesises evidence gathered from interviews with principal investigators, bibliometrics and interviews with stakeholders in the wider translational research community.

5.1 Overview

The projects funded in the broad, enabling and methodology initiatives differ in substantial ways to those funded under the focused portfolio described in the preceding section. The projects funded under these initiatives were not expected to directly contribute to the development of a specific product, but instead the initiatives aimed to support work that provided tools for translation, or new knowledge that might be particularly applicable to translational research in industry or academia. Many projects were intended to reach an endpoint (e.g. establishment of a patient cohort or development of a new method) by the end of the grant, so the value of this research will be reflected more strongly in take-up of the resulting tools by users (academic or private sector) and the knowledge produced, rather than in further progression and commercialisation outcomes.

This is evident in Figure 5.1, which illustrates the distinct outcomes arising from projects funded via these initiatives in terms of attracting further funding from funders within or beyond the MRC remit, in terms of collaboration with the private sector, the formation of spin-out companies or the citation of their publications in clinical trials / guidelines or patents (based on interviews with lead investigators and bibliometric analysis).

Figure 5.1 Proportion of interviewed projects from the directed translational research portfolio with selected outcomes



Source: Interviews with principal investigators and bibliometric analysis

[On bridging the **Valley of Death**] … acknowledged the MRC's contribution to supporting high level discovery science to underpin translational research and providing seed funding to bridge the valley of death between discovery science and translational research, which has led to cultural changes in the research community. By investing substantial resources, the MRC was seen by several interviewees to have helped to de-risk a number of research areas such as precision medicine and regenerative medicine.

Statement from summary of key stakeholder interviews

5.2 Broad translation

Interviews undertaken with grant holders from the broad translation research initiatives within MRC's directed translation portfolio included a sample of 37 grants awarded a total of £21 million. The awards varied considerably in size, with the two precision medicine consortia awards alone totalling £2.4 million. The sample also included nine of the larger awards from the TSCRC which totalled £9 million. These TSCRC awards were determined to have a mix of discovery science and enabling objectives. The portfolio included several innovative funding mechanisms, many of which were introduced by the MRC in the latter half of the decade covered by this study which meant they had less time to develop outcomes (numbers in parenthesis state the numbers of projects examined through interview):

- **AZ Mechanisms of Disease** (Seven projects) – this initiative offered research groups the opportunity to use deprioritised compounds in pre-clinical and clinical studies to investigate mechanisms of disease and inform the development of potential therapeutic interventions[19].

[19] The AZ Mechanisms of disease was initially an arrangement brokered with AstraZeneca, this was later replaced with the MRC-Industry Asset Sharing Initiative, which added assets from six other pharmaceutical companies https://mrc.ukri.org/funding/browse/industry-asset-sharing-initiative/mrc-industry-asset-sharing-initiative/

- **Precision Medicine** (Two projects) – Complex undertakings to discover and understand clinically important disease stratification to investigate disease specific mechanisms and treatments.

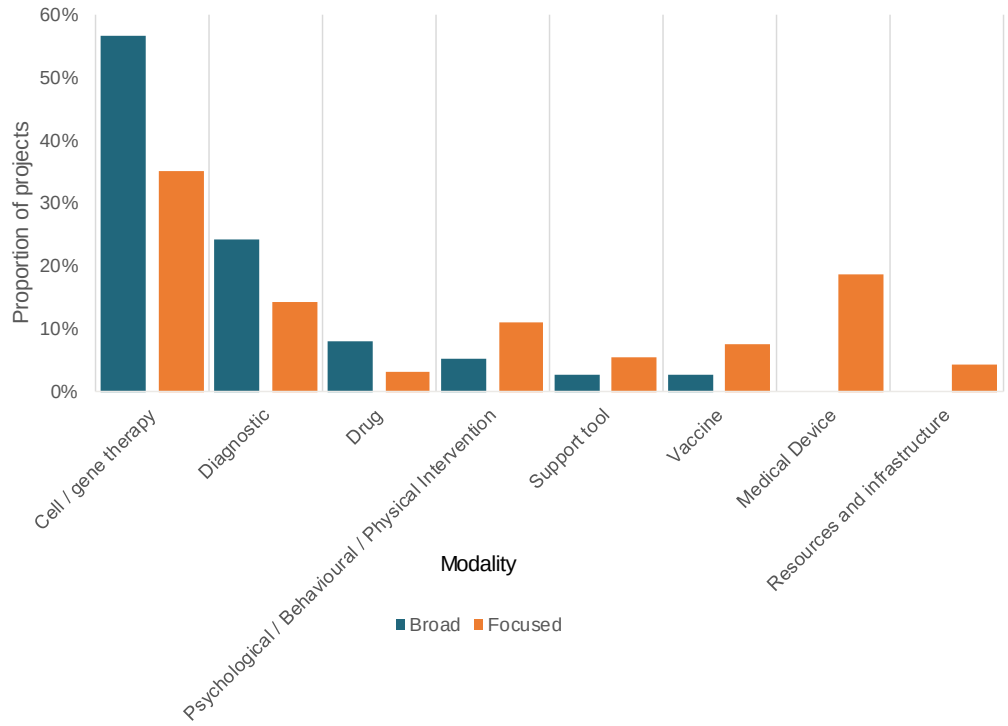
- **Experimental Medicines** (Twelve projects) – Investigations undertaken in humans to understand mechanisms of disease or provide proof -of-concept for new interventions. This initiative was later replaced with the Experimental Medicine Challenge Grants[20].

Two other initiatives were included in this portfolio: Industrial Collaboration Awards (Seven projects) and 9 projects funded through the Translational Stem Cell Research Committee were included (with four awards from this initiative allocated to the enabling portfolio).

5.2.1 Characteristics of projects

The intent of the funding calls under this group differed from the focused translation portfolio in that they had an emphasis on enhancing understanding of fundamental disease biology to inform the future development of therapeutics (rather than solely supporting product development). Aligned with this objective, the investigators for approximately a quarter of projects (10 of 37 cases) indicated their primary aim was to improve understanding of biological mechanisms. However, over half of the investigators interviewed expressed a strong interest in contributing to developing new therapies (20 of 37 cases), while a little under a quarter (7 of 37 cases) had elements of both. The initiatives also differed from the focused portfolio in terms of modality (see Figure 5.2), with a greater percentage of small molecule and advanced therapies based-projects, and less research on medical devices.

Figure 5.2 Contrasting modalities for grants included in broad and focused portfolios



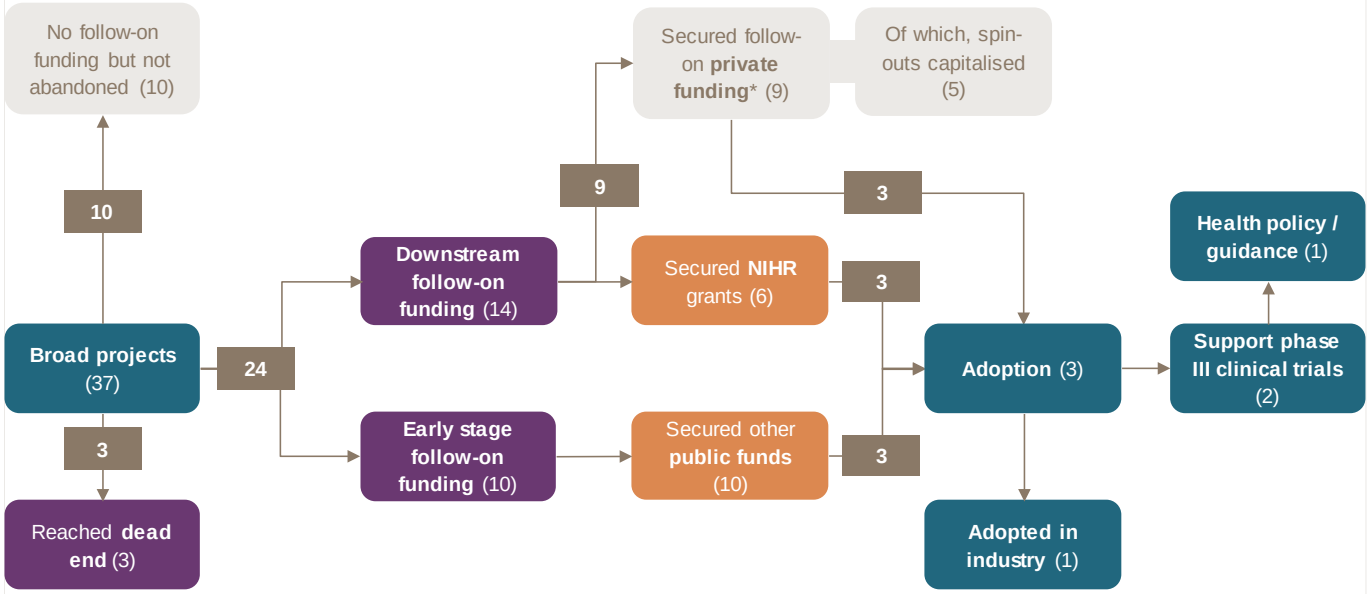
Source: Interviews with principal investigators

[20] https://mrc.ukri.org/funding/browse/experimental-medicine-challenge-grants/experimental-medicine-challenge-grants-discovery-science-in-humans/

5.2.2 Overview of Outcomes

Figure 5.3. provides an overview of progress made by the broad translational projects interviewed. It should be noted that several of the studies funded in this grouping involved clinical trials that had only recently been completed at the point the lead investigator was interviewed and, while the grant was complete, the lead investigator had not completed the relevant analysis or had only produced preliminary findings. As such, it is arguably too early to make a judgement regarding the success of many of these projects.

Figure 5.3 Impacts of grants funded under broad translational portfolio



*Includes follow-on funding from industry for further research, licensing outcomes where there is evidence that the licensee has invested resources in taking the project further, and spin-outs that have been capitalised by external investors.

Source: Interviews with Principal Investigators

In terms of the outcomes associated with this groups of projects:

- **Further funding:** 38 percent of projects attracted funding that could be considered beyond MRC's remit and 27 percent secured funding to do further work within MRC's remit, in both cases a higher proportion than in the focused portfolio. Some of the projects in the portfolio required both further experimental studies to test understanding of biological mechanisms and further clinical work in more robust and larger trials, before industry were likely to consider funding further development.

- **Private funding.** Across the broad translation grouping, 24 percent of grants received follow-on private sector funding to develop the core asset of the initial MRC grant, and 62 percent received further public funding. Eight of the nine grants receiving follow on private funding focused on therapy development, the only other grant receiving follow on private funding was a project repurposing an existing AZ compound to inhibit MMP-9 in patients with idiopathic pulmonary fibrosis which had a strong discovery science focus.

- **Funding for clinical studies:** Six projects out of 37 received follow on funding for clinical studies, a higher proportion than compared to the focused portfolio. 14 projects completed or progressed

to phase II clinical trials, while two grants progressed to Phase III trials. These clinical studies included work on:

- A behavioural / psychological intervention using virtual reality to overcome Self-Critical Attitudes
- Cannabidiol as a novel therapeutic agent for patients at high risk of psychosis
- A combined allergen immunotherapy and antibiotic approach for the treatment of chronic atopic dermatitis
- A stem cell-based treatment strategy for Age-related Macular Degeneration (AMD)
- Understanding predictors of patients with early rheumatoid arthritis and stratifying the patient population

- **Citations in health policy guidance:** One of these projects led to citations in health policy guidance. It aimed to provide a proof of concept for combining anti-bacterial treatment with allergen desensitisation to improve symptoms in adult individuals with severe atopic dermatitis. Findings from the grant led the principal investigator to investigate further the role of interleukin (IL)-4 inhibitors in treating moderate to severe atopic dermatitis, and to a NICE guidance recommending the use of an anti-IL-4 compound (dupilumab).[xxxi] Alongside, the grant led to a successful Phase IIa trial to test ANB020 sponsored by AnaptysBio, a selective inhibitor of interleukin-33 (IL-33).[xxxii] Planning for a Phase IIb trial to test ANB020 is ongoing.

- **Commercialisation outcomes:** Although the projects funded had less explicit commercialisation objectives than those funded under the focused portfolio, there was still evidence of commercial outputs from the portfolio. Across the projects sampled, eight grants resulted in one or more patents being awarded on the core asset, and four grants leading to licensing agreements, and five grants resulted in spin-outs (including one emerging from investigations of a deprioritized compound described in the Box 8 below).

Box 8. Edinburgh Molecular Imaging using smart probes for in vivo imaging

Edinburgh Molecular Imaging focuses on developing small molecules and peptides that target and specifically bind with cancerous cells and other diseased tissue. The company emerged from two MRC grants, one using an existing AZ compound (AZD1236) to inhibit MMP-9 in patients with Idiopathic pulmonary fibrosis, and a second grant to develop smart probes to highlight MMP-9 and administer compounds to the target area. It has received around £15 million in public funding from the Wellcome Trust, EPSRC and three MRC grants, and has received Series A investments from Epidarex Capital, Scottish Investment Bank and Wren Capital. It is currently involved in a phase IIb clinical trial testing a novel fluorescent compound for easier and more precise localisation of colorectal cancer.

- **Knowledge spill-overs:** Of the ten projects to improve understanding of biological mechanisms in the broad portfolio, all were still producing knowledge outputs, such as publications and presentations, at the time of the interview. One project had developed a new animal model to study Hepatitis C, which has since been used to undertake mechanistic research on the Zika virus, and another contributed to the formation of Edinburgh Molecular Imaging (see box 8). In terms of knowledge outputs more widely, 13 percent of awards in the broad portfolio produced papers that were cited in clinical trials, 1 percent produced papers cited in NICE guidelines, and 10 percent produced papers cited in US patents.

5.3 Enabling translation

A sample of 27 projects awarded a total of £18 million were selected from initiatives which share the aim of enabling research translation by providing new biomarkers, models, research tools and materials (from a portfolio of 95 awards totalling approximately £75 million). The projects within this category were awarded through the following initiatives:

- **Biomarkers:** the development of potential biomarkers for their predictive and prognostic capability for the diagnosis of disease, disease heterogeneity and underlying mechanisms, susceptibility, exposure or response to interventions.

- **Models of human disease:** the development and validation of animal models for evaluation of human disease mechanism: in vivo, in vitro or in silico. Primary activity areas in the funded projects include biological and endogenous factors in the areas of detection or therapeutics.

- **Regenerative Medicine:** the enhancement of scientific knowledge and understanding, as well as the development of new tools and technologies for regenerative therapies, with underpinning support from UK Regenerative Medicine Platform (UKRMP) Hubs. Some of the regenerative medicine projects were designed to standardise procedures for stem cell research. Note, we only report on one of these awards here because the other awards were for underpinning capital investments.

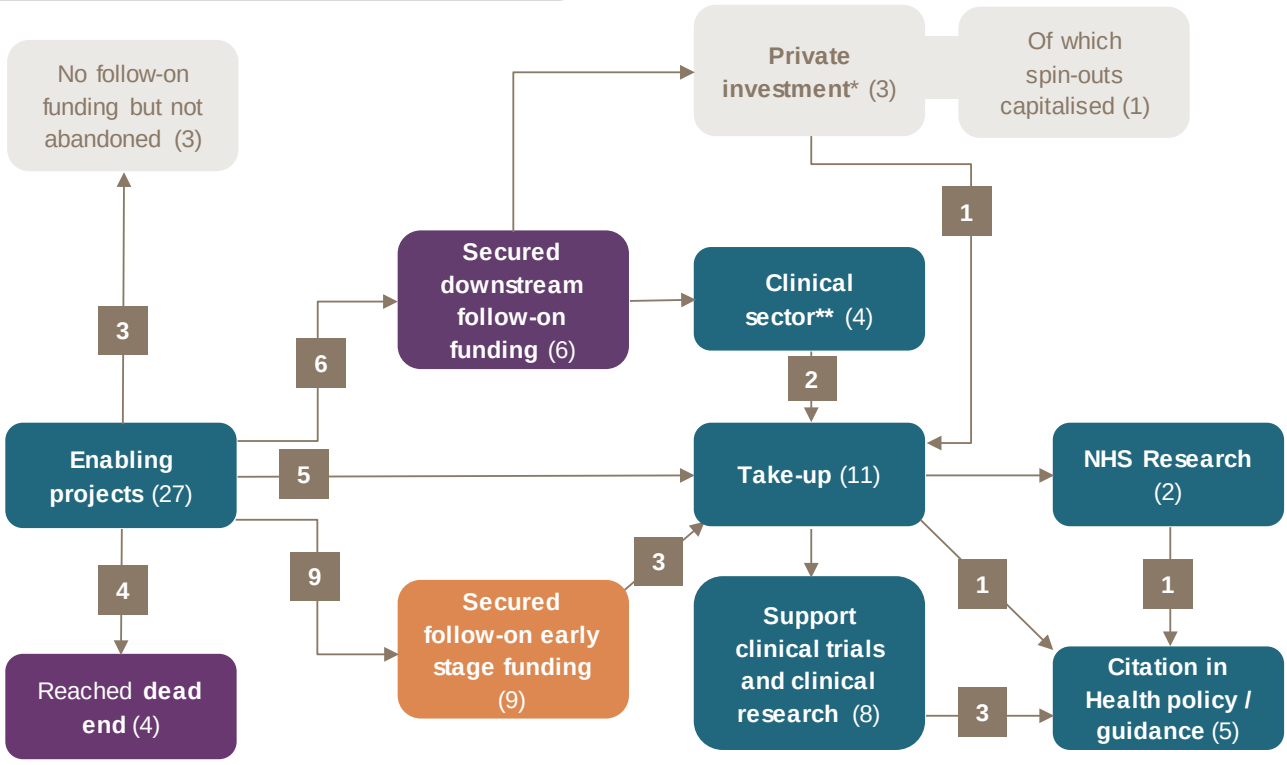
- **Joint Patient Research Cohort Initiative (JPRCI):** the creation of small, extensively defined groups of patients to help detect, treat or prevent disease in areas of high unmet need or where there are bottlenecks in turning research into therapies.

Four TSCRC projects were also interviewed in the sample. The projects discussed here are predominantly focused on the development and enhancement of outputs to support translational research via the production of research or diagnostic tools, methods, techniques, procedures and guidance.

5.3.1 Overview of outcomes

Figure 5.4. below provides an overview of the outcomes achieved by projects funded under the enabling translational research grouping.

Figure 5.4 Outcomes from the enabling portfolio



** Includes follow-on funding from industry for further research, licensing outcomes where there is evidence that the licensee has invested resources in taking the project further, and spin-outs that have been capitalised by external investors.*
*** One project received both clinical and private sector funding.*

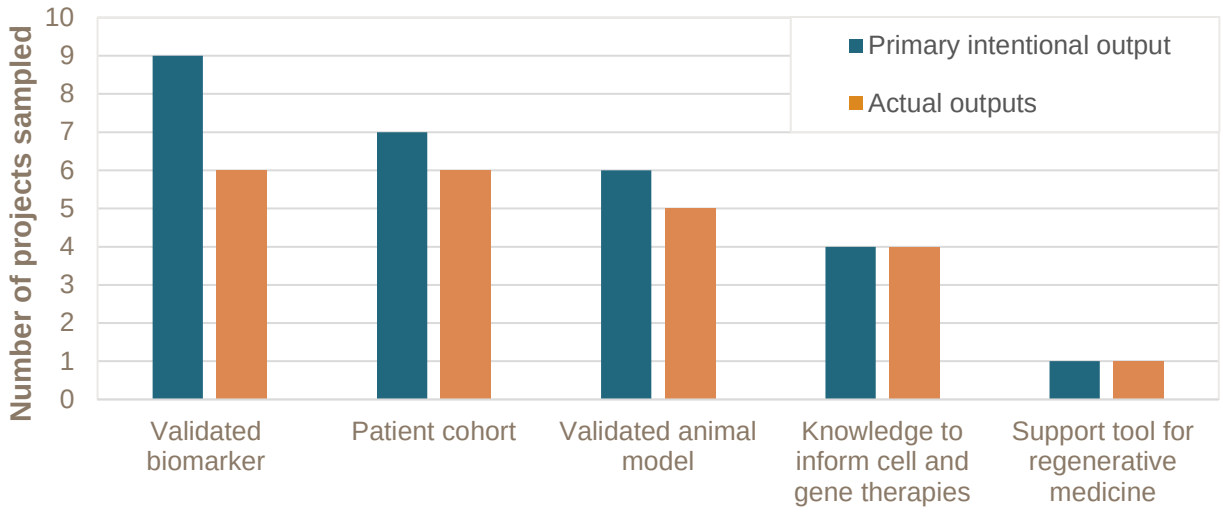
Source: Interviews with Principal Investigators, excludes four awards that provided capital equipment

5.3.2 Development and validation of tools for enabling translational research

As illustrated in Figure 5.5 below, a high share of projects funded under this grouping culminated in the successful development of their intended tool for enabling further translational research. Biomarker projects appeared to carry the highest level of risk. Three of the six biomarkers were not validated, either because the results were inconclusive (one project), or because they were proven to not be useful (two projects). Nevertheless, although the numbers were small, one or two of the interviewed Biomarker projects led to interesting translational outcomes. In contrast most of the Models of Disease projects led to their intended output (so appeared to be lower risk translational projects), but there was no evidence yet of later stage translational outcomes from these projects.

These outcomes were partly supported by further funding attracted from MRC and other sources. 59 percent of principal investigators reported they received further public funding to develop the core asset, with four projects receiving clinical sector funding. Three projects (11 percent) also reported that they attracted private investment (including one project which received both private investment and clinical sector funding). Around a quarter of researchers indicated that they would need further funding to progress the project's core asset.

Figure 5.5 Development of tools for enabling translational research



Source: Interviews with Principal Investigators

5.3.3 Take-up of new research tools

As highlighted above, a key measure of success for this grouping of projects is how far the resultant tools have been taken up in wider research:

- **Take-up of tools:** The interviews with principal investigators indicated that eight of the twenty-seven projects sampled produced research tools that were then subsequently used to support clinical trials and clinical research (this includes one grant where the resource was used to purchase imaging system equipment to support regenerative cell production). For example, a biomarker, developed as part of a project, has been used as a support tool to help predict the success of new treatments for antidepressant drugs (to reduce the level of resource invested in testing drugs that are likely to be unviable). This biomarker has been used in collaboration with pharmaceutical companies, specifically for Phase I studies with novel compounds. Turning to the Models of Disease initiative, while five of the six animal models were validated, evidence of further application from the principal investigators in the interviews was limited.

- **Enabling of translational research:** There were also some examples of successful enabling of translation, in the form of the production of knowledge. For example, the team undertaking the research within one TSCRC project, where the intention was to use liposomes as a potential delivery vehicle for dentine matrix, came up against practical difficulty in encapsulating a large matrix preparation in liposomes. The team managed to secure several subsequent funding awards, following the project, to progress their work leading to the discovery that they could incorporate liposomal carriers into hydrogels, and these are cellulose gels as an injectable system for the treatment. The researcher was clear that this progress would not have been possible in the absence of the underpinning biology carried out as part of the MRC TSCRC award. Another example of successful enabling translation was a project, funded by the TSCRC, aiming to translate a unique nanopattern which promotes stem cells from the bone marrow to become bone forming cells in vitro with the intention of generating new orthopaedic implants. The aspect of the project which was patented was the delivery of nanopatterning in strontium, which came about as the team were not able to transfer the pattern into titanium (their original objective).

- **Impact on health policy, guidelines and clinical practice:** There was evidence from interviews with principal investigators of impact on health policy, health guidelines or clinical practice resulting from enabling research funding. Investigators from five of the twenty-seven projects reported that their research had been cited in both domestic and international health policy or guidance. While the citations were typically part of a wider pool of citations from different sources the range of sources the projects have been cited in is worth noting.

    - The Population-based Ankylosing Spondylitis [PAS] cohort has been cited in NICE and OMERACT (Outcome Measures in Rheumatology) guidance.

    - The type 2 diabetes in childhood: building a platform to support novel intervention strategies cohort was referenced in the NICE guidelines on childhood diabetes, in the International Society for Paediatric and Adolescent Diabetes guidelines and in the National Paediatric Diabetes Audit.

    - The MRC Centre for Translational Research in Neuromuscular Disease Mitochondrial Disease Patient Cohort (UK) was used as part of evidence to the House of Lords on mitochondrial donation (and subsequently the law was changed) as well as clinical guidelines on the management of mitochondrial disease.

    - Those involved in the characterisation of the United Kingdom Thrombotic Thrombocytopenic Purpura (TTP) patient cohort have influenced the British Committee for Standards in Haematology (BCSH) guidelines on TTP and thrombotic microangiopathies.

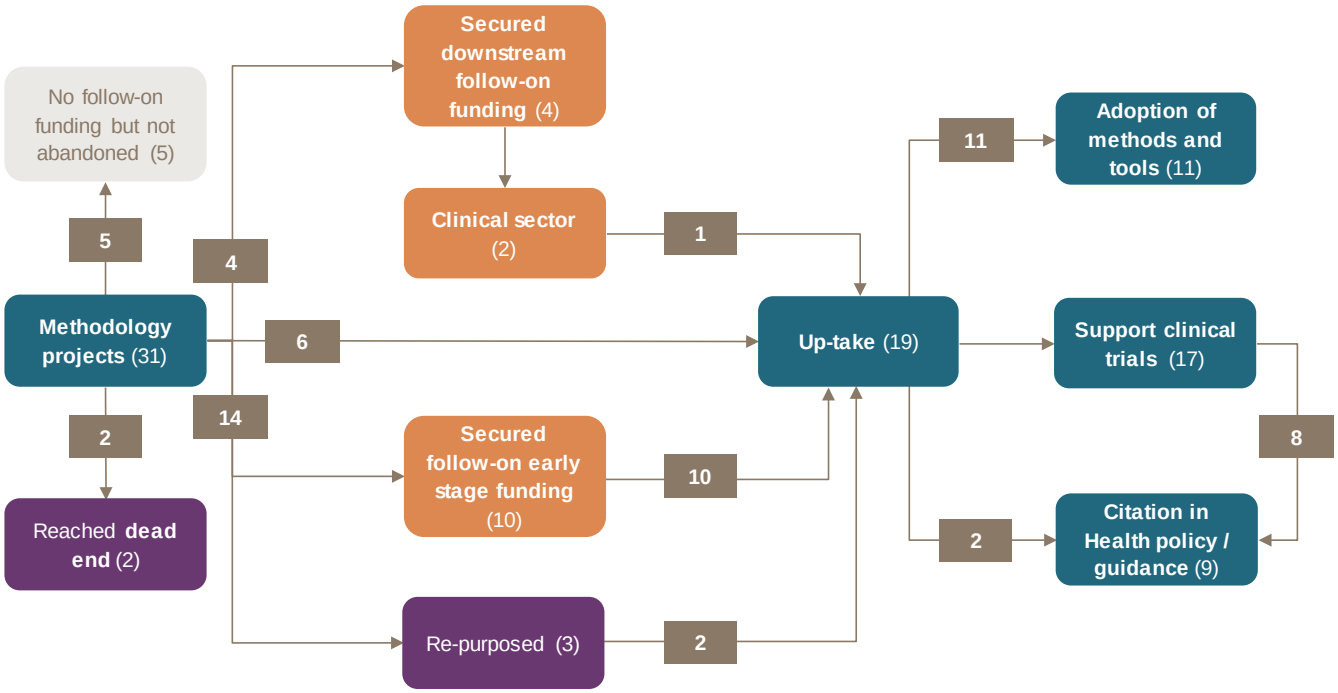
Bibliometric analysis of the whole directed translational portfolio showed that 7 percent of projects funded through the JPRCI were linked to publications cited in NICE guidelines. Across the enabling portfolio, 1 percent of awards produced papers cited in NICE guidelines, and 11 percent produced papers cited in clinical trials, whilst 13 percent produced papers cited in US patents.

5.4 MRC-NIHR Methodology Research Programme

The MRC-NIHR Methodology Research Programme (MRP) aims to support research which informs research practice, policy and healthcare. The MRP seeks to improve efficiency throughout the biomedical and health-related research process across four areas: experimental design (synthesis, approaches, conduct); data interrogation (analyses, interrogation, inference); implementation (context, evaluation, management); and knowledge management (dissemination, visibility, usability).

Over the decade, the MRP has had an annual budget of £5 million including a £1 million contribution from NIHR for activity relevant to its portfolio. Funding is almost entirely through 3 years (or less) duration project awards. To date, the total MRC investment runs at £39 million. Thirty-one interviews were conducted with MRP project leaders, covering awards totalling £12 million: approximately a third of the portfolio. Figure 5.6 below is a summary of the outcomes produced by these projects.

Figure 5.6 Outcomes from the methodology research programme



Source: Interviews with Principal Investigators

5.4.1 Development of new methodologies and tools

Outputs generated by the Methodological Research Programme (MPR) can be broadly grouped into four categories:

1. **Methods and models** – the development of existing or new statistical methods or models. For example, statistical methods for the analysis of single patient data and development of statistical methods for modelling repeated measures in a life course framework.
2. **Software packages and tools or source code** – the production of software or code, usually to support a method or model, for example computer software to run analysis on large quantities of data to model longitudinal data.
3. **Knowledge** – the generation of new knowledge or principles to guide research, disseminated most commonly via publication, but also supplemented with conference presentations, workshops, and attendance at meetings.
4. **The Hubs for Trials Methodology Research (HTMR)** – provision of extensive support and advice to researchers with questions about the use of nonstandard methods in trials, both individually and collectively through the network and its working groups, spanning all aspects of trial prioritisation, design and conduct with opportunities for application in complex health care interventions.

It is difficult to provide a simplistic measure of the reported benefits of the methodology projects within scope. However, if delivered and disseminated successfully, these projects are likely to produce benefits for researchers, statisticians, epidemiologists and clinical trialists, as well as regulatory bodies. An example of MRP impact is in more

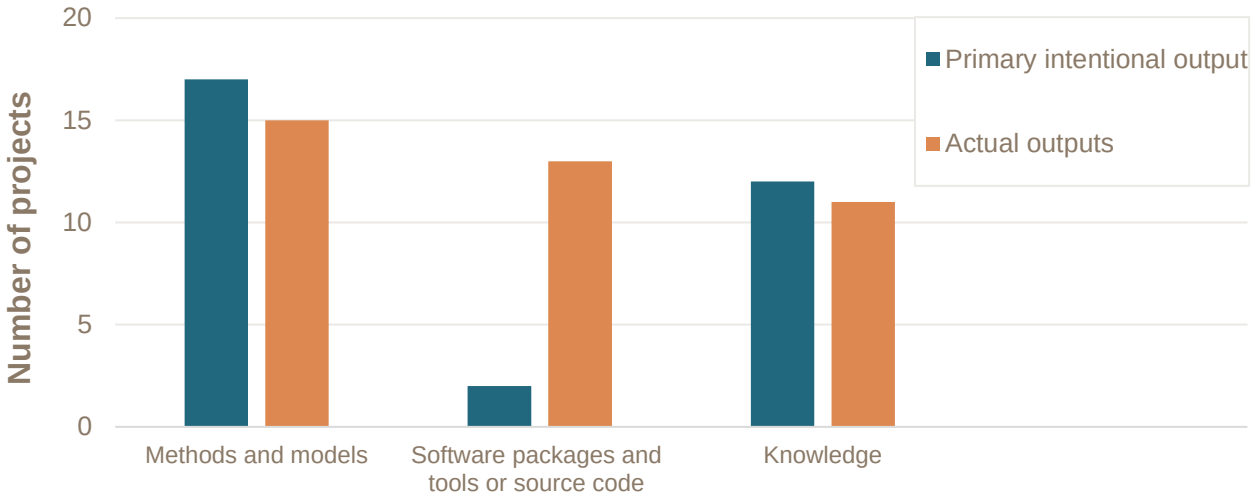
efficient clinical trial methodologies; these save time, reduce the number of participants that need to be recruited and enable more accurate and reliable trial data to be produced.

Figure 5.7 below shows that almost all projects produced the primary output intended by the grant[21]. Of the projects that explicitly intended to develop methods and models (of which there were 17, and includes two HTMR), all but two succeeded to this effect:

- The methods developed as part of one project did not perform well enough to warrant sharing more widely, however the team did publish software.
- In the other project, the necessary data were unavailable, so the team changed tactic and developed a tool for use instead in veterinary practice.

The two projects that intended to produce software tools succeeded in doing so. A further eleven also produced software packages and tools or source code, generally to accompany methods or models that had been developed as part of the grant. There were twelve projects where the primary intent was to produce new methodological knowledge in the form of publications, or formally disseminated via other channels. At the time of interview, all but one project had achieved this, and one did not publish its negative results.

Figure 5.7 Development of methodologies



Source: Interviews with Principal Investigators

5.4.2 Funding for methodological research

The majority of the 31 projects resulted in products, in the form of either models, software or code, as well as knowledge. The researchers secured funding to progress these products and apply them further. Fifteen out of the thirty-one projects went on to receive further funding to continue developing the method, model or tools. The organisations supporting this follow-on funding include NIHR, the Department of Health and Social Care, NICE, the Bill and Melinda Gates Foundation. The MRC supported the development for a third of these projects (five of fifteen).

[21] All grants funded within this programme would result in new methodological knowledge, however a share of projects specifically stated in the objectives that they would develop new methodologies.

Although the researchers were able to secure further funding from a variety of sources to progress methodological research, there is a perception among the researchers that they, and others within the methodological community, are heavily dependent on the MRP for funding. Without this funding, it was suggested that the methodologies (and supporting tools) discussed here would not have been developed. In five of the thirty-one cases, the principal investigator reported a lack of further funding as the main barrier to continuing to develop the planned methodology.

5.4.3 Take-up of new methodologies and tools

Principal investigators reported that knowledge was disseminated via academic publication and / or through conferences, meetings and workshops. There were, however, examples of wide adoption of the methods produced from these thirty-one methodological projects: MRI software that is used in tens of thousands of labs across the world, a prototype system for use in clinical trials with around 70 users of prototype system around the world[22], a diagnostic test accuracy tool that has been widely cited and widely used[23], and around 1000 reported downloads of some software on open source. However, six of the seventeen researchers whose primary intent was to produce methods or models were not able to provide concrete examples of take-up beyond their direct teams and close networks.

Bibliometric data suggests that the MRP awards have been highly cited in clinical trials, with 17 percent of the 105 MRP awards producing papers that have been cited in clinical trials as determined by analysis of *clincaltrials.gov*. This influence on clinical trials is significant; only the JPRCI initiative involvement is greater. The higher proportion of these projects cited in trials would be expected given that all JPRCI projects were designed to develop cohorts for trials while only a subset of MRP awards are targeted at trial methodology.

5.4.4 Impact on health policy, guidelines and clinical practice

There is evidence from interviews with principal investigators of impact on health policy, health guidelines or clinical practice resulting from the MRP. Nine of the thirty-one projects interviewed influenced health policy or health guidelines, both in the UK and internationally, with six of these having significant impact (i.e. beyond being cited among other contributors). For example, the statistical prediction methods developed in one project have been widely used during the Ebola and Zika virus outbreaks; they support real-time decision-making during an outbreak. This project also contributed to the WHO HIV testing and treatment guidelines. Another project created a tool, cited by NICE on its website as a recommended tool, features widely in NICE guidelines[24]. Bibliometric data shows that six percent of papers produced from MRP funded research have been cited in NICE guidelines. MRP outcomes shows greater evidence of impact on health policy than the other components of the translation research portfolio (Figure 5.1).

[22] RobotAnalyst is a tool used to support the literature screening phase of systematic reviews. RobotAnalyst is designed for searching and screening reference collections obtained from literature database queries. For more details see http://www.nactem.ac.uk/robotanalyst/

[23] QUADAS-2 is a tool for use in systematic reviews to evaluate the risk of bias and applicability of primary diagnostic accuracy studies. For more details see https://www.bristol.ac.uk/population-health-sciences/projects/quadas/quadas-2/

[24] https://www.nice.org.uk/process/pmg6/resources/the-guidelines-manual-appendices-bi-2549703709/chapter/appendix-f-methodology-checklist-the-quadas-2-tool-for-studies-of-diagnostic-test-accuracy

5.4.5 Industrial engagement

Interviews with principal investigators reveal limited engagement with industry in MRP-funded research. Of the 31 projects, 6 of these involved an industry partner. Researchers were more likely to draw on the specialist research skills and knowledge (and thus collaborate with), others from within their own institution, or indeed across other academic institutions. None of the 31 cases went on to receive follow on funding from a private source to develop the core asset. One researcher (who did not have an industrial partner), reported that the lack of engagement with drug companies makes it difficult to assess industry needs.

5.5 Section Summary

- This section provides an overview of the outcomes from projects funded via all initiatives outside of the focused portfolio (discussed in Section 4), this is a diverse portfolio subdivided into three areas; broad, enabling and the MRP.

- The **broad** initiatives differed from focused projects by including elements of understanding fundamental disease biology to inform the development of therapeutics. These projects had strong results with respect to progression beyond the MRC remit with a higher proportion of projects advancing to clinical studies than was found in the focused portfolio. With half of projects in the broad portfolio expressing an intention to develop a product there was also good evidence of commercialisation outcomes with 14 percent of broad projects linked to the formation of a spin-out company, comparing favourably with 18 percent of focused projects.

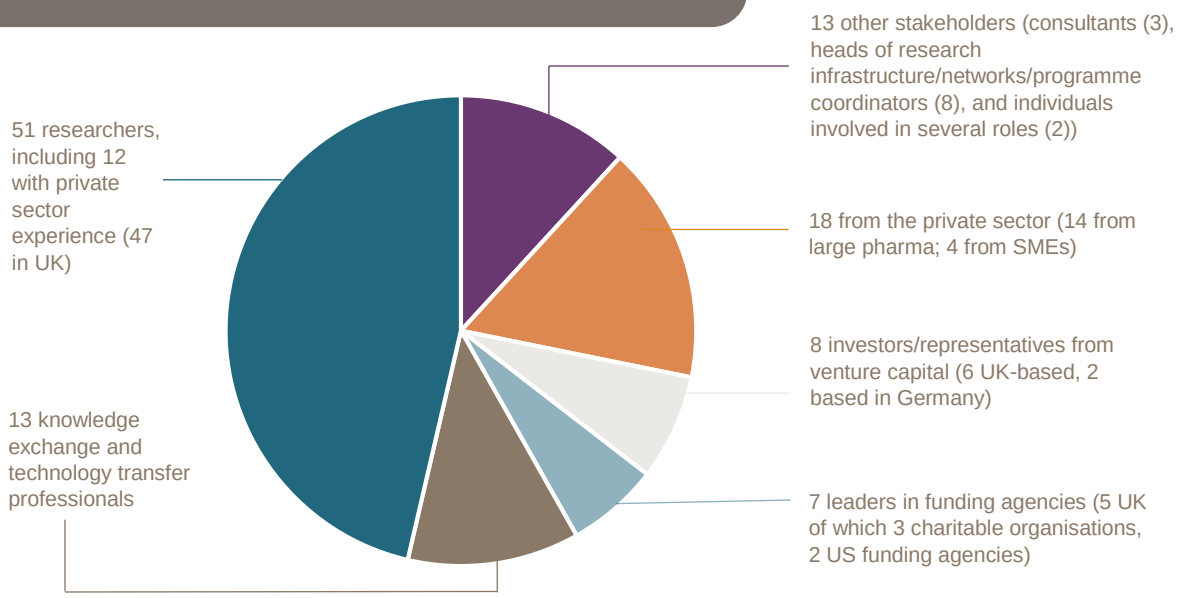
- Enabling projects aimed to deliver new biomarkers, models, research tools and materials and so the success of these projects should primarily be measured in terms of whether the work led to the intended tool and then importantly whether this output was then utilised by others. The evidence was that a high proportion of these projects had been successful.

- The MRP was found to have delivered the anticipated products, in the form of either methods or models, software or code and knowledge and in a small number of cases there was evidence of significant wider utilisation of these products. However, around a third of projects could not provide any evidence that their outputs had been utilised more widely than their direct teams and close networks, and the level of industry engagement was relatively low.

6. Changes in translational research landscape in last 10 years

The following is a summary of a literature review on the Research and Development (R&D) landscape and comments made by multiple key stakeholders during the interview process. The extract covers the areas where the translational landscape more broadly, or MRC activities specifically, were discussed. A total of 110 key stakeholder interviews were conducted. These involved senior decision makers from a wide range of organisations in the biomedical sector (Figure 6.1 shows the proportion of stakeholders from six different areas of the sector).

Figure 6.1 Key stakeholders interviewed in the evaluation



6.1 Changes in the broader R&D landscape

Industry has continued the shift (already evident in 2008) from all in-house discovery to collaboration with or licensing from academia and biotech SMEs, or purchase of small innovative companies. Companies tend to focus more on late (Phase II / III) clinical development and distribution of products; the discovery science underpinning new therapies and subsequent pre-clinical and early clinical evaluation have increasingly become the domain of academic centres, partnerships and SMEs[xxxiii]. This development was driven by high failure rates coupled with the rising cost of later-stage translational research.

This has been paralleled by changes in public policy and public funding in the UK, including:

- A strong government focus on the life sciences as an engine for economic growth (e.g. Cooksey report 2006; *UK Strategy for Life Sciences 2011*; and the *UK Life Science Sector Deal 2017*)

- Increased emphasis on demonstrating impact from public funding, initially focused on Research Councils, and later a strong emphasis on the research community reporting via the Research Excellence Framework (REF)
- A new MRC strategy and funding programme for translation, matched by initiatives from some charities.

The view is that as a combined result:

- The culture of the academic research community shifted, with more investigators interested in conducting translational research and open to collaboration with industry, and an increase in translational research skills in the academic community
- The boundary between industry and academia has become more porous, with better engagement from both sides and an enhanced understanding of the value each can bring to one the other
- The volume of translatable research coming out of academia has increased, with technology transfer office (TTO) professionals and investors seeing a higher quality and quantity of translatable discoveries
- Several UK universities substantially increased their capabilities to support commercialisation, by establishing / expanding Technology Transfer Offices (TTO) and Translational Research Offices (TROs) (e.g. University College London, Imperial College, Cambridge)

6.2 Changes in the translational research funding landscape

Between 2000 and 2015, government expenditure on health R&D in the UK rose from $1.4 billion (approx. £892 million based on historical exchange rate) to $3.4 billion (approx. £2.25 billion)[xxxiv]. The proportion of investment for translational health research across public and charity organisations was estimated to have increased by 9.3 percent between 2004 and 2014[xxxv]. The UK took the lead in Venture Capital raised in 2016, with the largest number of biotechnology sector financings of any European market. Total venture financing amounted to $590 million, or 30 percent of all European Venture Capital[xxxvi]. Correspondingly, interviewees reported that the UK's top universities had seen an increase in the level of capital available from VC funds.

Key stakeholders broadly agreed that the UK is now better equipped for translational research than it was 10 years ago in terms of people and facilities. Public funders (MRC, NIHR, Innovate UK) and Wellcome have significantly contributed. The funding landscape diversified, with the establishment of the MRC's translational research funding streams, NIHR's support for Biomedical Research Centres (BRCs), enhanced translational funding from charities (e.g. Wellcome, CRUK), and European Commission research programmes (such as the Innovative Medicines Initiative (IMI)). The MRC was seen to have had a positive impact on the UK's translational research landscape, by investing in translation, de-risking research areas (e.g. gene therapy and regenerative medicine) and facilitating academia / industry interaction and collaboration (e.g. asset sharing schemes; appointment of industry representatives to review boards).

6.3 Research developments

Research developments over the last 10 years included:

- A move from single observational data to using large datasets from multiple sources, e.g. combining 'omics, imaging, and patient reported data. Data integration is seen as a key future research area.

- A shift from animal models towards human model systems
- A shift from small molecule drugs to biologics / molecular medicine
- The emergence of novel modalities and technologies, e.g. gene and cell therapies, regenerative medicine, gene editing enabled through CRISPR-Cas9, CAR-T cell therapy / immunotherapy
- Maturing of the digital health field

6.4 MRC funding schemes

The MRC is considered a global leader in supporting translational research and establishing innovative partnerships with industry (often ahead of other UK funders), which in turn has driven changes in the level and nature of translational research activity and research culture in the UK. MRC has developed two funding schemes focused on direct translational outputs. However, some key stakeholders cautioned against shifting too much funding away from discovery science, crucial for feeding the innovation pipeline.

6.4.1 Developmental Pathway Funding Scheme (DPFS)

The DPFS is seen as the key translational research funding stream in the UK, helping to bridge the gap between discovery science and translation. The scheme is well designed and considered to have succeeded in moving assets further along the developmental pathway and in improving collaboration between academia and industry, thereby changing academic researchers' attitude towards translational research and enhancing their skills in this area.

The view was that the DPFS should be maintained or expanded. There were positive views on the DPFS milestone driven approach, the requirement for researchers to set out how their science will reach patients, the composition of funded teams (including researchers across disciplines and sectors), and the grant selection process via the DPFS review panel, combining individuals with high-level industry, VC, basic research and clinical expertise. It was however highlighted that areas such as digital health, diagnostics and devices were not as well represented as drug development within the DPFS portfolio and review panel.

6.4.2 Confidence in Concept (CiC) scheme

Views of the CiC programme were positive across the board. It was seen to have progressed translational research by:

- Enabling testing of ideas emerging from discovery science, with fast failure as a positive outcome
- Allowing universities to support multi-disciplinary and high-risk projects (often without clear route to funding), and to capture further funds, e.g. industry or DPFS, if proof of concept is established
- Providing an opportunity / lowering the entry barrier for interested academic researchers (especially early career researchers) to engage with translational work and acquire the necessary skills
- Driving a cultural change at universities by providing a devolved translational research budget to facilitate improved connections to investors and industry (e.g. by including them as advisors or reviewers of projects)

6.5 Enablers and barriers of translational research

The most important factors in enabling translational research highlighted by key stakeholders were: skills, collaboration, the right mindset (attitudes and culture), and funding. Institutional support and local translational research ecosystems (clusters) were also mentioned.

6.5.1 Skills

While academic researchers felt that translational skills had improved, significant knowledge gaps remain. Learning occurs predominantly on the job, i.e. by trial and error.

Many interviewees identified a lack of commercial expertise among UK academic researchers, e.g. relating to regulatory requirements, commercial finance, and the ability to position technologies within the current commercial context. Overall, the UK ecosystem is seen to lack entrepreneurs with experience in commercialising innovations, especially when compared to clusters in the USA.

Suggestions to improve translational research, commercial, and entrepreneurial skills included:

- Expansion of training, e.g. as a requirement for access to CiC funding, embedded into the early training of scientists or at MSc level, or as part of regular academia / industry workshops
- Access to expert advice, e.g. via mentoring schemes or by providing additional funding for consultants on translational projects. The Wellcome Seeding Drug Discovery and the Wellcome Translational Research Partnership schemes were mentioned as a positive example in this respect.

Many interviewees emphasised the need to increase researchers' ability to move between academic and industry positions, as this fluidity was considered essential to building strong collaborations and networks.
Interviewees also highlighted a range of disciplines with current skills gaps, especially relating to data skills (data science, AI, machine learning, bioinformatics). The USA and China are frontrunners in this area, with the UK in danger of falling behind. Other areas with perceived skills shortages are the clinical sciences, such as clinical pharmacology and experimental medicine.

6.5.2 Collaboration

Collaboration is seen as an essential component of translational research, bringing together the many required skills (which are beyond a single research group). Translational research requires a culture of collaboration.

Academia-industry collaboration: Attitudes to collaboration between academia and the private sector have improved: many interviewees held the view that nowadays, industry seeks academic input to inform early stage R&D projects, and academic researchers are aware that moving their research along the translational pathway requires collaboration with industry. Representatives from TTOs agreed that a culture change was evident in academics' views of industry collaborations, which were suspicious and standoffish in the past and are now warmer and more open.

However, barriers to collaboration remain:

- The issue cited most frequently related to the lack of team science in academia. As a result, academic researchers do not have the skills for working in large teams across disciplines and sectors.

- Finding the right collaboration partner with complementary expertise can be difficult. This process remains mainly serendipitous, e.g. through chance encounters at meetings. Relevant contacts in industry are not easily identifiable, and small companies lack resources to dedicate to liaison.

6.5.3 Funding

While interviewees concurred that more funding for translation is available now compared to 10 years ago, they broadly agreed that several funding issues remain, falling into three main categories:

- MRC translational grants were too short-term, and project based, covering only short stages in translational pathway. To improve the situation, interviewees suggested extended grant durations, covering multiple translational steps would speed up progress through the development pathway. More funding through CiC-type schemes, and faster turn-around times in the proposal process would also be an improvement. The Wellcome Seeding Drug Discovery grants were cited as a good model, providing a larger funding envelope which allows proof-of-concept as well as further steps to be tackled.
- Individual research councils, charities and the NHS are considered too siloed in their funding approaches.
- The MRC and NIHR were seen to overlap in some areas of research, but nonetheless complement each other well and form part of the improved UK ecosystem for translational research support. MRC researchers benefit from NIHR infrastructure, support staff and expertise.

Views on gaps in the funding landscape included the following:

- A gap between early translation and the DPFS was cited most frequently. An increased level of pump-priming is needed to move promising innovations to the point where they are ready for DPFS funding. Where available, CiC grants help but are still insufficient to fill the funding gap or meet local demand.
- Many interviewees identified a gap post-DPFS, e.g. from DPFS to EME or from DPFS to industry-VC investment, as technologies are often not yet sufficiently advanced to move on.
- Many interviewees pointed to a funding gap related to computational / *in silico* approaches, machine learning, artificial intelligence, as well as methods for data integration / big data.
- Some interviewees, mainly researchers, did not see specific gaps, but that the overall level of funding was insufficient (per project and number of projects funded), with funding being spread too thinly.

6.5.4 Culture and incentives

University reward structures: The current reward structures and promotions in the academic sector do not align with the main outputs of translational research. The current promotion system does not allow researchers to gain industry experience and return to academia (due to the break in their publication record).

6.5.5 Institutional support, TTOs and IP

Universities increasingly recognise the utility of technology / knowledge transfer in achieving and showcasing impact. The level of support varies considerably between institutions. TTO professionals agreed that it was difficult to recruit staff with commercial expertise, and that TTOs, especially outside London, Oxford and Cambridge, are generally understaffed and under-resourced. In addition, researchers now present more viable translational ideas; while this is a positive development, it places a further strain on university support functions.

6.5.6 Local clusters and thematic networks

Working within the right translational research environment is an important factor in driving progress. Access to clinical research infrastructure, and more specifically NIHR BRCs, was considered a key success factor.

6.6 Knowledge transfer mechanisms and barriers

6.6.1 Academia-industry

The main mechanisms of knowledge transfer between academia and industry rely on direct relationships. Academic researchers build their own networks by presenting at conferences, attending industry partnering conferences or contacting companies to explore interests; industry experts find academic researchers via the published literature, patent databases and through their academic alliance and liaison units.

6.6.2 IP continues to be a key barrier to knowledge transfer (and more broadly collaboration)

IP negotiations can be lengthy and inefficient. Interviewees from industry explained that universities overvalue their IP and conversely, several interviewees from both academia and industry highlighted that companies are also at fault. There is a need for better IP-sharing models between commercial and non-commercial organisations, leading to win-win situations, reducing delay due to extended negotiations, and ultimately reducing distrust between the sectors.

6.6.3 Academia-clinical environment

Most interviewees agreed that access to NIHR infrastructure is a key factor in the successful development of technologies for and within the NHS. The main issue highlighted is the increasing pressure on the NHS to deliver clinical services and the situation was perceived as worse compared to 10 years ago. Clinical staff are limited in the amount of time they have for research. The MRC Clinical Academic Research Partnership (CARP) scheme was highlighted as an exemplar scheme to support clinicians in research.

6.6.4 Academia-policy

Key barriers to knowledge transfer between academia and policy makers were:

- A lack of influencing and communication skills within the academic community
- Academic researchers' attitude that informing policy is not their responsibility. They hence do not allocate time to communicating research findings with policy relevance to this audience.
- A lack of incentives for policy makers to seek scientific evidence.

6.6.5 Academia-investors

Investors set out a range of criteria when making investment decisions, including: the calibre of people involved, a sensible tech transfer process, the market position of the technology, current trends in VC investments, and whether or not prior grant funding (MRC or NIHR for example) has been awarded, which provides validation and reduces the potential magnitude of VC investment required.

A key barrier to VC investment is the lack of commercial and entrepreneurial skills within the UK's academic community coupled with a lack of incentive for academics to spin-out and form companies.

6.7 Summary of section

- 110 influential stakeholders from a wide range of organisations (academia, industry, funding agencies, investment firms, technology transfer offices), both in the UK and overseas, were consulted regarding the impact that MRC has made on translational research.

- The views received from this important cross-section of key stakeholders in biomedical research were consistently positive about MRC's contribution. The interviews validated evidence gathered in the literature search that there has been a substantial shift in academic culture over the last ten years. More investigators are interested in conducting translational research, more are open to collaboration with industry, and there is an increase in translational research skills in the academic community.

- Many interviewees highlighted that MRC's directed initiatives had catalysed part of this shift. The DPFS is seen as the key translational research funding stream in the UK, helping to move assets further along the developmental pathway and in improving collaboration between academia and industry, interviewees were extremely positive about its design and recommended that it continue.

- Similarly feedback on the CiC scheme was positive. It was seen to have progressed translational research by enabling testing of ideas emerging from discovery science (with fast failure as a positive outcome), allowing universities to support multi-disciplinary and high-risk projects (often without clear route to funding), and to capture further funds, e.g. industry or DPFS, if proof of concept is established, providing an opportunity for interested researchers to engage with translational work and acquire the necessary skills, and facilitating improved connections to investors and industry.

- The most important factors in enabling translational research highlighted by key stakeholders were: skills, collaboration, the right mindset (attitudes and culture), and funding. Stakeholders highlighted that improvements were still needed to support team science, to broker appropriate partnerships, to encourage moves between industry and academia, to provide expert technology transfer support, and to provide longer-term support to projects in any health area. Excepting the funding and skills issues raised, these were areas in part outside MRC's influence.

7. Findings and opportunities for the future

This evaluation has summarised the outputs of ten years of MRC investment in translational research since the Cooksey review. MRC's approach to translation has been continuously refined across this period, adapting to the evolving landscape and building on the early results of previous initiatives.

We conclude that the UK is now better equipped to support translational research than it was 10 years ago following significant investment by the UK government through MRC, NIHR and Innovate UK and by the charity sector. Funding through MRC and NIHR is considered to provide continuity of public funding across the translational landscape, although there remain opportunities to streamline the offering so opportunities for funding are clear to both academia and the business community.

Translational development is a long and iterative process, requiring a strong discovery science evidence base, sustained financial support and flexibility of approach, alongside mechanisms to recognise and reward activity which may fall outside traditional academic work. MRC's translational funding schemes have enabled this by maintaining and leveraging the existing strengths of UK academia. MRC support has had a significant impact on the culture of UK translational research and provided a strong brand to attract downstream investment. The MRC schemes have supported a step forward in approach and scale of resource, enabling a UK drive to strengthen academic translational medicine, while recognising that different parts of the system need different interventions at different times. This in turn has built skills, developed careers and generated wealth and opportunity through downstream investment. The return on investment is clear. Both the evidence presented in this evaluation and the commentary from the stakeholders consulted emphasise that support for translational research remains crucial and the UK has a strong foundational base from which to continue to grow.

Core successes for the MRC in the last ten years have been growing the translational ecosystem in the UK and the de-risking of areas previously unattractive to industry. Looking to the future, key aims will be to build on the maturing landscape and further enable innovative development and address any identified gaps. Robust and agile support for successful programmes, tied to clear mechanisms to quickly identify and terminate failing programmes, will be important, alongside continued openness to emerging areas of opportunity. Consultees have highlighted that care should be taken to maintain and replicate the success that the DPFS has had in identifying and providing long-term support for gene therapies and other advanced modalities from 2008 into new technologies as these develop. While the evidence is that advanced biological therapies will remain a large, important, and diverse area for MRC for many years to come, new areas are already becoming apparent, for example around Artificial Intelligence-based products or early disease detection and the MRC should make sure that the promotion and design of translational schemes is suitable to support these also.

The findings from the evaluation are summarised below, leading into an overview of the opportunities for future refinement.

7.1 Summary of findings

7.1.1 MRC support for translational research

Over the past decade the MRC has introduced a programme of new initiatives, supported in part by additional government funding, directed toward supporting early phase, academic-led, translational research projects. Since 2008 MRC's investment in directed translational research has grown from zero to fourteen percent of total MRC expenditure (approximately £80 million per year in 2018). Across the MRC portfolio support for basic discovery science has been maintained, and the proportion of non-directed funding for projects with some translational intent has remained constant over the decade, so all growth in translational research has been managed through the directed route. MRC directed funding has been secured by research organisations throughout the UK, but unlike MRC's portfolio overall, a majority (65 percent) has been spent in institutions outside of London, Cambridge and Oxford. Institutions and regions show some tendency to specialise in the translation work they pursue, for example; advanced therapy research is particularly strong in London, whereas the development of medical devices and small molecule drugs are strengths for institutions outside of the South East.

The MRC did not expect translational projects to deliver highly-cited publications, the priority was to develop innovative ideas to the point where they could be translated beyond MRC's remit. Despite this the citation of publications from MRC translational research was found to compare favourably with bibliometric measures from the rest of the MRC portfolio and the outputs from translational and non-translational NIH and Wellcome research portfolios. This measure of academic impact demonstrates that MRC funded translational research is internationally influential.

7.1.2 Progress of MRC translational projects and impact in the private sector

Approximately 60 percent of MRC funded translational projects were found to have advanced to a later stage of translational development during the tenure of their MRC support. This is evidence that a majority of MRC funded projects are actively moving along the translational pathway. Importantly a third of MRC's directed translational projects were found to have secured funding to support work beyond MRC's remit within the period evaluated, and this was suggested to be a useful proxy measure (from the point of view of the MRC) of projects that had successfully translated.

Projects supported under MRC's directed translational research initiatives have involved private sector collaborations, generated knowledge that has been commercialised via the establishment of spin-out companies, and licensed intellectual property to a greater extent than non-directed translational MRC projects. The results show that the MRC's directed initiatives have expanded the pipeline of product development projects and encouraged new academic / private sector interactions beyond what is possible via non-directed routes for funding.

A diverse range of industry partners were involved with MRC supported projects. Projects with private sector collaboration were more likely to secure funding for later phase translational work and more likely to progress to clinical trials, highlighting that private sector involvement was helpful in identifying and accelerating projects with commercial potential. These collaborations did not always survive the duration of the project, in some cases this may be due to the project being identified as having low commercial potential, but in other cases this was due to changes in priorities of either the academic or industry partner.

Since 2008, a total of 134 spin-outs were attributed to MRC projects across the entire portfolio, representing between three to seven percent of new UK life science companies formed since 2008. Over half of all MRC attributed spin-outs trace their origin to a project supported under the directed translational research programme, including currently all the most highly valued companies. The small number of highly capitalised firms have attracted over 40 percent of all investment in the pharmaceutical, biotechnology and medical device firms established since 2008, a substantial slice of UK investment activity. This underlines the importance of companies based on MRC research in the current UK life-science landscape.

Companies focusing on advanced therapies were highly represented in the MRC-linked spin-out companies (fourteen percent of spin-outs versus three percent in the industry more widely) this appears to be a result of the MRC's sustained long-term support provided to this field and the progress toward clinical studies that these projects have made. Other subsectors were underrepresented, most significantly the emergent fast-growing digital health sector (one percent of spin-outs versus thirteen percent in the industry more widely). This may highlight an opportunity for the MRC to encourage the translation of results from recent investments in data science and to increase partnership with the digital health sector.

7.1.3 Focused translational research initiatives

The MRC focused translational portfolio mainly comprises the ongoing CiC and DPFS initiatives. 68 spin-out companies were incorporated to exploit the results of research funded through the focused portfolio (although it is important to note that underpinning research may also have been supported by other initiatives). 30 of these companies raised a total of £1.1 billion of external equity investment, with three progressing to an Initial Public Offering (IPO). These companies were valued at £2.7 billion (accounting for over 99 percent of the total economic value arising from the directed translational research portfolio). The conclusion is that CiC and DPFS have been a major driver of product development leading to successful commercialisation outcomes.

In the time covered by the evaluation and where this could be determined, a little under 20 percent of CiC projects progressed to secure follow on funding from the DPFS, industry or led to a spin-out. CiC projects are early stage, small scale and high risk. In contrast 38 percent of DPFS projects (which are larger scale and longer duration projects) moved along the translational pathway to a stage beyond the MRC remit. For both schemes this was considered strong progression and sets a benchmark that can be revisited in future.

The remainder of projects either led to further fruitful discovery science investigations or were no longer being pursued. Reasons for projects reaching a dead end were in the main scientific or technical (e.g. failing to show efficacy in clinical studies), but a minority of projects were shelved due to it becoming clear that the economics of the approach were unlikely to be viable. These findings are important as there might be cases where the likely market for an intervention (where appropriate) could be assessed in advance of taking a decision to fund a project.

The evaluation validated a wider body of research that shows the pathway from discovery science to health intervention is a long-term process. Projects funded in this portfolio were typically built on an underpinning platform of fundamental research, and early stage laboratory work, and generally would require substantial further refinement before the underlying technologies could be adopted into health systems. It was not therefore surprising that few examples of MRC projects funded within the last decade led to new interventions adopted into practice. There is every reason to believe that the existing advanced translational projects will develop into clinical practice in the coming years and that the following projects in the pipeline will continue to mature and give rise to more opportunities for commercialisation and increased health benefits. Some modalities progressed more rapidly (e.g. those developing psychological, behavioural and physical interventions or support tools) due to less complex routes to adoption.

7.1.4 Other support for translational research

The evaluation also examined outcomes from projects funded via all initiatives outside of the focused portfolio, roughly half of MRC's expenditure on directed translation over the decade. This is a diverse portfolio and we subdivided it into three areas; broad, enabling and the MRC-NIHR methodology programme (MRP).

The broad initiatives (e.g. precision and experimental medicine) differed from focused projects by including elements of understanding fundamental disease biology to inform the development of therapeutics. These projects had strong results with respect to progression beyond the MRC remit with a higher proportion of projects advancing to clinical studies than was found in the focused portfolio and good evidence of commercialisation outcomes. 14 percent of

broad projects linked to the formation of a spin-out company, comparing favourably with 18 percent of focused projects.

Enabling projects aimed to deliver new biomarkers, models, research tools and materials and so the success of these projects should primarily be measured in terms of whether the work led to the intended tool and then importantly whether this output was then utilised by others. The evidence was that a high proportion of these projects had been successful.

The MRC-NIHR MRP was found to have delivered the anticipated products, in the form of either methods or models, software or code and knowledge and in a small number of cases there was evidence of significant wider utilisation of these outputs. However, around a third of projects could not provide any evidence that their outputs had been utilised more widely than their direct teams and close networks and over the time period examined, no projects secured private sector funding to develop these assets further.

7.1.5 Views from stakeholders in translational research

110 influential stakeholders from a wide range of organisations (academia, industry, funding agencies, investment firms, technology transfer offices), both in the UK and overseas, were consulted regarding the impact that MRC has made on translational research. The views received from this important cross-section of key stakeholders in biomedical research were consistently positive about MRC's contribution. The interviews validated evidence gathered in the literature search that there has been a substantial shift in academic culture over the last ten years, with more investigators interested in conducting translational research, more being open to collaboration with industry, and an overall increase in translational research skills in the academic community. Many interviewees highlighted that MRC's directed initiatives had catalysed part of this shift.

The DPFS is seen as the key translational research funding stream in the UK, helping to move assets further along the developmental pathway and in improving collaboration between academia and industry. Interviewees were extremely positive about its design and recommended that it continue. Feedback on the CiC scheme was similarly positive. It was seen to have progressed translational research by enabling testing of ideas emerging from discovery science (with fast failure as a positive outcome), allowing universities to support multi-disciplinary and high-risk projects (often without clear route to funding), and to capture further funds, e.g. industry or DPFS, if proof of concept is established, providing an opportunity for interested researchers to engage with translational work and acquire the necessary skills, and facilitating improved connections to investors and industry.

The most important factors in enabling translational research highlighted by key stakeholders were: skills, collaboration, the right mindset (attitudes and culture), and funding. Stakeholders highlighted that improvements were still needed to support team science, to broker appropriate partnerships, to encourage flexibility of movement between industry and academia, to provide expert technology transfer support, and to provide longer-term support to projects in any health area. Excepting the funding and skills issues raised, these were areas in part outside MRC's direct influence.

7.2 Future opportunities for continuing investment

Linking the outputs of the evaluation to MRC's thinking about the future of translational research, there are clear opportunities to streamline schemes and investments to maximise outputs and continue to grow UK translational research. These are summarised below, broken up into sections reflecting the evaluation structure,

7.2.1 Funding Opportunities – Directed translational schemes

The two major ongoing directed MRC schemes are the CiC scheme and the DPFS (see section 4). CiC is considered an important scheme for pump-priming and enabling early translation, and an important feeder for DPFS bridging the

gap between discovery science and substantial translational funding as well as being a tool to drive innovation. CiC has facilitated a shift in culture and attitude at the local level, enabling translation in universities across the UK by engendering organisational buy-in and leveraging industry investment.

DPFS is considered uniquely placed in the UK and has gained international recognition as a successful intervention to drive the academic development of therapeutics, diagnostics and devices further down the developmental pathway. The milestone driven approach and DPFS review process, involving high level industry, VC, and clinical expertise with an in-depth knowledge of translation and product development are viewed as the main enablers of DPFS's success.

Opportunities:

- The short-term nature of the current translational project funding approach can be restrictive, and an individual award is typically insufficient to enable major progress or broad impact, greater flexibility is required. The need to **expand the scale and scope of translational funding** is recognised as essential for MRC to remain as a leader in this field, noting that different funding interventions are needed at different stages for different technologies.

- **No Gap support** – there is a need to better manage the tension between continuity of funding and ensuring that the right projects move forward. For example, the ability to support extended grant durations covering multiple translational steps, with expedited but robust review at critical stage gates to ensure that projects remain competitive, will speed up progress through the developmental pathway towards patient benefit and / or commercialisation. However, simply lengthening the duration and volume of project funding is not enough and there is also a need for better training, monitoring and mentoring to support such programmes.

- **Streamlined opportunities to reverse translate outputs from clinical work** across sectors to enable mechanistic insight, potentially tied to broader, more ambitious programmes of investment, could further grow and support translation, furthering bilateral links with discovery science.

- **MRC's translational strategy should be regularly refreshed and marketed** to ensure that it continues to build on preceding successes, address any identified gaps and safeguard a sustained continuum of funding, In particular, it will be important to ensure its suitability to support, de-risk and develop innovative technologies, including the development of appropriate cross discipline funding schemes with other funders to remove perceived barriers to interdisciplinarity while building a consistency of approach across the UK landscape.

7.2.2 Skills, Training and cross sector working

In general, the level of translational research skills has improved over the last decade, although some of the long persistent issues of training, career development and culture of cross sector working remain. UK skills gaps in translation have been discussed in many fora[25] and the results of this evaluation's interviews largely reflect the same conclusions. For example, a lack of commercial knowhow is considered pervasive across the university sector and a barrier to driving translation, while the UK ecosystem is still seen by many overseas experts as lacking serial entrepreneurs with experience of commercialising innovation.

In 2007/8 MRC was aiming for a substantial increase in training and capacity building in areas relevant to translation. Our assessment is that substantial progress has been achieved mostly through university-level development of

[25] For example, the Academy of Medical Sciences (AMS) and the Association of the British Pharmaceutical Industry (ABPI) discussed bridging the pre-clinical to clinical boundary at a joint meeting in 2018, and highlighted skills shortages https://acmedsci.ac.uk/file-download/36971834, the ABPI reported on skills gaps pertinent to the life science industry in 2015 https://www.abpi.org.uk/media/1134/skills_gap_industry_executive_summary.pdf.

training programmes and changing expectations for non-clinical and clinical trainees; coupled with hands-on experience gained in translational projects. Continued support for translational skills will remain an important priority for the MRC.

Opportunities:

- How, alongside UKRI initiatives, MRC could encourage more early career researchers to gain experience of translational working (e.g. through CiC) and enhance mobility between academia and industry sectors.
- Whether additional funds for more focused skills-gap schemes (e.g. training posts specifically in translation, potentially working across a portfolio of projects) might allow faster change and faster growth.
- Whether the landscape offers suitable opportunities for talented and motivated researchers to readily upskill, gaining an understanding of entrepreneurship and developmental pathways across sectors.
- How career pathways and incentives can be adapted to reduce the barriers to academic careers in translational medicine.

7.2.3 Collaboration and fostering innovative partnerships

Over the last 10 years attitudes to collaboration between academia and the private sector have improved and there is a notable increase in the numbers of open innovation[26] schemes enabled by industry. MRC's aims to develop more collaborative programmes with industry have been achieved successfully in the large Precision Medicine clinical consortia; but in earlier stage research and in more focused work there isn't an equivalent general mechanism for partnership building and support. The AZ Mechanisms of Disease Initiative was ground breaking, and MRC's leadership in translation and industry engagement has influenced culture and collaboration in general, but MRC should consider how it will drive up the level of meaningful collaboration in future.

Tightly focused, ambitious, projects such as those funded through DPFS have led to important new company formation and SME growth, but have less often contributed to and benefitted from collaborations with more established companies. To fully develop the UK's potential here, collaborations exploring disease mechanisms, providing valuable insight into novel targets or biomarkers; or addressing common challenges in emerging technologies or safety would be a useful addition. MRC did not sustain biomarker or models of human disease programmes for multiple cycles of funding, but the results from the small sample of outcomes suggest that when well designed, the results can be impressive.

Opportunities:

- The expectation that the numbers of academic industry partnered projects would increase over the decade has not been realised and this needs further evaluation. Exploring opportunities to enable meaningful academic / industry partnerships concentrated around an identified gap of target identification and validation will be undertaken.
- Proactively support brokering and networking activities to enable collaboration, building on the current precision medicine approach – critical understanding of disease biology and pathways remains the preserve of academia but can enable translation and underpins downstream partnerships with industry. More visible and flexible pathways for academia to link into industry resources and skills for product development, alongside improved visibility for industry of relevant biologic insight, offers a clear path to health impact.
- Increase recognition and visibility for industry leads on academic proposals, codifying the move away from a transactional relationship towards a partnership.

[26] Open innovation refers to the trend for the private sector to look externally for sources of innovation, by co-operating with academia and other firms, rather than relying mostly on intramural R&D.

- Extend MRC reach across all relevant business sectors beyond biopharma, for example to include sensor developers or commercial manufacturers, to support and explore the development of innovative collaborative (e.g. co-development) partnership models and ideas

7.2.4 UK Translational environment

The evidence supports the premise that the UK translational environment has improved over the decade through significant investment. However, several commonly cited barriers and enablers remain (as illustrated in the sections above) and further work to grow the translation and innovation culture and mindset is needed. Examples might include the level and type of institutional support for translation and IP, recognition of translational outputs for university careers and via the REF, access to enabling infrastructure, resources and capabilities and proximity to local clusters and networks. At the strategic level, a lack of coordination between funders and the complexity of the funding landscape has been highlighted.

The creation of UKRI has already started to pay dividend in boosting the UK translational ecosystem and more effectively enabling cross Research Council-Innovate UK and Research England working through its challenge led Strategic Priorities Fund and through the pioneering Industry Strategy Challenge Fund, bringing together academia and industry to deliver on the UK's ambitious Industry Strategy. It will be important to continue to work closely with external commercial thought leaders to ensure that the needs of the various industry sectors are considered when developing future opportunities.

While we continue to develop and refine the UK landscape, there is a need to ensure that we are not entirely inward looking and need to work synergistically in a collaborative international setting if societal challenges are to be resolved.

Opportunities:

- Development of a comprehensive UK roadmap for national infrastructures, clusters and capabilities for industry and academia, highlighting strengths and gaps enabling co-investment with business or with other funders to build focused infrastructure around areas of opportunity and need.
- Coordination between UKRI and other major funders, such as the NIHR on translational research infrastructure to identify and bridge gaps, avoiding duplication and eliminating unnecessary shifts in process or approach between funders.
- Creation of a simplified UK translational funding map.

Translational research is a central theme in the new MRC Delivery Plan. In ten years from now, some of the initially high-risk ideas among the projects evaluated should be delivering real benefits to patients. Realising this will be largely beyond MRC's control, but MRC's crucial role will be to consolidate the successes outlined in this report (such as the emerging advanced therapy field), widen approaches to new areas (such as digital health) and identify and build up as yet unimagined fields of biomedicine. Achieving this will be challenging, and will require new resources, but is vital to deliver with the UK's ambition to be a more research-intensive economy.

Annexes

A1 – Summary of methodology

A more detailed description of the evaluation methodology is provided in Annex A2.2.

A1.1 Inception phase

Ten scoping interviews (both phone or face-to-face) with former and current MRC staff associated with translational research funding and a parallel review of all major documentation relating to the MRC's directed translational research initiatives was conducted to inform the design of the evaluation. The aim of this exercise was to build understanding of the objectives, development and strategic direction of the MRC' translational research investments and define an overarching evaluation framework describing their anticipated outputs, outcomes and impacts. This was summarised in a logic model (details in the evaluation framework at Annex A2.1) which informed design of the relevant research instruments.

A1.2 Literature review:

A literature review was conducted by Technopolis from October to December 2018 to understand the translational research landscape in the UK, global activities in this area and what works. The review used keyword search strings to identify relevant peer-reviewed literature from PubMed and grey literature from Google searches and websites of government departments, research funders, international organisations, and professional associations. Emphasis was placed on identifying evaluations of translational research programmes so that learnings could be identified and synthesised into a summary of common bottlenecks and key ingredients of translational research. Countries and regions of interest included the USA, Canada, Australia, Hong Kong, the European Union, Norway, Germany, UK and Catalonia. The full literature review can be accessed via Annex A2.3.

A1.3 Bibliometric analysis

Analyses of publication output of MRC awards funded over a 10-year period from 2008 to 2017 was conducted by Science-Metrix[xxxvii] as part of the evaluation. The overall MRC portfolio included all types of award. The analysis was carried out to calculate the citation uptake of publications supported by the MRC, and to compare with the US National Institutes of Health and Wellcome, across various data sources, such as guidelines, patents and clinical trials. This analysis also enabled a comparison of the relative performance of MRC translational research funded via different initiatives. The full details of the bibliometric analysis can be accessed via Annex A2.5.

A1.4 Interviews with principal investigators

In-depth qualitative interviews were conducted with 250 principal investigators, representing a sample of all eligible awards across the entire MRC translational research portfolio. Additionally, the sample was designed to reflect geographical regions (i.e. different institutions or hubs) and gender, age and ethnicity of the investigators. 179 interviews were conducted with researchers who received a directed translational award (including 20 interviews with researchers who received CiC funding), 49 interviews were conducted with researchers who received an award that had been identified as having some stated translational intent from the non-directed portfolio and 11 interviews with investigators who received other awards (with no stated translational intent, but with some reported translational outcomes). Interviews were conducted via Skype or Webex and were recorded (with the interviewees consent) for analysis purposes. The fieldwork ran from 6 December 2018 to 18 March 2019. Interviews typically lasted between 45 minutes to an hour. The discussion guides used for researcher interviews can be accessed via Annex A2.4.

The transcripts of the interviews were then coded against a framework of project outcomes by Ipsos MORI. Outcomes included in the framework emerged from discussions between MRC, Ipsos MORI and Technopolis, and this data was used for semi-quantitative analysis of project progression.

A1.6 Interviews with Key Stakeholders

In-depth qualitative interviews were conducted with 109 stakeholders in Spring 2019. A sample of potential stakeholders was drawn from a list of more than 150 representatives from funding agencies, the private sector, academic institutions (researchers and TTOs), venture capitalists active in the life science sector, and those representing international organisations relevant to translational research and the life sciences sector. Interviews were conducted via telephone / Skype / Webex and were recorded (with the interviewees consent) for analysis purposes. Interviews typically lasted between 45 minutes to an hour. The transcripts of the interviews were then coded against a framework of themes by Technopolis. The discussion guides used for key stakeholder interviews can be accessed via Annex A2.4 and a summary of the results can be accessed via Annex A2.6.

A1.7 Analysis of secondary data

A database of spin-outs emerging from MRC research was established by cross-referencing self-reported records from Researchfish® with administrative records of new companies incorporated by funded and unfunded principal investigators recorded by Companies House and evidence gathered from the interviews described above. This database was linked to other sources of information on company performance, including records of clinical trial activity held within Pharmaprojects, data on venture capital and other forms of investment captured by Pitchbook, and markers of growth contained within Companies House. A separate analysis, comparing marginal applicants to the DPFS was completed to explore that degree to which the outcomes observed could be attributed to MRC funding. The full details of this analysis can be accessed via Annex A2.7.

A2 – Supplementary material available online

A3 – Glossary

BBSRC	**Biotechnology and Biological Sciences Research Council.** The BBSRC is one of the constituent councils of UKRI, it invests in world-class bioscience research and training. https://bbsrc.ukri.org/
BEIS	UK **Department for Business, Energy and Industrial Strategy** is a ministerial department supported by 41 agencies and public bodies (including UKRI). https://www.gov.uk/government/organisations/department-for-business-energy-and-industrial-strategy
BMC	**UK BioMedical Catalyst (BMC)**. The BMC is a brand for selected Innovate UK and MRC initiatives in translational medicine. https://mrc.ukri.org/funding/science-areas/translation/biomedical-catalyst/
CARP	**Clinical Academic Research Partnership** is a new MRC funding scheme to support NHS consultants with a higher research degree, who are not currently research active to participate in collaborative high-quality research partnerships with established leading biomedical researchers https://mrc.ukri.org/news/browse/new-funding-scheme-supporting-clinical-research-capacity/
CAR-T	**Chimeric Antigen Receptor T-cell** therapy**.** A type of treatment in which a patient's T cells (a type of immune system cell) are changed in the laboratory so they will attack cancer cells
CiC	**Confidence in Concept.** CiC is an MRC funding scheme providing flexible institutional awards to support preliminary translational work https://mrc.ukri.org/funding/browse/confidence-in-concept-scheme-parent/confidence-in-concept-scheme-2017/
CRUK	**Cancer Research UK** is the world's largest cancer charity dedicated to saving lives through research https://www.cancerresearchuk.org
CTSA	**Clinical and Translational Science Awards** is a US NIH funding programme designed to improve the efficiency, quality and impact of the process for turning observations in the laboratory, clinic and community into interventions that improve the health of individuals and the public https://ncats.nih.gov/ctsa
DHSC	**Department of Health and Social Care.** The DHSC supports ministers in delivering the government's health and care priorities including the Long-Term Plan for the NHS. https://www.gov.uk/government/organisations/department-of-health-and-social-care
DPFS	**Developmental Pathway Funding Scheme.** DPFS is an MRC funding scheme for supporting academically-led translational projects https://mrc.ukri.org/funding/browse/biomedical-catalyst-dpfs/biomedical-catalyst-developmental-pathway-funding-scheme-dpfs-outline-mar-2017/

EME	**Efficacy and Mechanisms Evaluation programme.** The EME programme was established in 2008 and is jointly funded by MRC and NIHR with contributions from the health departments in Scotland, Wales and Northern Ireland. It bridges the gap between preclinical studies and evidence of clinical efficacy and has invested more than £180 million on studies evaluating interventions in the promotion of health, treatment of disease and improvement of rehabilitation or long-term care. Within these studies, EME supports research to improve the understanding of the mechanisms of both diseases and treatments. https://www.nihr.ac.uk/explore-nihr/funding-programmes/efficacy-and-mechanism-evaluation.htm
EPO	**European Patent Office**, the EPO examines and grants European patents and provides data about patent applications https://www.epo.org/about-us/services-and-activities.html
EPSRC	**Engineering and Physical Sciences Research Council.** EPSRC is one of the constituent councils of UKRI, it invests in world-leading research and postgraduate training across the engineering and physical sciences. https://epsrc.ukri.org/
GPCR	**G-protein-coupled receptors.** The largest and most diverse group of membrane receptors in eukaryotes
HRCS	**Health Research Classification System.** The HRCS is a two-dimensional coding approach for classifying health research which has been widely used by UK funders since 2004, having been established by the UK Clinical Research Collaboration to support strategic discussions about health research www.hrcsonline.net
HTMR	**MRC Hubs for Trials Methodology Research (HTMR),** were established to co-ordinate methodology research across the UK, act as an interacting resource for researchers wishing to develop new trial methodologies and train the next generation of methodologists. https://mrc.ukri.org/funding/science-areas/methodology-research/resources/#hubs
i4i	**Invention for Innovation** i4i is an NIHR funding scheme that supports the preclinical and clinical development of medical devices in areas of existing or emerging patient need https://www.nihr.ac.uk/explore-nihr/funding-programmes/invention-for-innovation.htm
IMI	**Innovative Medicines Initiative (IMI).** The IMI is a public-private partnership between the European Community, represented by the European Commission, and the European Federation of Pharmaceutical Industries and Associations (EFPIA) committed to developing new medicines. It is the largest such partnership in the life sciences having provided a total of €5.3 billion of support for more than 130 projects. https://www.imi.europa.eu/
Innovate UK	**Innovate UK** (formerly the Technology Strategy Board) is one of the constituent councils of UKRI, supporting businesses to develop and realise the potential of new ideas, including those from the UK's world-class research base https://www.gov.uk/government/organisations/innovate-uk/about
Intramural	**MRC's intramural programme** refers to research undertaken in MRC's wholly owned Institutes and Units

IP	**Intellectual Property** is intangible property resulting from creativity, research etc. It may be protected using rights such as patents (for discoveries), trademarks or copyright (for written / recorded works)
IPO	**Initial Public Offering** the listing of company shares on a stock market for the first time
JPRCI	**Joint Patient Research Cohort Initiative** was funded by the MRC and NIHR with contributions from the health departments in Scotland, Wales and Northern Ireland to create new extensively-defined cohorts of patients to help detect, treat or prevent disease https://mrc.ukri.org/documents/pdf/patient-research-cohorts-initiative/
LifeArc	**LifeArc (formerly MRC Technology, MRCT)** was formed in the 1990s as MRC's technology transfer organisation. It has since become an independent charity and is sustained on the proceeds from discoveries it has helped translate to the market. https://www.lifearc.org/about/who-we-are/
MRC	**Medical Research Council.** Established in 1913 the MRC is the largest public funder of basic and early translational biomedical research in the UK, it is now part of UKRI. https://mrc.ukri.org/
MRI	**Magnetic Resonance Imaging** is a technique using strong magnetic fields, magnetic field gradients, and radio waves to generate images of the organs in the body
MRP	The **MRC/NIHR Methodology Research Programme (MRP)** is one of the main UK funding streams for methodological research which aims to inform research practice, policy and healthcare https://mrc.ukri.org/funding/science-areas/methodology-research/
NHS	**National Health Service** is the publicly funded national healthcare system for England and one of the four National Health Services for each constituent country of the United Kingdom https://www.nhs.uk/
NICE	**National Institute for Clinical Effectiveness** aims to improve health and social care in the UK by compiling guidance and advice https://www.nice.org.uk/
NIH	**US National Institutes of Health.** NIH is the main US public funder of biomedical research https://www.nih.gov/
NIHR	**National Institute for Health Research**. NIHR is UK's largest public funder of health and care research https://www.nihr.ac.uk/
NIHR BRC	**NIHR Biomedical Research Centre.** NIHR's 20 BRCs are collaborations between world-leading universities and NHS organisations that bring together academics and clinicians to translate lab-based scientific breakthroughs into potential new treatments, diagnostics and medical technologies. https://www.nihr.ac.uk/explore-nihr/support/experimental-medicine.htm
OLS	**Office for Life Sciences** within BEIS and the DHSC champions research, innovation and the use of technology to transform health and care service. Among other things OLS compiles the Bioscience and Health Technology database, a curated list of UK life science companies https://www.gov.uk/government/organisations/office-for-life-sciences

OSCHR	**Office of Strategic Co-ordination for Health Research.** The Cooksey report in 2006 recommended that OSCHR be established to co-ordinate UK health funding and improve support for translational research. OSCHR reports to both the secretary of state for Health and the secretary of state for BEIS (then Department for Trade and Industry) https://mrc.ukri.org/about/what-we-do/spending-accountability/oschr/
R&D	**Research and Development** describes innovative activities undertaken by corporations or governments in developing new services or products, or improving existing services or products
REF	**Research Excellence Framework.** The REF is a periodic assessment of the research excellence of all UK higher education providers run by Research England (part of UKRI). The next REF exercise is planned for 2021. https://www.ref.ac.uk/about/what-is-the-ref/
RMRC	**Regenerative Medicine Research Committee** was an MRC funding scheme that extended the work of the TSCRC beyond stem cell work into wider regenerative medicine, in 2018 the RMRC was discontinued as its work was sufficiently covered by the research boards and DPFS
SME	**Small to Medium Enterprise.** We use the European Union definition of an SME (https://ec.europa.eu/growth/smes/business-friendly-environment/sme-definition_en) a company that has less than 250 staff and turnover of less than €50 million per year
TRG	**Translational Research overview group.** One of MRC's four overview groups tasked with maintaining an overview of translational research, the TRG commissioned this evaluation and is chaired by Professor Dame Anna Dominiczak https://mrc.ukri.org/about/our-structure/strategy-board-overview-groups/translational-research-group/
TSB	**Technology Strategy Board** – the former name for Innovate UK (see above)
TSCRC	**Translational Stem Cell Research Committee** was established by the MRC in 2008 as a specialist funding panel to support for high quality research aiming to apply stem cell technology to improve human health, it provided the foundation for the successor RMRC
TTO / TRO	**Technology Transfer Office / Translational Research Office** refers to the department within a research organisation responsible for knowledge exchange, technology transfer and other aspects of the commercialisation of research.
UKRI	**UK Research and Innovation.** UKRI was established in 2018, the national funding agency investing in science and research in the UK. Operating across the whole of the UK with a combined budget of more than £6 billion, UKRI brings together the 7 Research Councils, Innovate UK and Research England (https://www.ukri.org/)
UKRMP	**UK Regenerative Medicine Platform (UKRMP)**. Established in 2013 by the BBSRC, EPSRC and the MRC, the UKRMP is a £42 million initiative that is addressing the key translational challenges of regenerative medicine. https://www.ukrmp.org.uk/
USPTO	**United States Patent and Trademark Office** is the federal agency for granting U.S. patents and registering trademarks (www.uspto.gov)

VC	**Venture Capital** is a form of financing provided by funds or firms to early stage companies, usually because they are deemed to have high growth potential
Wellcome	**Wellcome** is the world's largest charity supporting biomedical research (https://wellcome.ac.uk)

Endnotes

[i] The **Valley of Death** in research refers to a gap between early stage discovery science mainly conducted in academia and later applied work mainly carried out in the private sector. In 2008 an editorial in *Nature* expressed "concern that the resources being put into biomedical research, and the huge strides made in understanding disease mechanisms, are not resulting in commensurate gains in new treatments, diagnostics and prevention" https://www.nature.com/news/2008/080611/full/453840a.html. Investments in translational research help bridge this gap and cross the Valley of Death.

[ii] https://mrc.ukri.org/funding/science-areas/translation/

[iii] In 1973 MRC funded research led to the development of Magnetic Resonance Imaging (MRI) https://mrc.ukri.org/news/blog/behind-the-picture-the-humble-beginnings-of-mri/. Today more than 3 million MRI scans are performed by the NHS annually providing crucial information to clinicians. While manufacturers of MRI systems are largely based outside the UK (Philips, Siemens, GE, Toshiba), there has been a lasting economic impact in the UK of MRI beyond the original world-wide licensing of the technology to these firms (for example the market for superconducting magnets). Introduction of the technique created a global market for MRI systems that is now estimated at between $5 -$6 billion. In 1975 MRC research led to the discovery of monoclonal antibodies and in 1980 the technique for humanising them for clinical use https://mrc.ukri.org/news/blog/from-tool-to-therapy-a-timeline-of-monoclonal-antibody-technology/. Today 57 monoclonal antibody drugs are currently licensed for use, and the global market for these drugs is valued at between $100 and $120 billion. The licensing of this technology has brought significant returns to the UK, including more than £700 million over ten years to the MRC.

[iv]A key point in the history of support for academic translation is that in 1985, the UK government announced that the British Technology Group (BTG)
(formerly the National Research Development Corporation) would no longer have the
exclusive right to commercialise inventions deriving from university research and
resulting from Research Council funding. Since that time Research Councils and universities as employers of researchers have been active in commercialising their intellectual property.

[v] Formerly MRC Technology the technology transfer organisation for the MRC, LifeArc is now a UK charity focussing on biomedical translation and its work has contributed to launching four major humanised monoclonal antibody drugs to the market. A portion of the royalties from one of these (Keytruda®) was monetised in 2019 to create a $1.3 billion philanthropic fund for LifeArc to support collaborative research https://www.lifearc.org/news/news-events/.

[vi] A joint MRC/Department of Health delivery group had been formed in 2004 to align activities between MRC and NHS R&D, and this was strengthened with the formation of the Office for Strategic Co-ordination for Health Research (OSCHR) following the Cooksey review.

[vii] The Allocation of Science and Research Funding 2011/12 – 2014/15 (BIS, 2011) https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/422477/bis-10-1356-allocation-of-science-and-research-funding-2011-2015.pdf

[viii] The Allocation of Science and Research Funding 2016/17 – 2019/20 (BIS, 2016) https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/505308/bis-16-160-allocation-science-research-funding-2016-17-2019-20.pdf

[xii] The 2018 HRCS analysis is expected to be published by the end of 2019, and will be published at www.hrcsonline.net

[x] Some of the ways in which NIHR funding has positively impacted on UK translational research were set out a synthesis to mark the first 10 years of NIHR's work https://www.nihr.ac.uk/documents/the-national-institute-for-health-research-at-10-years-an-impact-synthesis-100-impact-case-studies/12172

[xi] See the Chief Scientists Office (Scotland) https://www.cso.scot.nhs.uk/; Health and Care Research Wales https://www.healthandcareresearch.gov.wales/about/; HSC R&D Division Northern Ireland https://research.hscni.net/

[xii] the UK Life Sciences Strategy (BIS, 2012) https://www.gov.uk/government/publications/uk-life-sciences-strategy

[xiii] These plans can be found in the 2008 MRC Annual Report https://mrc.ukri.org/publications/browse/annual-report-and-accounts-200809/

[xiv] The MRC Strategy 2014 – 2019, Research Changes Lives (MRC, 2014) https://mrc.ukri.org/publications/browse/strategic-plan-2014-19/

[xv] A Strategy for regenerative medicine (MRC, 2012) https://mrc.ukri.org/publications/browse/regenerative-medicine-strategypdf/

[xvi] The 20 universities in Figure 1.6 account for 49 percent of MRC expenditure between 2008 and 2018, other universities 6 percent, MRC Institutes account for 15 percent, other MRC Units 19 percent, with the remainder being transfers to other organisations and international subscriptions.

[xvii] Pressure sensors to help prevent pain for amputees (BBC News, 2014) https://www.bbc.co.uk/news/health-26891863

[xviii] Integrated interfacial sensors for assessments of lower limb prosthetics (MR/L013096/1) https://gtr.ukri.org/projects?ref=MR%2FL013096%2F1

[xix] Hydrogels – a unique solution for stem cell storage and transport (MRC News, 2015) https://mrc.ukri.org/news/browse/intellectual-property-hydrogels-a-unique-solution-for-stem-cell-storage-and-transport/

[xx] Therapeutic corneal stem cell delivery using hydrogels without the need for ex vivo expansion (G0900877) https://gtr.ukri.org/projects?ref=G0900877

[xxi] Atelerix company website https://www.atelerix.co.uk/

[xxii] Evaluating translational research: a process marker model Trochim *et al.* (2011) https://www.ncbi.nlm.nih.gov/pubmed/21707944

[xxiii] Monitoring wound status using multi-parameter optical fibre sensors (MR/R025266/1) https://gtr.ukri.org/projects?ref=MR%2FR025266%2F1

[xxiv] Development of a Novel Liver Dialysis Device (G0902211) https://gtr.ukri.org/projects?ref=G0902211
[xxv] Development of a software application for detection and monitoring of attentional deficits in delirium (MR/L023210/1) https://gtr.ukri.org/projects?ref=MR%2FL023210%2F1
[xxvi] Delbox and Delapp: diagnostic tools for delirium (MRC, 2014) https://mrc.ukri.org/documents/pdf/llhw-delbox-case-study/
[xxvii] Diagnostic test accuracy of a novel smartphone application for the assessment of attention deficits in delirium in older hospitalised patients: a prospective cohort study protocol BMC Geriatrics (2018) https://bmcgeriatr.biomedcentral.com/articles/10.1186/s12877-018-0901-5
[xxviii] The NIH focus for translational research is through the National Centre for Advancing Translational Sciences (NCATS). In 2018 the NIH appropriation for NCATS was $742 million with the condition that at least $543 million was provided to the CTSA program. https://ncats.nih.gov/about/center/budget/past
[xxix] Links might include principal, or co-investigators of MRC projects being named as directors of the spin-out company, there being a clear connection between the research supported by the MRC and the acknowledged assets of the company etc.]
[xxx] Affigo company website https://www.affigo.io/
[xxxi] https://www.nice.org.uk/guidance/ta534
[xxxii] http://ir.anaptysbio.com/news-releases/news-release-details/anaptysbio-presents-updated-data-anb020-phase-2a-atopic?ID=2333120&c=254208&p=irol-newsArticle
[xxxiii] de Vrueh, R.L.A. & Crommelin, D.J.A., 2017. Reflections on the Future of Pharmaceutical Public-Private Partnerships: From Input to Impact. *Pharmaceutical Research*, 34(10), pp.1985–1999. https://link.springer.com/article/10.1007/s11095-017-2192-5
[xxxiv] https://www.abpi.org.uk/facts-and-figures/science-and-innovation/global-public-funding-of-health-rd/
[xxxv] UK Clinical Research Collaboration, 2015. *UK Health Research Analysis 2014* *www.hrcsonline.net*
[xxxvi] *Biotechnology Report 2017: Beyond borders - Staying the course (*Ernst and Young, 2017) *https://www.ey.com/Publication/vwLUAssets/ey-biotechnology-report-2017-beyond-borders-staying-the-course/$FILE/ey-biotechnology-report-2017-beyond-borders-staying-the-course.pdf*
[xxxvii] Science-Metrix is an independent research evaluation firm http://www.science-metrix.com/?q=en/about-us/who-we-are

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