MRC Translational Research 2008-2018

Evaluation Report: Analysis of stakeholder interviews (Annex A2.6)

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ANNEX A2.6: Stakeholder interviews – full analysis

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1   Summary of stakeholder interview programme

A total of 110 stakeholder interviews were conducted. These included:

- Researchers: 51 researchers with public or charity funding, including 12 with private sector experience (47 in UK, 4 abroad of which 3 in US)

- Private sector: 18 representatives from the private sector (14 associated with a large pharma company, or with extensive background in large pharma; 4 active in SMEs)

- Investors: 8 investors / representatives from venture capital (6 UK-based, 2 based in Germany)

- Funders: 7 funders (5 UK of which 3 charitable organisations, 2 US funding agencies)

- Knowledge exchange / TTO: 13 knowledge exchange and tech transfer professionals: 4 at institutions in the Golden Triangle (Tier 1), 1 at a Tier 2 institution, 5 at Tier 3 institutions, 1 at a Tier 4 institution, and 2 in the tech transfer arm of a funder

- Other: 13 individuals categorised as 'other': consultants (3), heads of research infrastructure / networks / programme coordinators (8), and individuals involved in several roles (2)(It should be noted that many individuals consulted have been involved in multiple roles and sectors; a judgement was made as to the most appropriate category.)

98 individuals are either located in the UK or have recent extended experience of working in the UK. 12 individuals are predominantly located outside the UK; of these 6 are in the USA (2 funders, 3 researchers, 1 consultant), 3 in Germany (2 investors, 1 researcher), 1 in Singapore, and 2 work for pan-European organisations.

The following tables present a breakdown of UK researchers interviewed by institution, research intensity of the institution, and geographic location.

Table 1 Stakeholder interviews - Researchers

Name of institution	No. of researchers interviewed
Cambridge and Oxford Universities	7
Edinburgh University	5
King's College, Imperial College, and University College London	4 each
Queen Mary U, U Dundee, Newcastle U, Southampton U	2 each
Cardiff U, Lancaster U, U Kent, Nottingham U, St Andrews U, Queen's U Belfast, U Bristol, U Liverpool, U Glasgow, MRC-LMB	1 each

Tier of university by level of health research funding 2014*	No. of researchers interviewed (in brackets: with industry experience)
Tier 1 (more than £30 million)	25 (6)
Tier 2 (£15-30 million)	8 (1)
Tier 3 (£5-15 million)	12 (3)
Tier 4 (less than £5 million)	3 (1)

* https://hrcsonline.net/reports/analysis-reports/uk-health-research-analysis-2014/

Location of institution	Name of institution	No. of researchers interviewed (in brackets: with industry experience)
England		**36 (9)**
London	UCL, Imperial, KCL, Queen Mary	14 (2)
South East	Oxford, Southampton, Kent	8 (3)
East	Cambridge	8 (2)
South West	Bristol	1 (o)
East Midlands	Nottingham	1 (1)
North East	Newcastle	2 (1)
North West	Liverpool, Lancaster	2 (0)
Northern Ireland	Belfast	**1**
Scotland	Edinburgh, Glasgow, Dundee, St. Andrews	**9 (1)**
Wales	Cardiff	**1 (1)**

2 Changes in translational research landscape in last 10 years

2.1 Changes in the broader R&D landscape

Over the past 10 years, industry has progressively shifted from all in-house discovery to collaboration with or licensing from academia and biotech SMEs, or purchase of small innovative companies. This was driven primarily by high failure rates coupled with the rising cost of later-stage TR, due to the complexity of the underlying science and regulatory requirements, and led academic research to move into the gap that opened in early TR. Industry in turn started looking to collaboration with academic research groups to bring early TR into its pipelines. Large pharma companies often set up a number of strategic partnerships with key research institutions such as London, Oxford, and Cambridge universities and institutions around Boston.

Other factors driving change in the TR landscape were identified by number of interviewees:

- Industry realised that it was not efficient to compete in the early TR space and shifted to collaboration platforms and open science models in this 'pre-competitive' space, e.g. IMI. While interviewees agreed that these platforms have helped to improve collaboration activity in the TR community, some questioned how effective open innovation has been in terms of health impact.

- Large pharma companies reduced their UK operations, releasing an experienced TR workforce. Many of these TR experts retired, but some took on roles at UK academic institutions or started specialist CROs now active in the UK landscape. This helped to support the development of TR programmes at UK universities and publicly funded institutes.

- The '-omics revolution' and large data technologies have led to a recognition that population-based approaches and data sharing across organisations are needed to advance research efficiency.

In UK, the increased focus on translation was driven by the UK government's requirement for funders to demonstrate impact, which triggered the MRC to shift more towards TR, and the government's focus on the life sciences as an engine for economic growth in the UK. This was passed on to the research community through the introduction of the REF impact measures, the requirement for 'impact statements' as a component of proposals submitted to the MRC, and the inclusion of impact categories

in ResearchFish reporting. Other drivers mentioned were the inclusion of individuals from non-academic backgrounds on proposal review panels, the emergence of 'TR success stories' from academia which could function as models, and enhanced general awareness of progress elsewhere, e.g. in the US TR ecosystem (Boston, US West Coast).

As a result:

- The culture of the academic research community has shifted, with many PIs now interested in conducting TR and open to collaboration with industry, and an increase in TR skills in the academic community. Academic researchers who want to engage in TR now have the opportunities to do so; commercialisation and entrepreneurship are no longer frowned upon or considered 'low grade science' (but barriers remain, see section 'Culture and incentives'). One interviewee also commented that a lot more interdisciplinary research is taking place now, e.g. medical researcher partnering with engineers or directly applying for EPSRC grants.

- 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.

- As a result, the volume of 'translatable' research coming out of academia has increased. Representatives from TTOs as well as the investor community explained: The quality and quantity of translatable discoveries, and maturity of projects that investors see has 'improved tremendously over the last couple of years' as a result of increased funding in the ecosystem along with an increase in sources of non-private financing (allowing innovations still too risky for private investment to be taken a bit further until it is taken on by VCs). Another investor said: "In principle, I would say that the quality and the state of projects that come out of renowned research institutions like the MRC or Max Planck or Helmholtz has certainly improved since I started in the industry 20 years back. […] The biggest change has been really since 2010.". Academic researchers are increasingly using the spin-out route to commercialisation, generally to develop a technology to the point where it becomes interesting for a third party corporate entity.

- A number of UK universities have increased their capabilities to support commercialisation, such as TTOs and TROs (e.g. UCL, Imperial, Cambridge) – but others have not.

- A few interviewees from academic institutions felt that the increased emphasis on TR and impact had led to 'locking down of findings' through patents, hindering progress in discovery science by making it increasingly difficult to share information and collaborate. However, another described the academic researchers as "much more up now for just posting [their research] on a preprint server and letting other people see it, much less paranoid".

2.2   Changes in the translational research funding landscape

Interviewees from across sectors were in broad agreement that public funders and charities had strongly increased their focus on TR over the same period of time. Interviewees from all sectors explained that in the UK, the MRC and other funders established dedicated funding streams and the overall TR funding landscape diversified. This included the establishment of the NIHR, a large investment providing "excellent TR infrastructure" (but not available outside England), as well as enhanced TR funding from charities (e.g. Wellcome, CRUK) and through European research programmes. In addition to the MRC's dedicated TR funding streams, four interviewees (two researchers, two from private sector) called out the Wellcome Trust's Seeding Drug Discovery scheme as having been an important addition to the funding landscape.

Several interviewees from the venture capital community and researchers/KE professionals associated with the top UK universities also agreed that for the past 4-5 years, the level of capital available from VC funds had increased again (following the drop as a result of the financial crisis in 2008). However, a

few interviewees (two researchers, one funder) thought the overall level of TR funding at academic institutions had fallen, due to a decrease in investments from large pharma companies, and level public funding against a backdrop of rising research costs. A small number of interviewees, including investors, a representative from the private sector and a funder, thought that TR in the UK was now more difficult than 10 years ago, due to rising costs and increased administrative and regulatory burden. As one interviewee from the investor community commented: "I get a sense that translational research has got harder to do. Certainly, once you start getting closer to patients, it's harder, more bureaucratic, the clinicians have less power, it takes too long, it's too expensive. That's what I would generally say about most translational research. I think the UK has gone from being a good place to do translational research to a heavily bureaucratic and obstructive place to do translational research."

Interviewees across sectors (except 'other') specifically acknowledged the MRC's contribution to supporting high level discovery science to underpin TR and providing seed funding to bridge the 'valley of death' between discovery science and TR, 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 stratified medicine and regenerative medicine (mainly mentioned by academic researchers, but also individuals from other sectors). Several interviewees, both academic researchers and from the private sector, called out the MRC's important role in driving industry partnerships, as well as its efforts to improve alignment with other funders, e.g. in research consortia. Facilitation of academia-industry interactions and collaborations (e.g. by appointment of members of industry to review boards, and via asset-sharing schemes) was generally seen to have had a positive impact on the UK's TR landscape. As one interviewee with a career spanning large pharma and academia explained: "The MRC are, and I say this because I worked internationally, they are probably one of the best research funding councils on the planet, because the UK is very strong in it. But what they really did then was say, right, can we actually grease the wheels to bring a lot of the industry together? We were struggling as an industry to move some of the big challenge areas forward, because it was bankrupting every company individually. The MRC really got behind a lot of the pre-competitive work. They let us all come together into the same ballpark.". A few interviewees also commented that research over the last ten years had increased in 'back translation', i.e. understanding patient's basic disease and resistance mechanisms driving the next generation of studies, supported by increased interaction with care delivery organisations and patients.

2.3   Research developments

Interviewees highlighted the following broad research developments over the last 10 years:

- Many interviewees pointed to the move from studies based on single observational data to using large datasets from multiple sources, e.g. combining various -omics, digitalised imaging data, as well as patient-reported data (enabled through digital health technologies). This has brought with it the opportunity to:
    - Shift from a reductionist to a more holistic approach to disease and patient needs
    - Move to therapies tailored to the individual patient, rather than to populations (stratified medicine / personalised medicine)
- This shift was enabled by the 'data revolution' and the ability to share data across research groups.

    A future area of research identified by many interviewees related to the area of data integration, i.e. how to enable full analysis drawing on data from disparate data sources, involving computer science, AI and machine-learning. One interviewee pointed to the continued need for harmonisation of patient assessment, to enable comparable data to be collected.

Other developments mentioned were:

- A shift from animal models towards human model systems, responding to the high failure rate of animal models. This has led to increased use of patient samples/human tissue samples and cell cultures, and development of human biomarkers (e.g. in neurology).

- A shift from small molecule drugs to biologics/molecular medicine. This also shifted the 'location' of expertise: While capabilities in small molecules are much stronger in industry than academia, biologics capabilities are (also) strong in academia. There was concern that the shift towards biologics and the downsizing of large pharma in the UK would lead to a drying up of the drug discovery pipeline and loss of skills in medicinal chemistry.

- 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

- A few interviewees pointed to the maturing of the digital health field: While this area is still not taken as seriously as conventional health interventions, some applications have seen substantial successes in tackling major diseases (e.g. a reversal of Type 2 Diabetes in 30-40% of users).

2.4   The role of public funders

Interviewees broadly agreed that public funding has a fundamental role in TR, especially in three main areas:

- Funding the early stages of TR and de-risking innovation to the point where the private sector can step in, thus helping to bridge the gap (T1 gap) between basic and translational research

- Enabling high quality basic science / discovery science research to feed the TR pipeline

- Addressing areas of unmet need (e.g. antibiotics, mental health, rare diseases, infectious diseases) and of limited commercial interest (e.g. repurposing, prevention, paediatric drugs), particularly where there is high potential for impact

Other roles for public funding mentioned by some interviewees were:

- The creation and support of research networks and platforms across sectors and organisations, e.g. academic research groups, industry and NHS biomedical science base. A few interviewees mentioned working with regulators and nurturing interactions with SMEs as especially important.

- Funding and maintenance of key research infrastructure such as clinical trial units, patient registries and cohorts, catapults etc.

- Supporting novel, high-risk research approaches with potential for high impact

- Steering researcher behaviour by incentivising TR and cross-sectoral collaboration

- Training and investing in individuals and their career development

There was broad consensus among interviewees that the UK is now better equipped for translational research than it was 10 years ago in terms of both people and facilities, and that public funders such as the MRC, NIHR, Innovate UK and the Wellcome Trust have significantly contributed to this outcome.

Infrastructure and facilities for TR have also improved significantly. Public funding has played a role in creating and supporting these e.g. through measures such as InnovateUK's funding for Advanced Therapy Treatment Centres, the NIHR's BRCs and investments from the MRC such as the Dementia Platform, the Farr Institute, the Genomics England Data Centre, and the MRC CTUs. In addition, programmes such as the NIHR Invention for Innovation scheme (i4i), as well as the Biomedical Catalyst and other Innovate UK schemes have been important for growth in the SME sector enabling them to move their inventions to the next translational phase and leverage investment from outside sources.

2.5   MRC funding and individual schemes

Many interviewees from across stakeholder groups considered the MRC a global leader in supporting TR 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 TR activity and research culture in the UK. Two interviewees from the USA considered the UK's early TR programmes (e.g. DPFS, NIHR i4i) ahead of the US NIH in some respects; the latter were perceived as narrow and providing support only for the fairly well-established technologies. Two (other) interviewees, with academic research backgrounds, felt that CRUK had been the leader in enabling TR (e.g. "CRUK really led 15-20 years ago, driving to embed and educate drug discovery within the academic setting to ensure that the appropriate studies were done early in the course of basic research to ensure the right decisions could be made later on in the process."); these efforts were soon followed by the MRC and the Wellcome Trust. Another interviewee pointed out that the MRC was ahead of other research councils in supporting TR. Other interviewees pointed to the Wellcome Trust's Seeding Drug Discovery scheme as having been a strong driver of TR in the academic community. The technology transfer arm of the MRC, LifeArc (previously MRC Technology) was highlighted as a success story, having successfully collaborated with the private sector, supported spin-out activity and licensed IP, giving rise to economic benefit.

At the same time, a number of interviewees warned against shifting too much funding away from basic science, as this was seen as a key source of new material for the innovation pipeline. Nonetheless, a few interviewees also commented that the MRC has balanced its basic science and TR funding extremely well, continuing to support the best discovery science alongside increased facilitation of translation.

2.5.1   Developmental Pathway Funding Scheme (DPFS)

The DPFS was seen as the key TR funding stream in the UK, helping to bridge the gap between discovery science and TR. Many interviewees felt that the model is well designed, and functions very well, and hence should be maintained or even expanded. To quote one interviewee: "I think funding like Developmental Pathway is really important to sustain translational research through that valley of death, if you like, to enable the future to be seen and for it to be taken up by a company or brought into a larger company and taken to market.".

Most importantly, DPFS was considered to have succeeded in moving assets further along the developmental pathway, many of which have been acquired by companies or led to spin-outs like Meira Therapeutics.

There were positive views of:

- the milestone-driven approach and the requirement for researchers to set out how their science will reach patients (triggering a fundamental shift in thinking from 'interesting science' to 'impact')

- the composition of funded teams, bringing together players from across the TR ecosystem (academia, company, investors)

- the grant selection process. The DPFS review panel, which includes individuals with high-level industry, venture capital, 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. However, one interviewee highlighted the need to include a broader range of TR experts, e.g. with a background in diagnostics.

The scheme was seen as having assisted in improving collaboration between academia and industry, changing academic researchers' attitude towards TR, and upskilling of academic researchers. It was also commented that the DPFS (and Efficacy and Mechanism Evaluation [EME]) schemes had made 'repurposing' an acceptable research area for academic researchers.

There were conflicting comments regarding the availability of advice and mentoring for grant holders – interviewees mentioned both the value of mentoring provided by funding committee members from industry and the improvement the MRC could make by supporting projects through provision of expert

advice once they had been funded. Further, one opinion was that many DPFS projects continue to run even though it is clear that they will not meet their overall aim. These should be terminated to free up resource for other research.

A few interviewees highlighted that areas such as digital health, diagnostics, and medical devices were not represented at the same level as drug development within the DPFS portfolio and review panel. One suggestion was that the MRC should broker partnerships between DPFS grantees and industry to help smooth 'handover' and have a rolling open competition for awarding grants to prevent any delays in translation. The rationale for this recommendation was that teams would lose valuable time trying to make industry contacts themselves or waiting for grants to fund the next stage of development.

2.5.2   Confidence in Concept (CiC) scheme

All interviewees who mentioned the CiC programme were complimentary of the scheme and felt that it has had a strong positive effect on progress in TR by:

- Enabling testing of ideas emerging from discovery science, steering further efforts (with 'fast failure' as a positive outcome)

- Providing an opportunity /lowering the entry barrier for interested academic researchers (especially postdoctoral researchers) to engage with TR and acquire the necessary skills

- Allowing universities to support multi-disciplinary and high-risk projects (for which there is often no clear route to funding)

- Effecting a culture change at universities by providing a devolved budget for TR that facilitates improved connections to investors and industry (e.g. by including them as advisors or reviewers of projects)

- Enabling universities to capture further funds, e.g. from industry or DPFS if proof of concept is established

Most interviewees hence felt that 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 PIs engage in translation. That wouldn't have happened without the CiC […]. It has had a huge impact […], it was transformational."

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. For that reason, a number of interviewees recommended putting more money into the scheme. However, it was noted that availability of funding for subsequent stages of the translational pathway was a barrier to capturing the full impact of the pump-priming activity supported by the CiC scheme.

CiC was seen as an important 'feeder' scheme for DPFS, with successful projects often considering DPFS funding to aid progression along the translational/product development pathway. In turn, the DPFS projects, when successful were seen as candidates for the MRC/NIHR EME programme, which funds late stage TR. Many commented that this is how the whole TR pathway is covered between MRC and NIHR.

2.5.3   Other schemes

The MRC's partnering schemes with companies were seen as innovative and effective in fostering interactions and collaboration between academia and industry as well as improving the knowledge base. Examples included asset-sharing schemes, MRC Industry Collaboration Agreements (MICAs) and industrial CASE studentships. However, some issues were pointed out as well. One interviewee highlighted an issue with asset sharing schemes, such as the MRC/AstraZeneca partnership that "industry teams on these de-prioritised compounds have dispersed by the time the academic researcher starts the project, and there is no further clinical trial supply". Another interviewee questioned the

rationale for using deprioritised compounds for academic research stating: "if the companies have deprioritised it, there's a reason why". On the other hand, one individual felt that encouraging industry to share assets was in itself important as it enables not only TR but also interrogation of basic biological pathways, and another advocated having similar drug discovery/screening initiatives jointly with industry in areas of unmet need (e.g. rare diseases and infectious diseases). Among the few interviewees that mentioned MICAs there was a difference of opinion with regard to their impact, with one interviewee mentioning that the bureaucracy associated with them can be an issue.

The Proximity to Discovery funding stream was mentioned by a few interviewees as having led to increased understanding and collaboration between academia and the private sector despite being supported with a very modest amount of funds. Activities supported included people exchanges, often involving first time principal investigators or postdoctoral researchers, and university-academia events, discussion forums and presentations. This role in supporting cultural change was seen as the most important impact of the stream.

Several interviewees are following the implementation and impact of the Clinical Academic Research Partnership (CARP) scheme with interest. The scheme fills an important gap in the UK TR community, especially as pressures on the NHS (and the perception of low priority given to research in the NHS) had been a barrier to engagement of clinicians in research. However, one interviewee was unsure about whether the MRC should support such a scheme.

Interviewees had very positive views of MRC-supported research consortia and networks as these were effective in bringing the various players of the TR ecosystem together, enabling pooling of resources, infrastructure, and expertise. For instance, the Stratified Medicine Initiative was considered a very successful example of how researchers, companies, patient organisations and charities working in a particular disease area could be brought together to explore new molecular and cellular pathways from the point of view of precision medicine. One example given was the EMINENT (Experimental Medicine Initiative to Explore New Therapies) network involving the MRC, GlaxoSmithKline and five UK universities, which studies a range of inflammatory diseases. This collaboration represented a step change from previous models of 'handing over funding' to academic researchers to a truly collaborative approach of joint working.

Stakeholders with experience of the MRC's unit/intramural funding model stated that the model itself was key in their ability to do TR. In their opinion, the block grant gives units flexibility and autonomy to pursue projects in the manner that they prefer, allowing them to adopt a more team-based approach, take on more risk and be more generous with money, time and credit for the research.

Platforms and other infrastructure such as the UK Biobank, Dementias Platform UK, Health Data Research UK, patient cohorts and clinical trial units were noted as MRC investments that have made a great difference to the TR landscape in the UK. A couple of interviewees mentioned the Methodology Research Programme and Experimental Medicine Challenges and stated that both worked well. The latter was said to be instrumental in spreading awareness about experimental medicine and allowing researchers to address very specific scientific questions using human subjects.

2.5.4   Gaps in the funding landscape

Many interviewees mentioned gaps in the funding landscape. Most frequently cited was the gap between early TR and the DPFS. This is especially relevant for institutions without CiC funding, but also applies to institutions with CiC funding, as increased level of pump-priming is needed to move some of the promising innovations to the point where they are ready for DPFS funding. One interviewee pointed to a funding gap to take forward targets identified in screens, e.g. through the MRC-AZ/UCB discovery platforms. Suggestions included a larger envelope for CiC funding, or an 'earlier stage' DPFS funding strand.

A few 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. Especially the need for, and cost of, robust lead optimisation was highlighted. Coordination between funding streams was noted as an

important aspect, e.g. the need to apply the same prioritisation criteria in DPFS and EME committees so that successful DPFS projects are able to continue to the next step.

Several interviewees did not see any gaps in the MRCs portfolio. As one interviewee explained: "I think [the MRC's portfolio] is well thought through. I think when they've identified a gap along the translational path, they've tried to flood it, for example gaps within industry collaboration, gaps enabling researchers to access the DPFS-type funding. […] They have discussions around how to impact their strategy and they're taking advice from industry, they're taking advice from senior clinicians, from academic researchers with broad backgrounds […], they work hard to ensure a diverse set of opinions are heard.".

Other gaps highlighted by a small number of interviewees include:

- Interdisciplinary research, especially bridging MRC and EPSRC expertise
- Bridging research coming out of MRC-funded consortia to be taken on by an individual company (not many instruments available to move into Phase I studies)
- Experimental medicine
- Methodology and statistical approaches in early TR (which would improve reproducibility)
- Medical devices
- Public health research: population and community-level approaches; PHE undertakes strategically important research for the UK not conducted in Universities (e.g. radiation) but cannot receive UKRI funding

When asked about future developments, 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. Other areas mentioned included mental health and drug discovery/medicinal chemistry. A small number of interviewees expressed concern that too many funders (including charities) had shifted their focus on TR and feared that a funding gap for fundamental research was emerging.

Some interviewees commented that they did not see any specific gaps, but that the overall level of funding was insufficient (both, per project and number of projects funded) (see section Funding). A few interviewees were also concerned with MRC funding being 'spread too thinly'. Suggestions for improvement included taking a strategic funding approach by focussing on promising technologies not yet sufficiently de-risked to be taken up by industry, or formation of centres of excellence around specific themes (see section Local clusters and thematic networks).

3   Enablers and barriers of translational research

Interviewees commented that the most important factors in enabling TR were researchers with TR capabilities (skills) working in teams (collaboration), the 'right mindset' (attitudes and culture), and funding. Institutional support and thriving local TR ecosystems (clusters) were also frequently mentioned.

3.1   Skills

A range of skills were mentioned by interviewees, falling into three categories:

a) TR skills

b) Commercial and entrepreneurial skills

c) Skills in specific research disciplines

3.1.1   TR skills

Interviewees from all stakeholder groups consulted broadly agreed that academic researchers are increasingly aware of the TR skills needed to move their research along the TR pathway. However, while capabilities have improved, interviewees from all sectors agree that significant knowledge gaps remain. Validation studies and knowledge of standard industry models were highlighted as essential for reproducibility of academic research and for projects to be taken up by the private sector. A number of interviewees stressed that the necessary set of skills is best achieved through collaboration (see 'collaboration' below). Hence, academic scientists do not need to duplicate industry skills (and vice versa), but each needs side needs to be aware of requirements and processes on the TR pathway.

Many interviewees highlighted a lack of training in TR. Learning occurs predominantly 'on the job', i.e. by trial and error, as academic researchers have limited training in TR disciplines during their formal education and most have not gained TR experience in industry (see 'collaboration' below). While a few interviewees thought the MRC had offered useful TR courses, many considered training to be a crucial gap in the MRC's support activities. The need to address this issue was seen as increasingly urgent: The downsizing of large pharma operations in the UK over recent years has released industry experts who are now nearing retirement; with limited new talent being trained, the UK is at risk of permanently losing these critical skills.

Suggestions to improve TR, commercial (and also entrepreneurial) skills fell into three broad categories:

- Expansion of TR courses, e.g. as a requirement for access to CiC funding, as part of the CiC roadshow, embedded into the early training of scientists or at MSc level, or as part of regular academia-industry workshops to learn about each other's needs and capabilities

- Access to expert advice, e.g. via mentoring schemes or by providing additional funding for consultants on TR projects. The Wellcome Trust Seeding Drug Discovery and the Wellcome Trust Translational Research Partnership schemes were mentioned as a best practice example, providing mentors and experienced individuals to be included in the project teams. One interviewee suggested a type of tax credit system could be established to incentivise companies to allow their staff to take on advisory/mentoring functions.

- Opportunities for academic researchers to spend time working industry, e.g. fellowships and industry placements. One interviewee elaborated on this aspect, highlighting that it would be more effective to have industry select fellows they want to work with, i.e. matching their interest (rather than having MRC panels select from the pool of candidates).

One interviewee from industry provided an example of the difference in approach between researchers with industry experience and 'more academic' researchers: "The best collaborations are with ex-industry people that have gone out into academia. Some of the collaborations we have with academics are sometimes challenging because they don't really see, they don't really understand well how to progress their project forward. They're quite involved in their own piece of research and they want to go deep rather than going forward sometimes. It also depends on the institution - I do see a difference with the ones which have some industrial influence in their ranks versus those that are more pure science based."

3.1.2   Commercial and entrepreneurial skills

Many interviewees, especially researchers but also from across the other stakeholder groups, identified a lack of commercial expertise among academic researchers. Regulatory requirements, commercial finance, and the ability to position technologies under development within the current commercial context were among the skills highlighted as essential to consider early in the TR pathway in order to facilitate progression to market. These skills are (still) rarely present in academic settings.

Interviewees also commented that the UK ecosystems lacks entrepreneurs with experience in commercialising innovations, especially compared to the innovation ecosystems around Boston and the

US West Coast (see section on 'Entrepreneurial mindset'). However, individuals with entrepreneurial skills and experience are needed to function as models and as a source of advice in the local TR ecosystem.

A few interviewees thought the MRC had driven some improvements in this area, e.g. via the Proximity to Discovery scheme, and through the industry exposure academic researchers were getting as part of DPFS and CiC grants. Some universities have also taken measures to bring in entrepreneurs providing researchers interested in commercialising their technology with advice and direction. Such 'entrepreneurs in residence' can also function as 'innovation scouts', i.e. experienced entrepreneurs who proactively identify research projects with commercialisation potential. For example, King's College London recently hired an expert from Technion (Israel) for this role.

3.1.3   Skills in specific research disciplines

Interviewees highlighted a range of disciplines with current skills gaps.

Most interviewees from across all stakeholder groups (especially researchers and the private sector) pointed to a lack of skills related to data (data science, AI, machine learning, bioinformatics), required to benefit from the large amount of health-related data that has become available. The USA and China were mentioned as front-runners in this area, with the UK in danger of falling (even further) behind.

Several interviewees highlighted that clinicians were a crucial component of TR teams and expressed concern over a lack of skills in the clinical sciences, such as clinical pharmacology and experimental medicine. This was put down to the lack of incentives and opportunities for clinical scientists in general to engage in TR, as they have to deal with multiple barriers (increasing pressure on NHS services, low priority of research within the NHS, a lack of a clear career structure for clinician-researchers in the UK – compounded by falling grant success rates). One interviewee contrasted this with the situation in the US: "[When] one sees what is available in the US, one realises how crazy it is to do academic medicine in the UK. One really has to suffer through years and years of applying for grants and training, so on and so forth, which really is not seen in other countries around the world. […] It really shouldn't be about suffering, it really shouldn't be about sacrifice, there really is no need for that."

Other areas of skills gaps included medicinal chemistry and health economics.

A few interviewees would like to see more flexible fellowships, enabling researchers to learn skills in other disciplines and bring these skills back into their 'own' discipline.

3.2   Collaboration

There was broad agreement across stakeholder groups that collaboration is essential to progress in TR.

Collaboration was described as a way to bring together the necessary skills which – given the breadth of expertise required – is beyond a single research group. This includes both, a) collaboration across disciplines and universities, and b) linking up across sectors combining scientific expertise from academia with private sector R&D experience and the NHS (clinical expertise/access to patients). Successful collaboration requires that individuals come to the table with an open mindset, i.e. a 'culture of collaboration'. A few of interviewees pointed out that some of the most successful UK drug discovery projects had combined academic and commercial expertise within one team, e.g. Abiraterone (CRUK Institute for Cancer Research) and Keytruda (MRCT). The University of Dundee was also mentioned as an example of an academia-industry collaboration that 'works.

3.2.1   Academia-industry collaboration

Many interviewees, including both researchers and representatives from the private sector, felt that attitudes to collaboration between academia and the private sector had improved: While 10 years ago industry and academia still operated each in their own 'silo', industry nowadays seeks academic input

to inform early stages of their R&D projects, and academic researchers are aware that moving their research along the TR pathway requires collaboration with industry. Several interviewees, from across stakeholder groups, pointed out that 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'.

However, a number of barriers to collaboration were mentioned.

The issue cited most frequently related to the lack of 'team science' in academia. The performance metrics and reward structures of academic institutions (in the life sciences) do not place sufficient value on team science and fail to incentivise academic researchers in joining large collaborative projects (see section 'Culture and incentives'). Several interviewees pointed out that as a result, academic researchers did not have the necessary skills to work in large teams across multiple disciplines and sectors.

Another barrier relates to the difficulty of finding the 'right' collaboration partner with complementary expertise. This process remains mainly serendipitous, e.g. through chance encounters at meetings, or through targeted approaches (e.g. via contacts provided in publications). This is especially problematic for academic researchers as the relevant contacts in industry are not easily identifiable on company websites, and small companies without staff and resources to dedicate to academic liaison. A few interviewees suggested that the MRC could assist further integration across sectors by further supporting collaborative networks and platforms. One interviewee highlighted the MRC cohort scheme as an example of how academia, industry and the NHS can be successfully linked; another cited the Cell and Gene Therapy Catapult as very useful in this context as it provides academic scientists with a point of contact for engagement with companies. It was also suggested that the MRC take a more proactive role in supporting academia-industry connections, including through the organisation of informal networking events and setting up of a website where industry can gather information on current university research and identify stakeholders of the MRC funds. However, government funded portals or databases were not considered effective by TTOs. As one representative from a TTO commented: "We tried signing up to about six or seven portals simultaneously and did not get one single hit through any of those sites".

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 (and to enable academic researchers to acquire the necessary TR skills). This is currently blocked by the reward structures of academic institutions, leaving researchers trying to return from industry at a disadvantage over those who remained in academia (see section 'Culture and incentives'). One interviewee pointed to the US system of dual appointments between universities and industry; another suggestion was to offer flexible fellowships for academic researchers to work in industry (without a strict timeframe, as the duration needs to adapt to the research progress made).

One interviewee raised the issue of changes in company strategy, leaving collaborating academic researchers 'stranded' as projects are terminated (due to strategy rather than scientific reasons). Examples are GSK's recent withdrawal from fibrosis and respiratory R&D and Pfizer's terminating their neuroscience programme. These reorganisations left many academic research teams hanging; the suggestion was to require a ringfenced contribution from industry as a condition for funding collaborations. Another interviewee from academia was concerned that shared academia-industry platforms were really inequitable and knew of a number of cases where "they're actually highly exploitative".

3.2.2 Collaboration between basic researchers and clinicians

A few interviewees explained that collaboration between basic researchers and clinicians is crucial, highlighting two aspects: 1) Clinicians enable the 'circular' dimension of TR ecosystems, as they

understand patient problems and needs. This input is necessary to optimally frame the basic science hypotheses to be tested. 2) When discoveries advance along the TR pathway, clinicians can provide access to human tissues and experimental models, and eventually patients. Given the issues frequently encountered with animal models, this approach allows for accelerated progress into the clinic – or a 'faster failure' saving time and resources. However, challenges to collaboration with clinicians have increased as pressure on the NHS (and on service delivery) has intensified (see section "Culture and Incentives").

3.2.3   Collaboration across disciplines

Collaboration between academic groups was not seen as problematic; however, several interviewees highlighted the need to work across disciplines and barriers to these type of research projects. An example provided was the area of digital health, where health care practitioners and data scientists need to come together to gather patient data and use machine learning techniques to analyse the data and improve health outcomes. Another interviewee highlighted research areas that need to draw on both medical and engineering expertise, an example being research on air pollution which combined both aspects of human health and technology development to measure air pollution.

Barriers mentioned related to the lack of funding streams for some multidisciplinary areas ('projects falling between research councils'), and to cultural barriers, e.g. where medical researchers and engineers 'speak different languages' – and are housed in separate university departments.

A few interviewees considered 'place' an important driver for collaboration, facilitating interaction to start and implement projects, and sharing of resources and infrastructure (see section Local clusters and thematic networks).

3.3   Funding

While interviewees concurred that more funding for TR was available now compared to 10 years ago, they broadly agreed that a number of funding issues remained, falling into three main categories:

- the low level of overall funding available for TR in the UK

- the low level of funding available for individual TR projects

- the short-term nature of TR grants, failing to provide a continuous TR funding pathway

3.3.1   Overall level of funding available for TR in the UK

A few interviewees, including individuals involved in reviewing grant applications, noted that the overall level of funding for TR was too low in the UK, with many promising projects unable to secure further funding. One interviewee explained that this leads to funding committees selecting relatively conservative proposals, shying away from higher risk projects that propose to test the newest and most innovative approaches. A number of interviewees from across stakeholder groups pointed to the risk to TR investment post-Brexit. At the same time, there was a recognition that the MRC needed to balance funding for basic research with funding (the much more expensive) TR. A few interviewees recommended funders focus on strategic areas, both in terms of disciplines/technology and geography (see section Local clusters and thematic networks).

3.3.2   Size of TR grants

A number of interviewees highlighted that the level of current grants was insufficient to adequately cover the higher costs of TR, such as PK/PD and toxicity studies. As one interviewee from industry put it: "Of course funding is important [for TR]. And sufficient funding to ask and answer the right questions. There are some schemes that provide very, very small amounts and proof of concept funding; those sorts of funds do help answer a question but you could almost say they just take the project one step further into the valley of death rather than they bridge the valley of death.". A perception from abroad was that the

level of funding available in the UK was lower than in the USA, which has "a lot of places fully set up in terms of driving such translational studies, whereas in the UK, there are state of the art facilities […] specific to certain cities and certain centres, but much more variable outside of these".

3.3.3   Short-term MRC grants and the lack of a continuous funding pathway

Many interviewees commented that MRC grants are too short-term, covering only short stages in TR pathway. Researchers need to secure further funding at relatively short intervals, slowing down research projects (e.g. staff moves on). This represents a competitive disadvantage with research groups elsewhere drawing on published research findings (e.g. in US academia and industry). Many interviewees also explained that the lack of a clear, 'no-gap' funding pathway discourages academic researchers from engaging in TR.

While funding streams in the UK were considered more linked up now than a few years ago, some issues were highlighted, e.g. moving from CiC to DPFS (see section above) and from DPFS to EME. Coordination between funding streams was noted as an important aspect, e.g. the need to apply the same prioritisation criteria in DPFS and EME committees so that successful DPFS projects are able to continue to the next step. As one interviewee summarised the challenge: "Translational research is expensive and requires quite considerable money the further you go down the translational pipeline toward patients. So, it is expensive, but much of the funding is in tranches to milestones and this makes it difficult to have a continuity of effort - if you can only get the next amount, the next tranche of funding if you meet a certain milestone. That's certainly true for retention of staff and continuity of a coherent unit.". The Wellcome Trust Seeding Drug Discovery grants were cited as a good example of how to address this issue by providing a larger funding envelope, allowing proof-of-concept as well as further steps to be tackled.

Longer-term funding was also highlighted as important for studies that yield maximum value through follow-up, such as cohorts, especially as better, non-invasive tools for monitoring people are becoming available. However, as one interviewee explained: "In general, it is easier to propose a new study than to keep following up a group that has already been studied.".

Two representatives from the investor community highlighted that the UK 'piecemeal' TR funding landscape represents a disincentive for investment in the UK. Sufficient resources to advance a TR project quickly to the point where large pharma will take it on is crucial for investment decisions. Two interviewees from the investor and KE communities explained that investors tend to follow 'trends' in terms of the type of technology they invest in, e.g. "Trends come and go very quickly and so you can easily be sitting on something which was in fashion two years ago but not in fashion today, and you've lost your investment that way.". Others pointed to the need to quickly move forward once a patent had been filed. One interviewee from a funding organisation explained that the lack of public research funding, and hence the need to rely on VC funding, has led to many small single product companies being spun out from academia. Given their small size, these companies are bought up easily by larger non-UK industry, without benefit to UK productivity and employment. To address this situation, the MRC needs to fund TR teams at a much higher level; this enables bundling of products and drives TR further along prior to formation of a spin-out.

To improve the situation, interviewees suggested the MRC extend grant durations, make available more funding through CiC-type schemes, and speed up turn-around times in the proposal process. As one interviewee put it: "I think there needs to be much more joined up thinking that if you get funding for an animal study that demonstrates you can fix X, Y, Z with this therapy, there should be an implicit understanding that you will then be able to get the next tranche of funding without a big gap. And I'm not saying you shouldn't have to write a proposal but I think you should be able to write that very easily, have it assessed very easily and know that you're on a guaranteed path that if your basic proof of concept study works then you can move on." Another interviewee suggested that the California Institute for Regenerative Medicine was an example of how these issues could be handled well. A few interviewees also noted that short-term grants cannot support sophisticated research infrastructure (e.g. the inability to commit to service contracts for equipment). One interviewee made reference to Innovate

UK's Investment Accelerator Programme's helpful approach of providing UK SMEs with simultaneous grant funding and venture capital investment for early stage feasibility studies. This aims to give applicants confidence that investment will continue and reduce the time and resource required to find additional investment and grant funding. In addition, the scheme provides researchers with access to commercial acumen and insight into market opportunities.

As one interviewee summarised: "What makes a successful translational funding scheme is that it's a mixture of directed calls and open calls, it's generously funded because these things don't come cheap, the timescales are appropriate and the duration of funding is sufficient, and that there's an element of risk taking to allow some of the high risk stuff to be funded.".

3.3.4 Lack of coordination between funders

Many interviewees from across stakeholder groups highlighted the need for increased coordination between funders, in order to ensure strategic oversight to inform infrastructure investments, share best practice, enable funding of multidisciplinary projects (with 'data' highlighted as cross-cutting field), and reduce duplication, e.g. through multiple review of the same proposals.

The vast majority of interviewees felt however that individual research councils, charities and the NHS were too 'siloed' in their approaches. An example provided was the division in remits between the BBSRC (no TR remit) and the MRC, which had led to promising but 'non-standard' projects falling 'between' funders and being terminated. Failing to coordinate funding strategies and sharing platforms can also result in duplication of infrastructure investment; an example provided related to CRUK's building of five drug discovery units, which was followed by InnovateUK's investment in the Medicines Catapult. One interviewee from the research community mentioned the National Funders Forum, which had provided more clarity on funding initiatives for funders and researchers alike.

Other comments on coordination between funders included:

- The MRC's response mode funding is too conservative and not collaborative with other funders.
- Three interviewees specifically highlighted the division in funding remits between the MRC and InnovateUK, i.e. academia vs industry, as problematic. This drives 'artificial' decisions, e.g. academic researchers spin out their technologies early to be eligible for InnovateUK funding, even if further development in the academic environment would be of advantage, and reinforces the perception of a division between 'academic' and 'industry' research (when in fact they should be going hand-in-hand from the start of the TR journey). A representative from the investor community commented that many UK spin-outs are too small to scale up, and if their (single) technology is successful, are easily bought up by larger non-UK companies, leading to a loss of impact on UK productivity and employment.
- Funders could coordinate to take forward certain projects, e.g. discoveries emerging from consortia that are promising but outside the consortium's remit.
- Currently, the MRC, the Wellcome Trust, and CRUK are all targeting the same TR ecosystems and business models, following the simplistic TR progression models of a) Good science - TTO - licensing agreement with private sector - impact; or b) Good science – university spin-out – VC investment rounds – impact. Funders need to be aware of new types of innovation business models in the health space, and (at least between them) include these within their remit.
- One interviewee suggested the MRC work with organisations such as the Health Foundation and King's Fund to help define health care needs and inform MRC strategy.

Views diverged on the complementarity of MRC and NIHR. The majority of respondents felt they complemented each other well; while there was some overlap between the research funded, this worked well, and MRC-funded researchers were benefitting from NIHR infrastructure, support staff and expertise (and vice versa). Examples of synergy included the MRC-NIHR methodology research

programme. Four interviewees recognised the role of the OSCHR in coordinating research across the NIHR and MRC. However, other interviewees explained that there were overlaps and tensions between MRC and NIHR research areas, that the interface was confusing, and that (at least for some predominantly MRC-funded departments) interaction with BRCs and BRUs was minimal.

3.4   Culture and incentives

Interviewees' comments on culture as a barrier to TR fell into two broad categories – university reward structures and mindset of researchers in the TR ecosystem.

3.4.1   University reward structures

Interviewees broadly agreed that current reward structures and promotions in the academic sector do not align with the main outputs of translational research. The key measures of success in academia remain publications in high impact journals and follow-on funding. Progress along the TR pathway generally results in lower impact publications in the early stages, is riskier, and – if successful - takes 10+ years to yield health impact. The established model of 'academic superstars' with clearly attributable publications and grants is also not compatible with multi-disciplinary and possibly cross-sector TR teams. Most of the respondents cited a lack of reward for team science and collaboration as an important barrier to TR. The system puts academic researchers with interests in TR at a disadvantage compared to basic science colleagues, especially early career scientists who need to demonstrate their ability to publish in order to secure their career progression (while established PIs with large research groups can take the risk of delayed publications). As one interviewee put it: "It quite upsets me actually. The institutions want the kudos of great translational stories but they don't want to, they don't have very good mechanisms for rewarding the people who get them there.". And a representative of a top tier university commented: "I think if we want to really make a step change in the way people collaborate, we have to do something about getting away from how we reward success in science […] and some of the ways of thinking that are driven towards individual scientists rather than rewarding teams and in the whole way things are structured is driven around people making claims about what they did as an individual. […] I think perpetuation of the individualistic reward culture in science is really impeding progress."

It was also noted that the current reward and promotion system does not allow researchers to gain industry experience and return to academia. While movement between sectors is seen as a crucial aspect for 'upskilling' the academic TR workforce (see 'Skills' section), universities' focus on publications and grants when making hiring decisions puts scientists who spend some time in industry at a disadvantage. This includes fellowships, as stepping back into academic science is not guaranteed. Several interviewees also highlighted barriers clinicians face in engaging in TR: Clinical career progression depends almost exclusively on clinical competence and NHS service delivery; with the NHS under (increasing) pressure and low priority given to research, clinicians may find they do not have time to get involved in TR. The need for a clear career structure and support for clinical scientists was emphasised.

A number of interviewees recommended the MRC steer away from its perceived strong focus on publication record in the proposal review process and instead focus on enhanced recognition of TR outputs. The REF was also cited as leading to universities placing too much value on publication in general, although a few interviewees commended the REF's impact case studies, the MRC's requirement for impact statements, and the inclusion of TR-type output categories for reporting in ResearchFish. To bring about change in the recognition of TR, the US NIH NCATS requires institutions applying for grants to demonstrate how they are creating incentives and promotion/tenure structures which support the broad teamwork and collaboration driving TR.

3.4.2   Entrepreneurial mindset

While interviewees from across sectors broadly agreed that academic researchers' attitude to TR and collaboration had improved over the past 10 years, several interviewees from the research, knowledge

exchange, private sector, and investor communities noted that the cultural identities of academic and industry researchers remain distinct in the UK, and that the entrepreneurial mindset of the UK academic community lags behind that of researchers in the US. In addition, many researchers felt TR continues to be less valued than discovery science, being seen as 'less exciting', 'less prestigious', or 'second rate research' by the academic research community (and funding review panels).

Interviewees felt that the UK needs more role models for entrepreneurship, including through increasing the movement of researchers between the private sector, academia, and the investment community. The P2D funding scheme and entrepreneurs in residence were cited as good examples of how to improve the situation. Highlighting best practice, a representative from the private sector commented: "Now the place I have seen this done best is at MIT in Boston, so MIT, Massachusetts Institute of Technology. They have about 5000 students, 4000 of which are post docs, and a key part of their post-doctoral training is business skills. What emerges out of MIT to a greater or lesser extent are scientist entrepreneurs who understand what is required to start a business, who understand the funding routes that might be available to them to start a business. That culture of creating scientist entrepreneurs I do not believe exists anywhere in the UK.".

3.5   Institutional support, TTOs and Intellectual property

The government's impact agenda has resulted in universities increasingly recognising the utility of TT in achieving and showcasing impact. As one interviewee from a TTO explained: "Technology transfer has now very much risen up to become the third thing that universities are expected to do. And I think that is coming now to the point where the senior management of most universities have picked that up, and that message is now starting to reach down to the academics as well that you are employed to do research, to teach students and to create impact from that research".

However, many interviewees noted that the level of support varies considerably between institutions. For example, Cambridge, UCL, Oxford, and Imperial College were highlighted as 'top of the class', providing support function such as TR advice, TROs (in addition to TTOs), a network of connections and exchange with entrepreneurs, and 'model' academic entrepreneurs within the department. Other universities were described as having limited TR capabilities and unable to offer the necessary level and/or quality support - with one example given where a single TT officer was responsible for the portfolio of the entire university. Representatives from TTOs agreed that it was difficult to recruit staff with commercial expertise, and that TTOs were generally understaffed and under-resourced.

Institutions also vary in their approach to licensing and commercial rights/IP. Many interviewees explained that IP negotiations continue to be challenging and negotiations time-consuming and costly. This situation has gotten worse in recent years as universities have built up their TTOs and TROs and focus on IP has increased. Representatives from both academia and industry held the view that universities often overvalue their IP. TTOs can get 'bogged down' in the minutiae of contracts, delaying negotiations which can ultimately lead to the deal or collaboration being dropped altogether. A few interviewees from industry explained that companies consciously avoid engaging with universities known to overvalue their IP and to be difficult to deal with, even if they are interested in research at these institutions. Conversely, a number of interviewees from both academia and industry highlighted that companies are also 'at fault' in failing IP discussions, placing a low value on academic IP (e.g. compared to small biotech IP) and at times 'playing hardball' in negotiations. One interviewee with a KE background highlighted that funders can also delay the licensing process at the stage where they have to provide consent on the negotiated deal.

Opinions on the importance and role of institutional support and TTOs was mixed; while a few researchers felt that KT is – and should be – primarily driven by the individual researchers, with TTOs supporting only in the later stages of TR, others thought that the low level of TTO support at their institution was an issue, and that increased support would accelerate progress. Several interviewees, including from TTOs themselves, pointed to a lack of industry experience among TTO staff, often science PhDs, hence lacking experience and judgement, e.g. in negotiating licensing deals.

A few interviewees felt that TTOs in the UK place too much emphasis on income from licensing, rather than taking a longer-term view on return from royalties or milestones. This was related to the fact that TTOs had to 'self-fund' their operations, and hence needed to focus on early stage revenue streams from their institutions' innovations. Representatives from universities/TTOs in turn pointed to the rising demand for contracts associated with translational grants or working with industry, such as multiple agreements with DPFS or consortium partners, driven both by funding the MRC has made available and repeat business from industry relationships established over the last ten years. In addition, researchers now present more viable TR ideas; while this is seen as a positive development, it is placing a significant strain on university support functions.

To improve issues related to the variability of TTO support, three interviewees suggested the creation of a centralised resource for knowledge transfer in the UK (rather than relying on the small TTO team present at smaller universities). One interviewee suggested this could also include access to a group of TR experts with whom academic groups can discuss project ideas and gather advice.

The Cambridge accelerator 'Start Codon' and CRUK's support functions were named as examples of important institutional support. In the case of the latter, a researcher from academia described the support provided by CRUK's Drug Development Office (in handling interactions with the regulator and ethical approval), and by Cancer Research Technology as crucial, including in-house laboratory capability as well as business development functions and connections with the venture community.

One researcher highlighted the importance of funding through the institution, such as the ability to apply for small amounts of money for taking the next step in translating findings or to support entrepreneurship. This funding could be through MRC funding such as the CiC, or opportunities from within the institution, e.g. the example of a scheme was provided which enables people to take three months out to develop a business plan, scope a market and decide whether launching a company is 'the right thing for them to do'.

A small number of researchers pointed out that as a result of the increased understanding of IP in academic institutions, researchers have limited how and when they share their findings with the research community. This presents a barrier to research progress and collaboration, both with industry and between universities. (At the same time, other researchers felt that enhanced connectivity through the internet and platforms such as Twitter and YouTube have accelerated sharing of information.)

Most interviewees agreed that 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. The MRC's university-industry partnership schemes were seen to support the development of these models, providing a process through which joint projects can establish a transparent IP situation from the outset. One interviewee (from the private sector) cited the MRC's AZ/UCB platform as an example of 'where it works well'. Another interviewee highlighted that assessment of DPFS proposals provides helpful input and advice at the start of TR research projects and suggested that the MRC continue to provide IP support throughout the grant. Other suggestions for improvements included:

- active promotion of best practice examples from the MRC portfolio, to serve as models
- the MRC take an active role in how IP is handled rather than delegating IP to the universities, as TTOs are often too busy to consider all opportunities
- an 'Attorney in Residence' or 'Attorney on call' scheme

Three interviewees pointed to the high cost of patenting, with universities struggling to cover the costs. One researcher with private sector experience explained that this is a particular issue for international patent applications (PCT). These need to be filed 18 months after the UK patent to continue protecting the IP. Many UK universities do not pay for the international patent, letting the IP lapse and thus reducing the value of the asset – which in turn leads to industry paying UK universities a 'significantly reduced amount of money for it'. This was set in contrast to the situation in the USA: "What we would pay in the US for a product […] is maybe 10x more than what we would pay a UK [university] just because the

quality's different. Everything's there, the IP, the team helping to drive it, it's put together better. And so the UK is really missing out big time. Not building companies, not creating jobs and not creating wealth and letting it all go to the US which I find very hard as a passionate UK scientist." Two other interviewees advised against the current focus on patenting, as this blocks innovation resulting in costly IP processes without outcomes, and to focus on collaboration with the private sector instead.

3.6   Research infrastructure

Compared to other enablers and barriers, research infrastructure was mentioned less frequently.

A number of interviewees pointed to a need for data platforms that were both accessible and affordable for researchers, and able to manage the large amount of health-related data being generated.

Others were concerned about the lack of long-term infrastructure funding, as 'grant-to-grant' funding' is making it risky for universities to invest in equipment with long-term service contracts. Long-term funding is also required for infrastructure enabling the use of human samples and for following patients treated with new therapies such as gene editing to detect any long-term effects (20+ years).

3.7   Local clusters and thematic networks

Many interviewees from across stakeholder groups acknowledged that being embedded in the 'right' TR environment was an important factor in driving progress. Imperial College, Cambridge, Oxford and UCL were highlighted as examples in this respect, combining a 'critical mass' of researchers with translational skills with strong translational infrastructure, local networks of SMEs and large pharma companies, individuals with business skills, and proximity to the venture capital community. This functions as a fertile ground for collaboration, skills exchange, and KT, and attracts further funding and talent into the area. A few interviewees felt that differences in the ability to attract funding are potentiated by the fact that key academics and opinion leaders from Golden Triangle institutes sit on the advisory boards of many large funding programmes.

Other universities continue to operate in isolation, unable to access other players in the TR ecosystem. Most interviewees who commented on regional variation pointed to access to clinical research infrastructure and more specifically NIHR BRCs as a key factor. In regions of England where BRCs exist, there is better continuity of funding which attracts and retains the best researchers in the area. Two interviewees also noted that universities attached to academic hospitals traditionally have a better track record of successful translation for this reason. Five interviewees from Scotland pointed out that researchers at Scottish institutions suffer from not being able to access NIHR funding and infrastructure. One interviewee explained that while Scottish institutions have shown reasonable translational success, they do not receive the same level of funding as institutions in the Golden Triangle, and do not have the critical mass of skills and people to influence at the highest levels of government. Another requested the MRC take the absence of NIHR infrastructure in Scotland into account when planning their funding schemes.

Reflecting on the importance of the enabling environment, a number of interviewees suggested that TR funding was currently spread too thinly with "every little university starting a translational research centre". However, interviewees also recognised a tension between the need to build world-leading clusters of excellence, and the need to support science across the UK. A number of interviewees, especially from institutions outside the Golden Triangle, considered the unequal distribution of MRC support across the UK a barrier to TR, missing out on many opportunities to draw on specific regional strengths, as well as 'unfair' for tax payers in the less-supported regions. Suggestions included investment in a smaller number of Centres of Excellence for TR, both in specific locations and as virtual centres spanning the UK, with the latter allowing the cluster effect to spread beyond the immediate geography (and beyond the Golden Triangle). As one interviewee commented: "There are very good

skills in other parts of the country as well - and that's where most of the health inequalities and most of the populations that are ill are. It's really important that we make sure that the UK research infrastructure doesn't just become the Golden Triangle. That there is funding, and there is investment going on in the North and other parts of the country to make sure that we have the high grade researchers in those parts of the country as well, because they will be the people who are seeing some of the changes going on in this country.". Another interviewee explained: "I'd like to see, in a way, MRC to move out of London and to be seen everywhere around the country. I'd like to see it more visible so that the public and industry, places like I am here in [..], and universities get to know it as an institution because I think that would go an awful long way towards generating further trust which would enable this translation pathway to become even more effective.

4 Knowledge transfer mechanisms and barriers

4.1 Knowledge transfer: academia-industry

4.1.1 Mechanisms of knowledge transfer between academia and industry

The majority of interviewees explained that the main mechanisms of KT 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. A few interviewees noted a growing desire from universities to build larger more strategic partnerships with industry rather than focusing on KT on a project to project basis. Some interviewees also pointed to a KT route via university TTOs and TROs utilising their established networks (but a few others commented that they had little contact with their institutions' TTO). A number of interviewees explained that KT is greatly facilitated by engaging with industry very early in the research process. Considering issues such as regulatory pay or commercial finance very early in the process validates the trajectory towards commercialisation and de-risks the proposition from an industry perspective. This approach also reduces cost further down the development pipeline and ensures industry buy-in from the outset.

A number of interviewees expressed that over the last 10 years industry has become more willing to share data and expertise, especially for particularly challenging areas of clinical research such as antimicrobial resistance and Alzheimer's disease where previous failures have catalysed a behaviour change and a more proactive attitude towards knowledge sharing. Exchange of personnel between academia and industry was noted by several interviewees as a useful mechanism for KT and a good way of encouraging cross-fertilisation of skills and insight (see section Collaboration). Fellowship schemes such as CASE PhD studentships were highlighted as particularly useful as they provide for students to be exposed to the industrial research environment.

A few interviewees mentioned the MRC's partnership schemes, such as the Discovery Partnership with Academia (DPAc), or open innovation platforms, such as AZ's Open Innovation Network as impactful when considering KT, in terms of facilitating the creation of a shared-risk shared-benefit model. The Proximity to Discovery: Industry Engagement Fund and MRC Industry Collaboration Agreement (MICA) were also highlighted as useful modes of funding as they facilitate early industry engagement and collaboration within a project.

To expand the level of information exchange and KT, a few interviewees noted the benefit of co-locating industry within academic institutes, instigating cultural change and alleviating concerns associated with 'who owns what' to create a shared-risk shared-benefit model of translation. Other suggestions included a greater number of academia-industry studentships and fellowship schemes, recognised in university reward systems, to enhance movement between academia and industry and facilitate cross-fertilisation of knowledge and experience.

4.1.2   Barriers to knowledge transfer with industry

Many interviewees noted issues around **IP** as a key barrier to KT (and more broadly collaboration) between industry and academia. One example is the difficulty associated with defining an equitable share of the potential value of innovations for either party. For example, an academic researcher may have spent considerable time progressing the basic science to a point where industry is interested; while industry may require another 10-15 years to achieve an implementable innovation. Therefore, a model for a 'fair' hand-over has not yet been established.

Other issues included the **complexity of negotiations around IP** which can be lengthy and inefficient and a sense of 'paranoia' within academic institutes regarding IP ownership. Several interviewees noted that many TTOs are under-resourced, and that interactions with TTOs can be cumbersome and inefficient; representatives from industry explained that their companies avoid dealing with institutions known to 'be difficult' altogether (see section Institutional support, TTOs and Intellectual property). Other barriers mentioned were patent costs and the fact that academic researchers and TTOs are prone to overestimating the value of their IP, thus inhibiting KT to industry. A few interviewees stressed the need to develop a straightforward, understandable and manageable tech transfer process with clarity on how research organisations engage with third parties.

A number of interviewees noted the **lack of reproducibility of academic results within industry** as a key barrier to KT. Industry frequently need to repeat a significant proportion of the development that has been completed within academia to ensure it has been undertaken to an appropriate regulatory standard for MHRA audit requirements. When industry cannot properly validate these results, it becomes increasingly difficult to progress the work. In relation to this it was highlighted by a few interviewees that knowledge of industry standards is not widespread within academia, i.e. the experimental requirements that are necessary to make an asset industry consumable. This lack of knowledge then also becomes a barrier to KT.

Two interviewees suggested the MRC work more closely with other funders and regulators within the pharmaceutical/biotech/healthcare system to build a standardised approach to research and development within the UK. This could help to improve reproducibility of academic TR and reduce the amount of duplicated work. In the case of clinical trials, it could also reduce duplication in terms of each individual Institutional Review Board approving clinical trial protocols which can take a considerable length of time. One interviewee recommended the MRC engage much more closely with the MHRA to proactively move UK TR projects along the development pathway. Particularly post-Brexit, this was thought to provide the UK with a competitive advantage in the TR space.

Some interviewees highlighted a **lack of knowledge of key contacts** to approach in industry, or even non-governmental bodies such as NICE who would be useful to engage with early in the research process (see also section Academia-industry collaboration). Similarly, several interviewees felt that a clear mechanism for companies to learn about MRC-funded research is lacking, posing a barrier to engagement especially for SMEs who lack the resources to search for potential partners. It was suggested that the MRC take a more proactive role in supporting academia-industry connections, including through the organisation of informal networking events and setting up of a website where industry can gather information on current university research and identify MRC funded stakeholders.

Two interviewees suggested that universities could virtually communicate their CiC portfolio as a way of achieving this or alternatively create industry relevant speciality groups to steer engagement. An example was given whereby a university ran an internal call for proposals based on their CiC funding and invited an industry representative to assist them in reviewing the proposals, bringing broad industry insight into the type of research being suggested by academia at the time. This resulted in the creation of a number of joint industry projects over time, building trust and creating a platform for further collaboration.

In addition, a few interviewees noted the **importance of ensuring open access** to data and publications to ensure equitable access and to optimise dissemination.

Two interviewees cited disincentives for industry investing in academic research in the UK: the large overheads associated with academic research, and the fact that access to medicines via the NHS represents a small market for industry when considering the global market. Two other interviewees, from industry and academia, highlighted that MRC calls for proposals needed to be announced with sufficient lead time to assemble a cross-organisational team, especially when working with industrial partners. At the same time, the turn-around after submission needed to be as fast as possible to keep the momentum of the partnership going.

4.2   Interface with the clinical environment

4.2.1   Mechanism from academia to the clinical environment

Most interviewees who expressed a view on the mechanisms of KT from academia to the clinical environment agreed that access to NIHR infrastructure was key to the successful development of technologies for and within the NHS. Other mechanisms of KT mentioned were conferences and personal networks. A few interviewees highlighted the importance of engaging with clinicians and patients at the outset of any research project, to validate the need and applicability of proposed technologies and to optimise uptake once the research reaches the clinic.

Two interviewees noted the work of the Academic Health Science Networks (AHSNs) as impactful in terms of spreading research findings at the very applied end of the translational spectrum and promoting the potential benefits to the NHS.

4.2.2   Barriers to knowledge transfer to the clinical environment

The main issue highlighted relating to KT to the clinical environment was the increasing pressure on the NHS to deliver clinical services. The situation is worse compared to 10 years ago; clinical staff are very limited in the amount of time they can free up for research, and most hospitals are focussed on service delivery rather than placing value on research. Several interviewees noted that research is not on the top priority list for NHS trusts and therefore resource is not routinely set aside for experimental medicine. In addition, clinicians are limited in the amount of time they can prioritise for research based on their clinical responsibilities and current demand on NHS services.

Most interviewees who raised this point agreed that KT could be improved by increasing the level of funding for clinician scientist PhD programmes in order to create a critical mass of researchers who are able to interface optimally between academia and the NHS. The MRC Clinical Academic Research Partnership (CARP) scheme was highlighted as an attempt at facilitating this. Three interviewees thought that including individuals employed by the NHS on TR teams, and possibly co-funding their involvement, could be a useful mechanism for improving KT to the NHS.

A number of interviewees also expressed that the implementation of new and innovative technologies or interventions in the NHS is very slow, which can lead to a critical loss of momentum. This is based on a number of factors such as limited funding and resource to implement, the lack of a clear pathway to implementation in the NHS and the lack of a clear body at a national level dealing with implementation. Two interviewees also felt that there was a fundamental lack of willingness within the NHS to engage with or be involved in translational research. Two interviewees also noted the importance of understanding the difference between working in a clinical trial and working in clinical practice, emphasising that clinical trials need to be more representative of a real-world setting in order to get an accurate treatment signal with minimal risk of bias. This level of real-world evidence is also important for bodies such as NICE and NHSE when making policy and commissioning decisions. To that end it was noted by a few interviewees that signposting to the relevant points of contact at NICE and NHSE could be improved so that researchers can engage with the implementation process earlier in the research timeline.

A few interviewees expressed that implementation within the NHS was not solely driven by an evidence base to suggest clinical benefit but also by the culture within a trust or hospital. In some cases, clinicians can be reticent to change their clinical practice. Two interviewees noted that the MRC could take a more

proactive role to improve this situation, e.g. by organising stakeholder events involving academic researchers and NHS decision makers such as commissioners to create a forum for interaction between scientists and NHS staff.

4.3   Knowledge transfer: academia-policy

Key barriers to KT 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, and hence not devoting any time to communicating research findings with policy relevance to this audience

- A lack of incentives for policy makers to seek scientific evidence.

As one interviewee explained: "I think there's still a great lack of understanding amongst academic community of how policy is made, and of the opportunities to interact with policy makers and support them. And likewise, when policy makers come into their role, they are very resistant I think to engaging with the research community and the research literature."

The majority of interviewees who mentioned KT from academia to policy described instances where their institution had placed early career researchers in a government department or parliamentary office. It was felt this was particularly useful as it allowed upskilling and cross-fertilisation of knowledge, while also providing academic researchers with the opportunity to be exposed to new ways of thinking.

Two interviewees suggested establishing a knowledge broker role, within the MRC or at research institutions, to frame academic questions around the most pertinent policy issues and signpost opportunities to interact with policymakers.

4.4   Knowledge transfer: within the academic community

The majority of interviewees who raised this point agreed that the most common mechanisms of KT within the academic community are via the traditional routes of publication and conference presentations. Two interviewees highlighted the merits of publishing work on pre-print servers to ensure immediate dissemination and to avoid the traditional publishing route which has become slow and can lead to a loss in momentum. Paywall articles were also highlighted as a barrier to KT in this context based on the significant expense associated with accessing some journal repositories.

Social media sites such as twitter were mentioned by a few interviewees as a useful way to communicate research findings to fellow academics and stay up to date with the current research in their field.

Two interviewees highlighted the potential benefit of encouraging more interdisciplinary research, especially between the fields of biomedicine and the physical sciences, as a mechanism to stimulate KT within academia and to facilitate translational research more broadly.

4.5   Knowledge transfer: academia-investors

Interviewees, including representatives from the VC community, agreed that the number of investable discoveries coming from academia has increased over the past 10 years and that the level of investment available had increased over the past 3-5 years (see section Changes). A few interviewees noted that academic researchers were increasingly using the spin-out route to commercialisation, generally to develop a technology to the point where it becomes interesting for a third-party corporate entity.

Investors noted a range of criteria when making investment decisions:

- The calibre of people involved, i.e. whether they are from a reputable institution, the confidence in the researcher's ability and dedication, a solid track record in successful translation, an entrepreneurial mindset and willingness from the researcher to be involved in further development

- A sensible tech transfer process and clear direction of travel/next steps

- The market position, such as demand for the particular discovery that is being presented and competing technologies

- The current trends in VC investments: Science fields perceived as novel and 'trendy' drive investment by the VC community; examples include 'stem cells' and 'immune oncology'. Technologies that do not fit into current 'trends' are at a clear disadvantage, irrespective of merit

- 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

Very few interviewees mentioned mechanisms by which investors identify research. One interviewee explained that often investors identified research by tracking publications from well renowned professors in the field. Another noted that a particularly useful method was via sitting on the MRC review panel for CiC awards – which provides investors with the opportunity to identify projects early in their timeline and offer expert advice from the outset. Two interviewees also noted the MRC's role in engaging with investors, highlighting the benefit of investor input on review panels and the importance of ensuring an open dialogue to identify common ground and continue to learn from one another.

A key barrier to VC investment noted by a several interviewees is the lack of commercial entrepreneurial skills within the UK's academic community coupled with a lack of incentive for academics to spin out and form companies. A lack of mobility for academics to move to and from industry in order to cultivate these skills was also mentioned as a barrier.

Other barriers highlighted by interviewees included a lack of contract manufacturing organisations (CMOs) and contract service organisations (CSOs) in the UK; a significantly lower VC funding value per capita in the UK compared to the US; and (an investor's perception) that TTOs were reticent to provide all of the relevant information required for VCs to make a well informed decision.

To improve KT to investors, two interviewees made reference to TTOs with one suggestion being to ensure a single point of contact within the TTO so that discussions with investors remain focussed and efficient. A second suggestion was to create a mechanism whereby companies and TTOs work together to prepare a short business plan which can then be reviewed by a panel of investors who provide input and discuss the possibility of future investment.

5   Success in translational research

5.1   Successful translational research programmes

Many interviewees from across sectors consider the UK's and MRC's TR funding schemes excellent, and the MRC a front runner in establishing innovative partnerships with industry (e.g. AZ, GSK). This has driven collaboration, an increase in TR activity and a change in culture and mindset. The cluster around Cambridge, with AZ moving facilities, and the Crick Institute were mentioned as potentially emerging as European powerhouses of TR.

Other funding programmes highlighted as positive include:

- The Wellcome Trust Seeding Drug Discovery scheme, which provided mentoring and access to commercial expertise as well as a larger funding envelope. This created momentum to progress the TR and remain competitive, while also allowing a technology to be developed to the point where industry becomes interested. (Interviewees were wondering as to why this programme was discontinued.) [3 private sector representatives, 2 researchers, 1 funder (non-WT), 1 other]

- IMI, representing a large commitment from both industry and the public sector to create infrastructure and enable collaborative research. However, while interviewees agreed that the IMI has led to the development of improved collaboration models and enhanced communication between stakeholders in the TR ecosystem, a few interviewees questioned whether there have been

any impact on health and patients. [4 private sector representatives, 3 researchers, 1 KE professional)

- One researcher noted the California Institute for Regenerative Medicine (a funding agency of the State of California) as particularly successful due to its emphasis they place on integration with the private sector and prioritising the due diligence required to ensure that applications are suitable for implementation within the clinic up front.

- Other successful TR institutes and initiatives mentioned by interviewees included the Wyss Institute at Harvard, CRUK's Institute of Cancer Research, the University of Dundee, the NIH Accelerating Medicines Partnership, and JLABS in San Diego. Innovation in China was highlighted in relation to ease of access to health data and data science skills.

More generally, a number of interviewees from across sectors agreed on the benefit of having a more centralised approach both in terms of data collection/storage and patient recruitment to clinical trials. The NHS was highlighted as a unique asset to the UK in terms of providing the ability to work at scale. However, three interviewees (researchers and private sector) noted that the NHS still lags behind the Nordic countries in terms of electronic health systems and routine data collection. With this in mind, one researcher highlighted the Statens Serum Institute in Denmark, which links routine health data collected by the Danish health system with information stored within the Danish administrative register and biological material collected from a significant number of individuals. Researchers can use this infrastructure to collect patient data in a routine manner, greatly facilitating the scale and scope of proposed research.

5.2   Successful countries and regions

The US was recognised as home to the largest TR ecosystem, especially in and around Boston and on the West Coast. Factors influencing this success include: the large size of the US economy, significant venture capitalist investment coupled with investors' higher risk threshold, an engrained entrepreneurial spirit, a strong biomedical university base and research culture valuing TR and commercialisation, and the ability of individuals to move between the academic and private sector. Therefore, from the outset PIs tend to look to the translational potential of their research. One interviewee also noted that it is much easier to recruit patients to clinical trials within the US.

For example, interviewees who mentioned Boston as a hub for successful translation pointed to its ecosystem of brilliant universities, the abundance of large academic hospitals, the significant presence of large pharma and the level of venture capitalist, business angel and philanthropic funding available. Within the Boston cluster, a few interviewees highlighted MIT as a particularly successful institute. Factors influencing this success include MIT's ability to create multidisciplinary teams with specific expertise in engineering and computing, and its focus on providing scientists with the opportunity to develop their business skills. Crucially, entrepreneurial spirit is something that is actively encouraged at MIT.

Three interviewees highlighted Israel as a fledgling success story, having managed to generate a technology sector from the ground-up in a relatively short period of time. Interviewees pointed to academic culture which places equal emphasis on commercial activity and academic achievement as an enabler of this success. They also described a prevailing 'sense of urgency' in Israeli universities in terms of spinning out, and a positive attitude towards start-ups and the associated risk of failure.

The Netherlands was also mentioned by three interviewees as a country that punches above its weight in terms of translational research, owing to its small but sophisticated system of academic health science centres. Although there are only six throughout the country they ensure funding is contingent on some kind of translational activity. The centres are essentially owned by the university and operated as research hospitals. This prioritisation of research is crucial to their success when compared to the NHS which has competing priorities in terms of clinical service delivery.