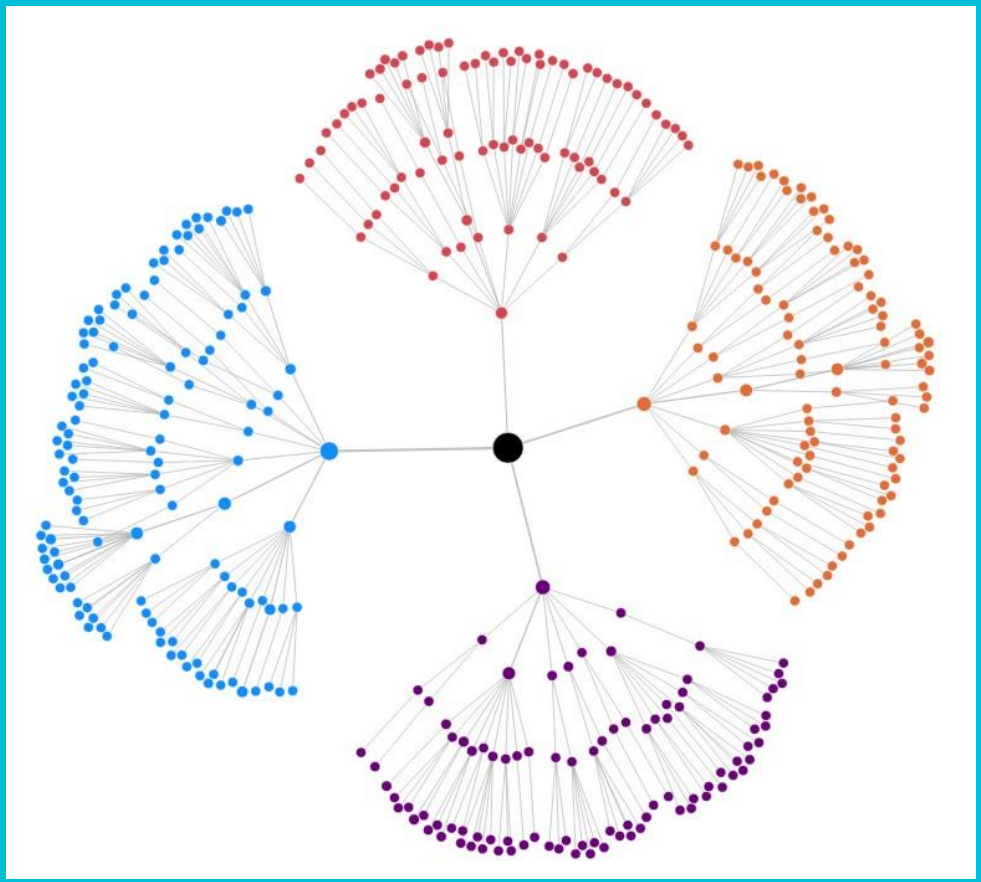
Medical Research Council

Clinical Research Infrastructure Initiative

Outcome and Evaluation Report 2019



Acknowledgements

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The evaluation programme was overseen by the CRII Evaluation Steering Group: Ian Viney (chair), Nathan Richardson, Helen Bodmer, Adam Staines, Jonathan Pearce, and Declan Mulkeen.

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Contents

Report Purpose:

1. To provide a brief review of the outputs and outcomes of the Clinical Research Infrastructure Initiative, funded 2015
2. To identify insights that might be applied to future infrastructure funding initiatives
3. To provide feedback to CRII partners and BEIS

The overall objective of this initiative was to establish innovative research infrastructure capabilities to:

i. catalyse scientific innovation in clinical research in the UK
ii. Enhance translational capability and partnerships with industry
iii. Enhance and add value to existing strategic investments of the partners and clinical research infrastructures

Section 1: Executive Summary

The MRC Clinical Research Infrastructure Initiative (CRII) set out to fund innovative technologies in areas of strategic opportunity. Support was provided for research that had existing momentum and also new areas that had future transformational potential. The £180 million initiative launched in 2015, attracted an additional £118 million from research institutions, industry and charities, and established 37 advanced technology capabilities across the UK (ANNEX 1). The capabilities comprise complementary analytical equipment for innovative data acquisition in areas of translation research. In many, the capability was integrated into existing facilities, enhancing their research potential and contributing to clinical or translational research across a dispersed community of users. By 2019, all Clinical Research Infrastructure Initiative (CRII) funded programmes were found to have succeeded in establishing the planned capabilities and all were producing research outputs.

- **Translational progress** - The objective of the CRII was to expedite translation of innovative research into clinical programmes, to accelerate existing translational research with advanced technologies and to instigate underpinning investigations into novel clinical applications. Two technologies have successfully been translated into clinical application and are currently being used in patient treatment programmes. A further 20 of the 37 capabilities are producing clinically focused research publications and pursuing targeted clinical applications.

- **Added value to existing investments** – Additional funding for existing strategic investments in DPUK (Dementia Platform UK) and Genomics England extended and strengthened the research communities served by these investments. DPUK developed and launched the DPUK cohort MR imaging database. This service is now live[1] and available to clinical and academic researchers beyond DPUK. A unique network of six PET/MR imaging facilities linked to dementia cohorts was also established. The Genomics England Research Environment provides access for translational researchers to the 100,000 Genomes Project (sequences with associated health data) dataset created by Genomics England.

- **Research direction** – Access to the innovative technologies provided by the CRII have accelerated and expanded the breadth of disease areas addressed by translational research programmes. Cutting-edge single cell isolation and characterisation capabilities have made possible precise phenotyping of vanishingly sparse cell types and cells within complex populations at scale, thereby speeding up development of theranostics for cancers and other health conditions. Access to the novel capabilities has increased implementation of existing and novel methodologies to previously unexplored disease applications (ANNEX 2).

- **UK global reputation** – The large investment in leading technologies in single cell characterisation, PET/MRI and 7Tesla MRI raised the UK academic profile for single cell research and contributed to the continuing UK prominence in imaging research.

[1] https://portal.dementiasplatform.uk/AnalyseData/ImagingPlatform

- **Rapid implementation** - Those interviewed as part of this review universally agreed that the limited time frame for implementation[2] of the CRII created many challenges that delayed or limited the full potential of the programmes. They identified that co-funding opportunities had been limited (due to the short time available to engage with a range of funders, research institutions and potential industry partners in preparing bids). Similarly, applicants had little time to carefully consider some of the challenges that they would face launching the novel technologies, to explore ways to co-ordinate research activities across related programmes, and to negotiate access to the latest technological updates.

- **Cross-sector collaboration** – Strong clinical links and NIHR BRC or NHS Trust financial support were evident for almost all capabilities (ANNEX 3). Additionally, a review of publications from projects using the capabilities has evidenced an expanded breadth of disease areas addressed by the translational researchers (ANNEX 2). In contrast, there is, as yet, little evidence of new private sector relationships developing as a result of the new CRII capabilities. Private sector collaborations were generally continuations of existing collaborations. The exceptions were in instrument and methodology advancements and a few early indications of exploitation of the new data by spinouts for product validation.

- **Networking of capabilities** - In the establishment of both data platforms and Single Cell Characterisation capabilities, the opportunities to benefit from UK-wide networking and collaboration were not fully capitalised upon. The interviewees felt there was scope for funders to have investigated effective networking structures to work through the common challenges. The initiative's generic requirement for networking did not generate motivation or commitment from the applicants to create effective focused networks. It was suggested that the MRC could do more in this area, and "can act as a conduit for joining things up".[3]

- **Addressing skills gaps** - Most programmes indicated some challenges in recruiting appropriate expertise to the capabilities; bioinformatic expertise, combined PET and MRI expertise and imaging physics expertise were singled out for mention by capability directors. This was true for capabilities across the UK but possibly more acute for programmes outside of the intense research centres of the south. In at least one case, Brexit also played a part[4]. The shortages were exacerbated by the simultaneous demand for similar expertise created by CRII across the UK. There is some evidence that large data platform projects such as Biobank and the Genomics England Research Environment support expansion of bioinformatics expertise in the UK. However, the challenge persists to support training and establish career paths based in these areas.

- **Sustainability** - Capabilities were expected to set out plans to work toward sustainable operation and access for their user community. Support from host institutions, external funding and cost recovery is currently ensuring that these capabilities can continue to operate but will not be sufficient to repeatedly renew the capabilities over the long term. Given the fast pace of technological advances in the areas funded through CRII, further capital investments will be needed for these to capabilities to continue to be internationally competitive.

[2]Funding availability was confirmed August 2013; Expressions of Interest were required by December 2013; April 2014 was the deadline for full proposal submission; awards were made July 2014 with the stipulation that all spend must occur before April 2016.

[3] From interview

[4] From interview

Section 2: Background

The 2011 government Strategy for UK Life Sciences highlighted that innovative multidisciplinary research with collaboration between academia, the NHS and industry, would be key to international competitiveness. This research would require new tools and techniques to probe more deeply into disease mechanisms and treatment effects in humans.

The MRC Clinical Research Infrastructure Initiative (CRII) was proposed to enhance UK clinical research capabilities with an emphasis on stratified and experimental medicine. The CRII was made possible by the (then) Department of Health (DH), confirming in August 2013, that they could contribute £150 million to the initiative. The DH required that this contribution be spent through the MRC by April 2016, which added a significant time pressure to the setting up and execution of the initiative. Between August 2013 and April 2016, the MRC created the funding call through iterative discussion with partners, assessed the applications, made allocations to the successful research organisations and monitored their projects to establish the new infrastructures. This timetable was achieved, but was very challenging for MRC staff, applicants and host institutions.

The MRC committed £23 million of its resources to the initiative and secured £6.5 million funding from other UK partners to extend the funding opportunity beyond England to the other regions of the UK and to provide limited staffing funds. The call for expressions of interest was communicated during the summer of 2013 and allowed just five months for the academic community to conceive, design, and co-ordinate the multimillion-pound research capability proposals. 48 applications were received and 30 were invited to submit a fully developed proposal by April 2014. An international, cross-sector expert panel considered and conferred 24 CRII awards in July 2014. The funding decisions were based on excellence, scientific innovation, probability of success, and value for money. To ensure that the goal of spending the £150 million DH contribution by April 2016, the MRC provided programme management to facilitate negotiation with equipment suppliers, to consult with University refurbishment teams, and closely monitor spend and implementation of each award against agreed milestones.

This initiative was a unique opportunity to initiate world leading research infrastructure, providing a transformative boost to UK medical research. However, the speed with which the initiative had to be launched raised concerns that opportunities for all stakeholders to fully explore avenues of co-funding for the initiative or individual projects, multidisciplinary research engagement, extended networking, and detailed consideration of the challenges intrinsic to working with innovative technologies.

Section 3: Methodology

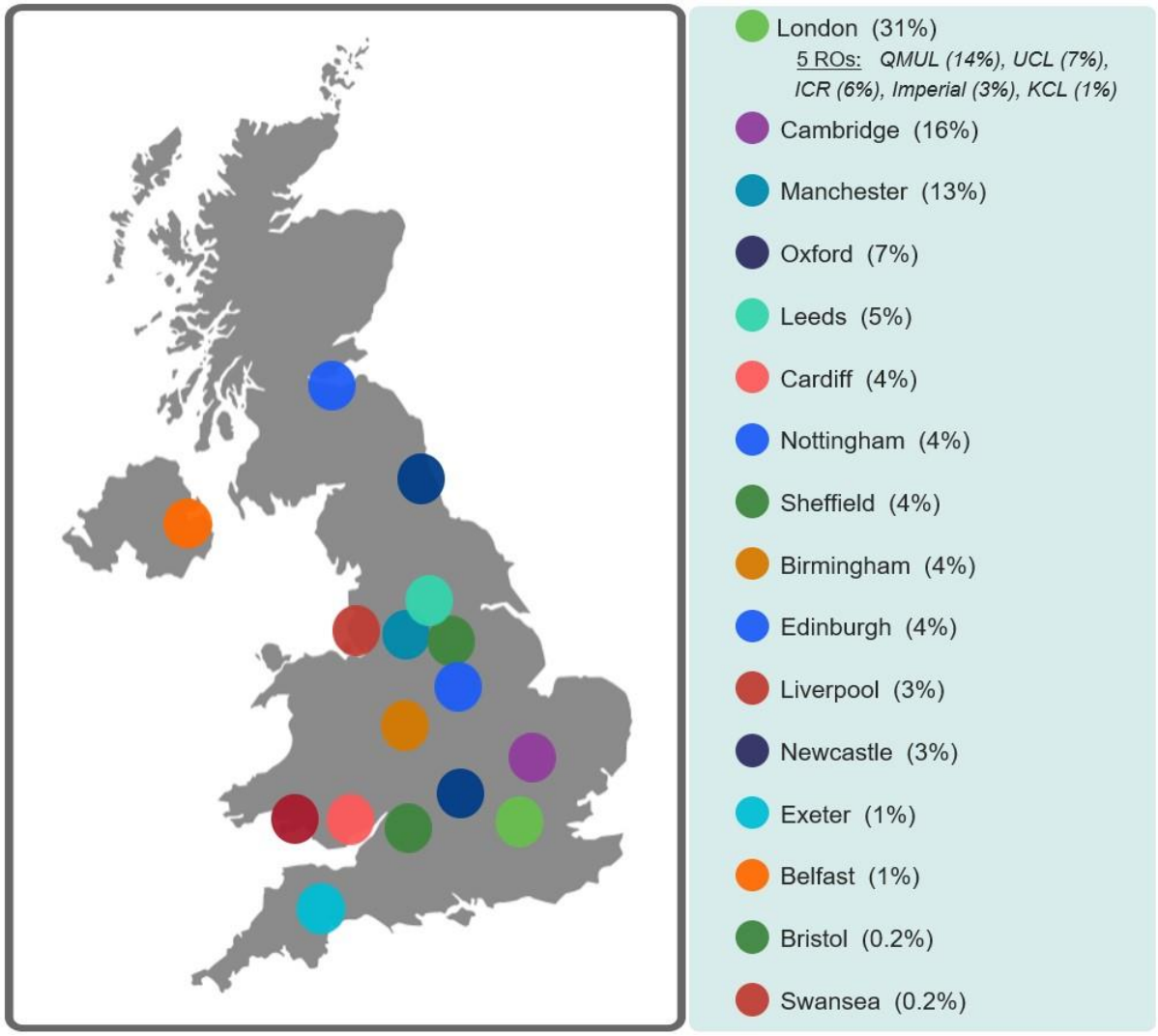
Detailed knowledge of how these nascent areas of research are being fostered by innovative technologies requires close monitoring of the development of the capabilities. MRC initiated a head office monitoring project to follow the development of the Single Cell Characterisation capabilities but due to MRC head office staff turnover, this project lost continuity so we lack details of how these facilities have developed over time. This contrasts with MRC's continuing interaction with the progress of DPUK.

Beyond the project management, we capture annual reports of output via Researchfish and we returned to the applicants in 2019 with a survey which was followed up by nine targeted interviews. Three recipients did not respond to the survey and provided minimal researchfish reporting. While this was a light touch evaluation, some desk research was carried out to validate or expand on the information already received. This combination of monitoring methods identified the overarching insights into the strengths and weaknesses of the programmes, afforded detailed examples of uptake and impact and provided general reassurance of where the investment has provided benefits.

Section 4: Funded Projects

The £180m CRII provided funding for 37 capabilities (ANNEX I – CRII funded capabilities) in innovative technologies to investigate new opportunities to improve human health and well-being across 20 research organisations covering the breadth of the UK (Figure 1, below).

Figure 1 – Geographical distribution of CRII capabilities by city



The funding panel invested in:

- Facilities at a single site that offer a national resource – these included the Magnetic resonance (MR) Linac Unit, Drug benefit-risk ratio analysis capability, and Genomics England data access platform.
- Facilities at a single site focused on providing advanced technologies to accelerate local research programmes for patient benefit – these included clinic-focused hyperpolarised magnetic resonance imaging facilities, a GMP stem cell facility, a naturally occurring human knockout database, a phenome centre, and a non-coding genomic variation database.
- Groups of related infrastructures to advance UK research prominence – these included the Dementia Platform UK (DPUK) and associated imaging facilities, and the eight Single Cell Characterisation (SCC) capabilities. The capital investment was distributed across a number of different sites.

The capabilities can mostly be grouped into four science areas using the advanced technologies they have in common (see Figure 2, below):

1) magnetic resonance imaging modalities (42 per cent of funding)

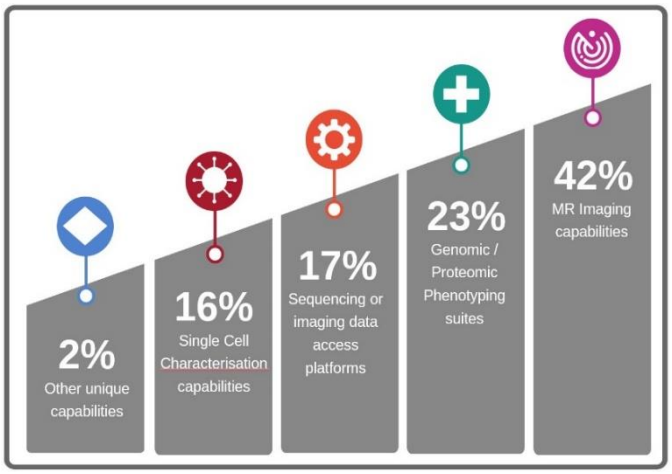
2) phenotyping equipment suites (23 per cent of funding)

3) data access platforms to patient sequencing and/or imaging databases (17 per cent of funding)

4) Single Cell Characterisation capabilities (16 per cent of funding)

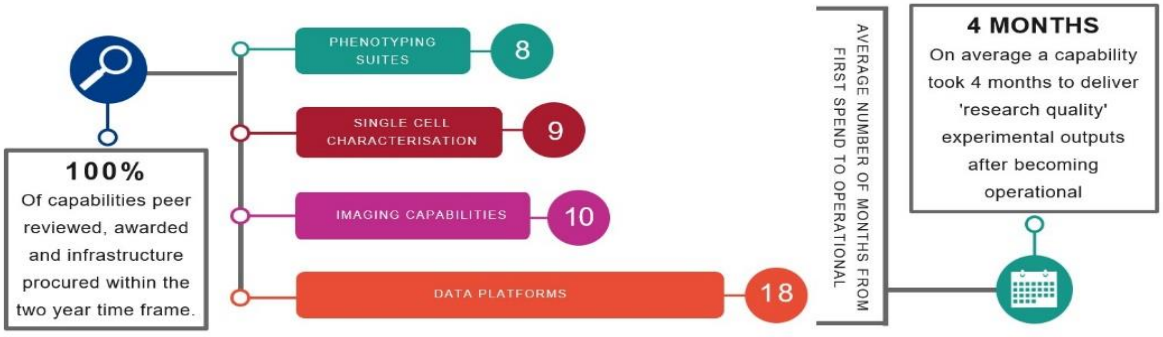
Three CRII programmes exploited different technologies from those of the four science areas ("other capabilities" in Figure 2).

Figure 2 – Distribution of funding across the four main science areas



The time line for procurement of many pieces of single supplier equipment combined with establishment of the capabilities was tightly managed. The data access platforms required the longest timeframe to become operational, potentially because the challenges of linking health and research data were the least explored at the time of the award (Figure 3, below). Significant experience in the establishment of magnetic resonance imaging facilities in the UK was available to bring the positron emission tomography magnetic resonance imaging (PET/MRI), 7Tesla magnetic resonance imaging (7T MRI) and other imaging modalities on-line efficiently. Cardiff, the recipient of a 7T MRI, was particularly grateful for the shared expertise developed in the separate MRC 7T MRI Network (funded in 2016). However, the rarity of 7T physics and combination PETand MRI expertise as well as other issues with the non-coil components of the imaging equipment seriously delayed availability of the full scanner capacity for many institutions. In four cases, unforeseen staffing or equipment problems delayed the infrastructure reaching its full capability until 2019 (Genomics England data platform, East London natural human knockout sequencing project, GMP stem cells production facility, and the Cambridge 7T facility). However, for most of the capabilities, the transition from operational to research quality data was a rapid one (Figure 3).

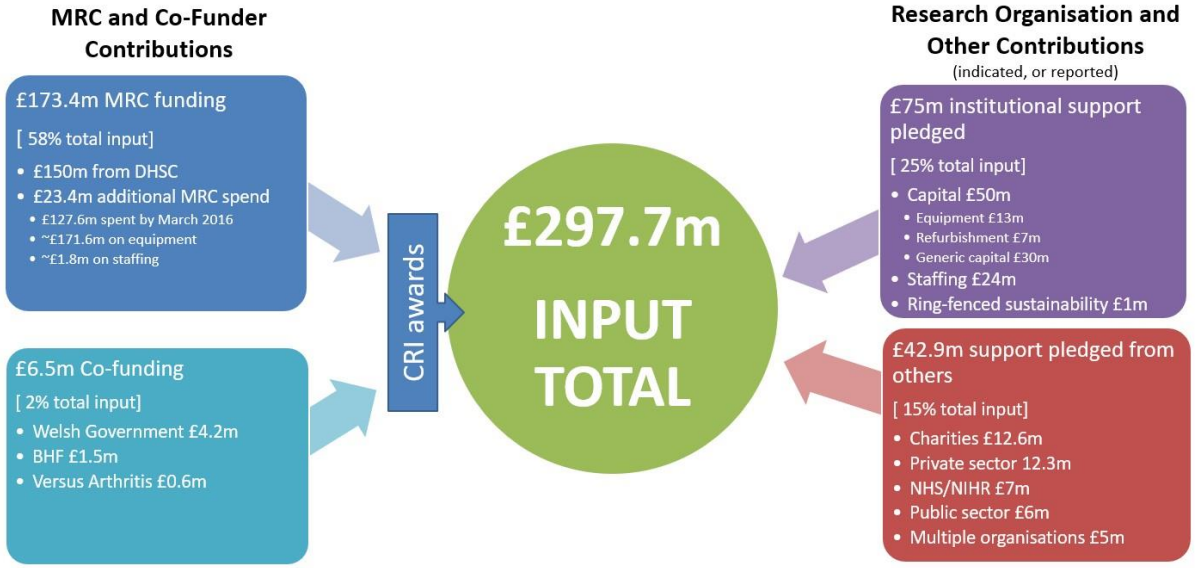
Figure 3 - Period for capability establishment



Total resources for infrastructures awarded

At the outset of the programmes, MRC awarded £179.9 million from DH and other co-funders and additional support for the infrastructure, estimated at £117.9 million (in cash and 'in kind' contributions), made by host research organisations and others (Figure 4) was reported.

Figure 4 – CRII capability input funding



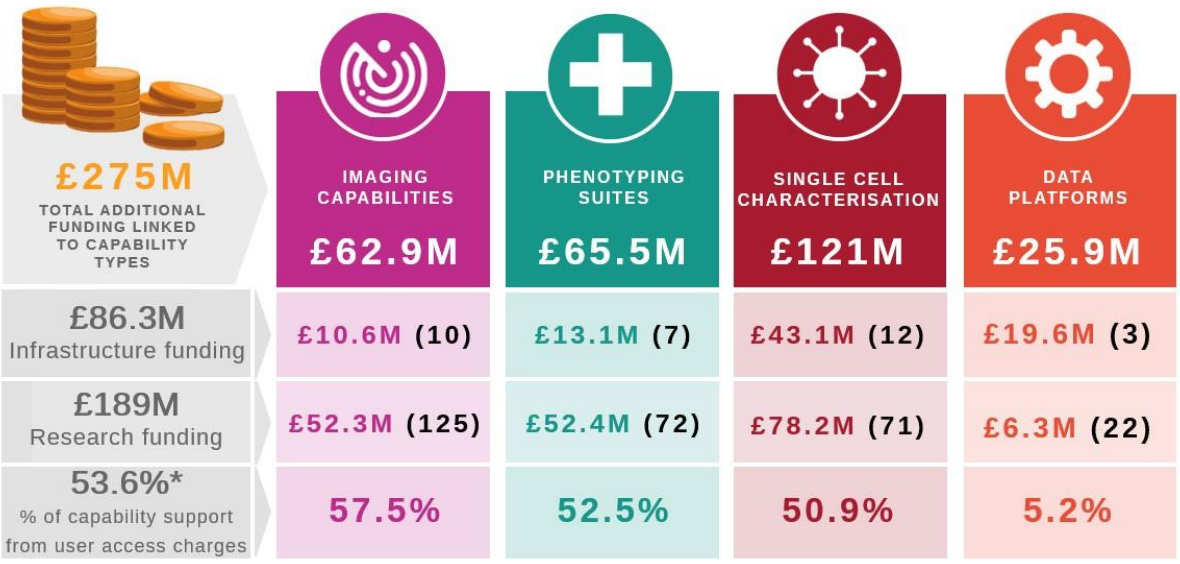
The investment from the research organisations in the capabilities was primarily focused on the imaging infrastructure and staffing (£43.6 million total) with only £8.2m for SCC capabilities, £16.7 for Phenotyping suites, £4.8 for data platforms, and £1.7 for the one-off capabilities. Whereas, other contributors invested in the SCC capabilities (£18.9 million; 44%) as well as imaging (£17.0 million; 40%). In many cases, this reflected the instrument manufactures' interest in further development of these advanced technologies in cell sorting and analysis. The type of support also varied between the technology areas with 66% of imaging support provided for infrastructure costs (refurbishment, building, equipment, etc) and 80% of SSC capability support pledged for staff costs.

In the post-award survey[5] and researchfish® submissions, the principal investigators reported an additional £275 million in follow-on funding had been secured through research awards, capability equipment awards and contributions from the host institution (a breakdown of this follow-on funding is in Figure 5) in addition to initial pledges. This funding has supported ongoing staffing, maintenance and improvement of the facilities (£86 million) as well as further research using the capability (£189 million). Approximately 54% of the running costs of the facilities (excluding data platforms for which there is incomplete data[6]) were recovered from user access charges.

[5] 2019 CRII evaluation programme

[6] The reported lower access charges for data platforms (Figure 5) is the result of three different issues: 1 data availability limitations resulting from their integration within the cost recovery system of a larger facility, 2) they have no or partial user charges or 3) only charge for commercial use

Figure 5 – Follow-on funding for CRII capabilities from post award survey and researchfish® further funding data



The number of incidences of further funding reported are contained within the ( ).

** Average excludes the proportion of access charges for data platforms, which is much lower than other science areas due to three different issues: (1) HPHI data availability limitations resulting from their integration within the cost recovery system of a larger facility, (2) DPUK data platforms have no or only partial user charges or (3) GeL only charges for commercial use.*

Section 5: Capability progress

Clinical translation and underpinning health research

The programmes funded through CRII were ambitious and far reaching in intent. At the point of funding, few programmes were expected to have direct clinical impact in the short term. For most awards, the anticipated short to medium-term goal was to accelerate development of innovative therapeutics or theranostics through increased momentum in translational research fields[7]. It is reasonable to expect that the facilities will take longer than just two to three years to mature and demonstrate their full contribution to clinical research.

While acknowledging that some of the projects may be at an early stage of this journey, we provide an indication of the 2019 translational position of the portfolio of capabilities (Figure 6 below) using a few basic metrics. From current evidence[8], 18 of the 28 programmes funded have produced valuable clinic-facing research, developed rich datasets and/or established user communities which indicate the strong potential for substantial progress in clinical therapies or understanding in the future. Outputs were assessed by extent of the intent to translate for patient benefit seen in the reported capability-associated publications and programmes of research.

Figure 6 - Matrix of project development

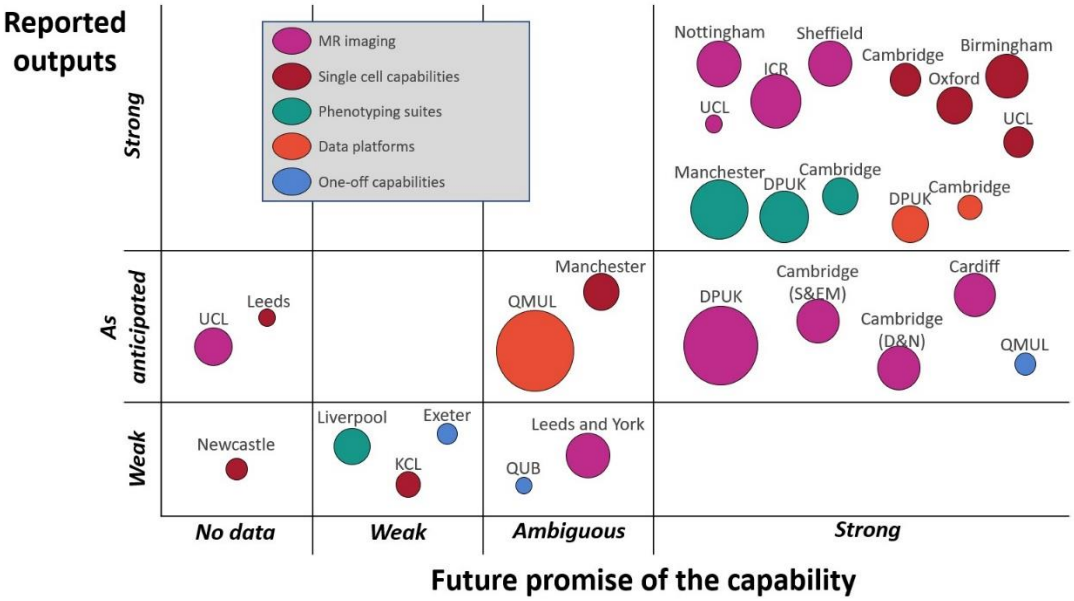


Figure note: Progress in reported outputs was assessed by evidence of advances in translational or clinical based research ('Strong') or evidence of advances in underpinning knowledge ('As anticipated'). Indication of future promise was assessed by evidence of development of novel data sets, a strongly engaged user community with expanding researcher up-take beyond the applicants and the originally stated disease areas, and/or broad dissemination and uptake of methodology and techniques developed. In some cases, there was no data available and in others the limited evidence or uncertainty made assessment of future promise unclear.

The DPUK programmes represent multiple capabilities: imaging (5), Phenome suites (6), data platforms (1). Bubbles are scaled to indicate relative investment.

Assessment of future potential was based on evidence that the facility was actively supporting an expanding research community engaged in both clinical and underpinning research,

[7] In some cases, this included discovery science research which enhanced understanding of human health and disease.
[8] Survey responses from 21 of the 24 awardees, researchfish reports, web investigation and detailed interviews with nine investigators have provided information on the progress, potential, linkages and outputs of the awarded capabilities.

addressing diverse disease areas (represented in Figure 7 below) and, in some cases, was developing clinically focused datasets of value to translational researchers. For four of the funded projects potential progress was difficult to determine, for three projects there was evidence that progress was limited and for three other projects no data for progress was available. The assessment of progress was based on reported[9] outputs in surveys, interviews and details available from facility websites, and took into account the programme objectives as stated in the application.

Figure 7 – Diversity of disease areas

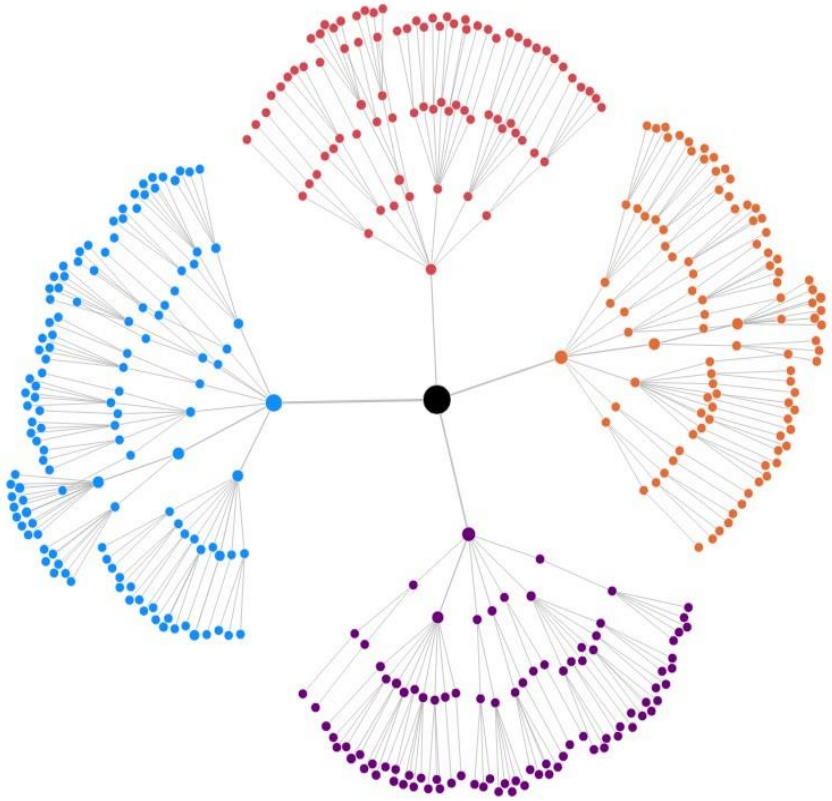


Figure note: The dots represent the distinct health conditions being investigated using the innovative technologies provided by the CRII. Each of the four science areas are indicated by a different colour.

[9] This assessment was based on data requested or evidence available in the public domain.

Imaging capabilities

The CRII funded or supported expansion of 14 MR imaging capabilities:

- six PET/MRI installations within the DPUK network of dementia researchers (Cambridge, Cardiff, Edinburgh, Imperial, Manchester and Newcastle)
- two 7Tesla MRI in Cardiff and Cambridge for research into neurological conditions with strong links to DPUK
- one 3Tesla MRI in UCL for research into neurological conditions with strong links to DPUK
- one 3Tesla MRI in Nottingham for imaging of thoracic, abdominal and musculoskeletal conditions
- one 3Tesla MRI in UCL for cancer theranostic development
- two projects expanding existing hyperpolarisation facilities in Sheffield and Leeds
- one linear accelerator for ICR for treatment management of a variety of tumour types

There was evidence that 12 of the 14 the imaging capabilities funded had advanced research toward clinical application and generated knowledge to better understand the development and progression of neurological and physical degeneration in a wide variety of health conditions (ANNEX 2). Programmes to develop two of these innovative technologies have resulted in translation into clinical treatment. The Leeds hyperpolarisation programmes has shown limited translational progress and there is little information concerning the UCL theranostic programme.

UK researchers are leading the world in clinical implementation of two innovative technologies: translation of, first, xenon hyperpolarised gas techniques and second, linear accelerator (Linac) radiology. Research programmes investigating their clinical potential of have existed for decades but the CRII investment provided the last lift necessary to apply these methods to the clinic. The first, hyperpolarised gas work carried out in the University of Sheffield POLARIS imaging centre has recently established clinical applications of human pulmonary imaging with hyperpolarised xenon (see case study below). Hyperpolarised gas is now regularly used for diagnosis and monitoring of lung conditions in Sheffield hospital trusts. Additionally, the technology is currently being trialled for use with a variety of other pulmonary diseases and explored for use in other body regions. Second, teams in the UK (2018) and in The Netherlands (2017) were the first in the world to use the MR Linac machine to treat patients by targeted radiation beams. The UK team at ICR received CRII funding for the Linac in January of 2015 and were treating patients by September of 2018. As of summer 2019, they had already treated 300 fractions of radiotherapy for patient groups. By 2020, treatment planning studies have established templates for the treatment of prostate, rectal, bladder and gynaecological cancer and patients were treated for the first time in the UK on the MR-Linac.

Case study: Expansion of state-of-the-art MR imaging infrastructure for pulmonary disease stratification: POLARIS
Prof. James Wild, University of Sheffield, MR/M008894/1

A research team led by Professor Jim Wild at the University of Sheffield has pioneered the use of hyperpolarized gases in MRI for measuring early lung disease, disease progression and treatment responses in asthma, cystic fibrosis, pulmonary fibrosis, pulmonary hypertension and chronic obstructive pulmonary disease (COPD). A CRI award in 2015 allowed the expansion of this technology, leading to advancements in patient diagnosis and a series of studies of how the method may be applied in various lung diseases. The funding helped the team substantiate the clinical applications of hyperpolarised MRI, by allowing them to run parallel xenon imaging at two major hospitals in Sheffield. Professor Wild stated," now we're performing clinical hyperpolarised xenon MRI scanning for the NHS and that's really been enabled by the infrastructure from the MRC CRI award". This subsequently led to the site becoming established as an NHS Clinical Referral Centre for Clinical Pulmonary Imaging in the North of England, with approximately 250 patients imaged through clinical diagnostic referrals in the past three years. The Sheffield Pulmonary Vascular Disease Unit (PVDU) is now one of the largest Pulmonary Hypertension treatment centres in Europe with a referral population of approximately 15 million patients. As a world first breakthrough to clinical practice for this technology, Professor Wild's group has established MHRA regulatory approval for the manufacture of xenon. These technical developments have been disseminated to other user communities in the UK and beyond; for example, the CRI funding allowed the team to develop a portable xenon polariser unit that can be transported in a van which they trialled with human lung imaging at Royal Papworth Hospital, Cambridge. The dissemination is also evident as knowledge and skills transfer from PhD students who have subsequently helped enable novice sites in the UK in hyperpolarised MRI acquisition technology, along with capability for building polarisers and RF coils for other sites. The team are also helping develop hyperpolarised gas imaging capability in sites such as UCL Hospitals, Manchester Wythenshawe Hospital, and Columbia University Hospital in New York.

The expansion also led to innovation on multiple fronts including further research into xenon polarisation and its applications, technological and design adaptations of MRI equipment to this modality, development of specific image acquisition and processing methodology, and physiological modelling computations to suit the high complexity of the lung. Consequently, there has been a high degree of integration of all these aspects within the University of Sheffield and its partner hospitals, as well as with external academic and clinical partners (UK and international), and industry. Although the POLARIS MRI Research Group already had an international reputation for competitive expertise in hyperpolarised MRI methodology and its biomedical applications, these newer developments and their dissemination would have been unlikely without the increase in capacity that the 2015 CRI award has allowed.

The initiative was transformative for the UK research infrastructure landscape. Six positron emission tomography magnetic resonance imaging (PET/MRI) facilities for dementia research were strategically located in close proximity to DPUK cohort populations at a time when the PET/MRI 'state of the art' was evolving rapidly. Installation of six cytometry of time of flight mass spectrometer (CyTOF) machines within single cell characterisation facilities quadrupled the UK population of this cutting-edge technology.

The largest CRII award provided additional support for the Dementia Platform UK (established in 2014) to transform the multi-modal imaging capability for research into Dementia. This was further strengthened with investments in Cardiff and Cambridge imaging programmes directed toward further understanding of neurological conditions more broadly: neurodegeneration, cognition, depression, etc. The funding provided DPUK sites with a variety of additional imaging equipment including the establishment of, or upgrade to, six PET/MRI capabilities. This investment in advanced imaging has had impact on diagnostic trials. For example, the multi-modal imaging studies enabled combination of detailed mapping of neurodegeneration and brain functional changes with imaging of associated molecular neuropathology. This increased capability has been integrated into the MRC/NIHR Deep and Frequent Phenotyping study. The outputs of the study, that aims to develop markers for progression of dementia, have been fundamentally enhanced by the DPUK CRII investment working with the infrastructure established by the NIHR Translational Research Collaboration.

The CRII awards have solidified and improved the original DPUK network. The CRII funding for computational capacity and interoperability has supported the creation of an accessible dataset incorporating imaging and patient data from dementia cohorts and other patient groups. The network has made advances in health data platform development and expanded clinical connections in Cardiff and other sites. The programme combines MR imaging, stem cell modelling for dementia research, and a UK-wide data sharing web for imaging methodology. The CRII investment was described as taking the early momentum of DPUK and solidifying the commitment from a broad research community to create this database and platform. *"If I had to ~~…~~ get the buy-in from all of the partners, that would have been much harder to do…the timing of the CRI capital call in relation to DPUK meant that ~~…~~we achieved something that we couldn't have achieved as easily otherwise."*[10]

Across the MR imaging capabilities, the investment has increased the potential for multimodal brain imaging on the same site and/or in proximity to cohorts. This increased practical efficiency has resulted in an increased number of multimodal studies undertaken. In alignment with the objectives of the CRII, this has also stimulated expansion into other areas of disease where the non-invasive insight provided by MRI can be effectively applied. Co-localisation of the variety of imaging technologies has allowed more precise determination of the best methodology to collect the data required. In the case of Cardiff, the proximity of the CRII 7Tesla and existing connectome scanner has attracted the CUBRIC scanning safety study in children leading into a study of children's epilepsy, a UK first. Among other novel studies, Nottingham is using its multimodal capability to investigate placental condition enabling identification of those at high risk of obstetric syndromes. The work on image guided therapies for prostate cancer at UCL has contributed to the 2019 launch of the MRC funded ReIMAGINE trial to demonstrate the diagnostic accuracy of imaging in comparison to the current PSA blood test. The PET and magnetic resonance imaging capabilities continue to develop new clinically relevant methodologies and underpinning knowledge and have expanded clinical trials into new disease areas. However, the translation to clinical use is still some way in the future.

The researcher interviews generally highlighted that the short time frame for establishing the capabilities caused problems. For the DPUK data portal, the CRII investment funded a vastly more useable and richer data portal than originally conceived. However, the restricted time

[10] From interview

for planning this at application did not fully anticipate the challenges of reworking DPUK plans, the team became committed to a prolonged development process, and the downstream impact was that there was no money remaining for data curation. In another case, the latest 7Tesla technology was six months away from launch at the time of the award but with the time constraints placed on award spend Cardiff was obliged to buy the existing, rather than latest technology. This may reduce the time their scanner is supported by the manufacturer and meant they had to work with a more awkward instrument configuration[11]. More broadly for the investment in UK imaging, more time would have allowed the 7Tesla facilities to provide a coordinated application that took advantage of technology developments and synergies between facilities.

The private sector relationships with the CRII imaging capabilities are generally continuations of long-term investigator collaborations with pharma e.g. funding PhD students to work with the new capability. The exceptions to this are those that involve the equipment manufacturers. Where new equipment has been provided, the manufacturers continue to maintain close relationships with the research laboratories. For example, Siemens, the 7Tesla manufacturer, extended the original placement of a scientist to oversee installation at CUBRIC to an open-ended position for scientific collaboration on 7Tesla clinical methodology at their own cost[12].

At the time of award, dual trained PET/MRI technicians were not available in sufficient numbers, so twice as many staff were initially employed to ensure availability of the expertise required. However, DPUK have reported that training for dual expertise has progressed and skill shortages have been reduced. The PET expertise skill shortage had been identified by the MRC in 2009 when a training programme for post-doctoral researchers was established. This was discontinued in 2013 when it became clear that the researchers trained were not retained in academia in the UK.[13]

While accessibility of multi-modal imaging on the same site was highly valued by those interviewed, the PET/MRI scanner, as opposed to having a separate PET scanner and a 3T MRI, was not universally seen as more efficient. However, the broad distribution of leading-edge imaging technology, PET/MRI and 7Tesla MRI, across the UK was reported to have contributed to the UK maintaining[14] its reputation as a leader in brain imaging techniques.[15]

[11] From interview
[12] From interview
[13] From 2017, *MRC Review of Positron Emission Tomography (PET) within the Imaging Research Landscape*
[14] UK imaging reputation has been maintained by constant development in the field and because the software package FSL, arising from Oxford in the late 1990's, remains one of the two main tools used for image analysis globally.
[15] From interviews

Data access platforms

Three data access platforms were specifically funded in the CRII:

- cohort MR imaging and health data for DPUK
- patient imaging and health data for the Stratified Medicine Core Laboratory at Cambridge
- the Genomics England Research Environment, based at QMUL, for linked clinical and Genomics England sequencing data.

The three platforms were designed to provide researchers and clinicians access to data from advanced technologies, imaging or sequencing, linked to patient health records. Interviews with researchers directly involved with development and/or use of these data systems highlighted the major impediment of linking live or complex health data with the research analysis data (imaging, sequencing, etc.). The challenges encountered proved far more difficult than anticipated. The interviewees reported the common challenge created by uncertainties around data ownership, stringency of data security and engaging with data managers. It was repeatedly pointed out that data sharing, for secondary use, was a very low priority for the NHS, while a very high priority for translation focused researchers. One interviewee felt that the limited time available to design the CRII projects had prevented the development of effective routes to address these problems, leading to false starts and delays in finding a resolution[16]. As of August 2019, all data platforms appear to be complete and are accessible, but there were severe delays and limitations in expected usability due to unanticipated challenges. Despite the fact that the data platforms shared similar problems, there was no evidence of collaborative working to more efficiently overcome these issues.

The **DPUK cohort MR imaging database** is now live[17] and available for researchers beyond DPUK. The intent was to make this dataset useful for both translational underpinning research and for clinical use. Lessons were learned from the highly praised UK Biobank data access platform. The establishment of the platform linking all the DPUK research sites was completed on time and to the agreed budget. The subsequent harmonisation of cohort patient data took longer and is only now being accessed by the community.

The aims of the **Stratified Medicine Core Laboratory** at Cambridge were to deploy a computer platform for biomedical imaging (particularly for data generated in the Wolfson Brain Imaging Centre), to allow patient data linkage, and to allow this data to be shared. All three aims have been partially met. However, there was a long delay in access to some of the PET/MR imaging data and developmental work is still ongoing for patient linkage and data sharing.

The original objective of the **Genomics England Research Environment** data access platform application was "*to integrate high-fidelity clinical phenotypes and whole genome sequence data from these patients with electronic health data from primary care, hospital episode statistics, and outcomes*"[18]. It was intended to give easy access to large volumes of sequencing data to academic researchers. Research publications, while still just a few in number, indicate valuable data for clinical decision making will arise from this project, using the clinical phenotypes captured at the time of genome sequencing. However, the data platform (The Research Environment), has been unable to integrate genome sequence data from patients with their electronic health data from primary care, hospital episode statistics, and outcomes. There is minimal e-health data accessible within The Research Environment. It is unclear how this integration can be developed further from the information available to this evaluation.

[16] From interview
[17] https://portal.dementiasplatform.uk/AnalyseData/ImagingPlatform
[18] From the UK Infrastructure for Large-scale Clinical Genomics Research CRII grant application

The GE data access platform was an extremely ambitious project considering the limited experience with data platforms of this size and complexity at the time of funding. Additionally, the designation of the primary user group for the integrated data has shifted over the course of the project to NHS clinicians and away from academic researchers. Unforeseen technical limitations required a significant redesign of the infrastructure halfway through the development; this delayed completion for more than a year. While the limitations in fundamental design of the current GE platform could not have been anticipated five years ago, they do highlight the need for a cultural shift in data sharing, ways of working across data controllers whilst respecting robust governance systems and privacy/security, and platform design, with respondents suggesting one solution could be a move toward fewer but multi-tenanted trusted research environments[19]. The GE 100,000 Genomes Project was completed in 2019 and this data is available on the Research Environment. Researcher uptake to access that data is gradually increasing. However, using the sequencing dataset remains very awkward when performing complex analyses on bulk sequences and extremely difficult when investigating disease areas requiring access to additional e-health data. This is inhibiting an expansion in use of the dataset while acknowledging more broadly that it is still very early in the development of strategies to cope with this complex data analysis space. Usability within The Research Environment will improve, no doubt, and iteration with researchers is active and responsive but it will take time.

Interviews with researchers responsible for CRII data management platforms revealed missed opportunities for pooling resources and expertise to resolve similar problems. Many of the issues are still challenges for these projects. While networks are becoming established for data platform development, the perception is that the discussions focus on the general overarching issues instead of targeted problem solving. One researcher suggested, “networks which are just about a brilliant meeting of the minds around thoughtful things that may matter in twenty years, but if you're talking delivery, then those networks need to have a task and finish” [directive].

[19] From interviews

Single Cell Characterisation

The CRII investment in advanced cell isolation techniques alongside detailed single cell phenotyping equipment linked to an informatics infrastructure was to accelerate understanding of individual cell characteristics for diagnostics of cancers and other health conditions as well as of the underlying biology through complex immunophenotyping of cells. CRII provided a technologically transformational investment in single cell characterisation for the UK through the establishment of eight suites of equipment designed to isolate, sequence, and characterise at the level of single cell precision. Single Cell Characterisation (SCC) capabilities were created in Birmingham, Liverpool, Manchester, Newcastle, Cambridge, UCL, KCL, and Oxford. For six of these centres, the leading-edge technology, cytometry of time of flight mass spectrometer (CyTOF), was a key component of the equipment funded. The installation of six CyTOF machines within single cell characterisation facilities in 2016 quadrupled the UK population of this cutting-edge technology (from two to eight). The existing two capabilities requested equipment to complement the analytical strength of the CyTOFs they possessed.

Mass cytometry, or CyTOF, is a variation of flow cytometry in which antibodies are labelled with heavy metal ion tags rather than fluorochromes. Readout is by time-of-flight mass spectrometry. This allows for the combination of many more antibody specificities in a single sample, without significant spillover between channels, than previous approaches. The first commercial set-up for such experiments was developed at Stanford University in 2011[20] and the potential for the approach to transform single cell characterisation rapidly became apparent[21].

There is clear evidence that five of the eight SSC capabilities are making possible new avenues of research with the potential to lead directly into improved diagnostics, prognostics, and new therapies within the next five to ten years. While there is no progress into the clinic as yet, interviewees and survey responses indicate that the funding has increased the volume of work possible (by an order of magnitude) transforming the pace of the research and leading to plans for more translational work. Evidence for the other three capabilities was lacking.

"Up to that point [the time of CRII funding] *we were in a situation where I think where we were typically processing tens of cells, sometimes hundreds of cells for experiments, but moving to thousands of cells was a major endeavour. And the funding allowed us to invest heavily in robotics platforms to...to really...I think that was a real paradigm shift in what we were able to deliver, so we went quite quickly to a pace when we could process thousands of cells in a single experiment, relatively straightforwardly… to allow us to really change the throughput to...by an order of magnitude really, so that was definitely transformative"*

Access to single cell characterisation (SCC) equipment has allowed researchers to work at scale: for example, to generate genomic, transcriptomic, proteomic and metabolomic data for thousands of cells in a given disease or developmental context. These advances in underpinning knowledge have yet to translate into direct patient benefit but the potential routes to new diagnostics or/and treatments is evident. One example, seen in Oxford, has been the impetus for the launch of the Therapeutic Acceleration Laboratory (TAL). The purpose of the TAL is to collect and analyse samples from patients in clinical trials according to GCLP[22] standards, so that the information can be fed back directly to influence patient management within that clinical trial[23]. Applying single cell characterisation techniques into the study of

[20] Bendall SC, Simonds EF, Qiu P, et al. Single-cell mass cytometry of differential immune and drug responses across a human hematopoietic continuum. *Science*. 2011;332(6030):687–696. doi:10.1126/science.1198704 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3273988/

[21] Doerr, A. A flow cytometry revolution. *Nat Methods* **8,** 531 (2011). https://doi.org/10.1038/nmeth0711-531

[22] Good Clinical Laboratory Practice

[23] From interview

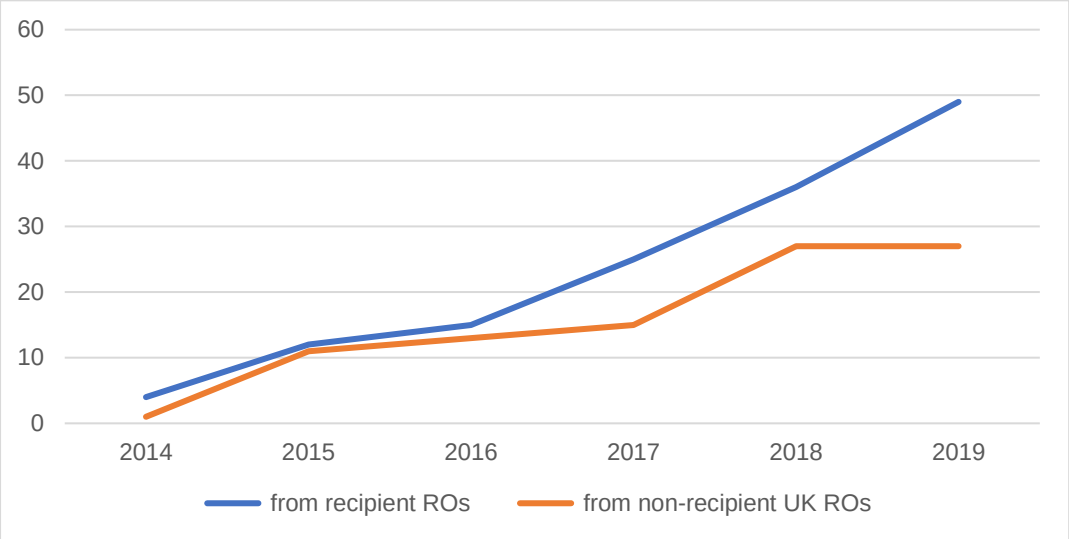
diseases such as cancer has been particularly fruitful. For example, it not only allows the cataloguing and characterisation of the heterogenous population of cancer cells within a tumour but also their responsiveness to chemotherapy. Studies are underway to understand the tumour microenvironment before and after the tumour responds to chemotherapy and/or ionising radiation therapy. The infrastructure has allowed single cell characterisation technology to be used to generate pilot data in other disease areas that are, unlike cancer, not immediately obvious targets for benefiting from this technology: for example, gaining insights into inflammatory bowel syndrome and other autoimmune disorders. The increase in applications for single cell characterisation analysis in the UK, made possible since the CRII funding, has generated interest in an expanding community of skilled researchers as evidenced by the growing uptake of use of the UCL SCC capability in pathologists' research programmes.

To address the challenges faced in using this new technology, MRC required networking plans to be explicitly laid out in the applications from all groups receiving funding for SCC capabilities, however, there is no evidence of the described networks having been established. Groups in Birmingham, Oxford, UCL, and Cambridge have established strong research communities based around the exploitation of the SCC capability; however, interviewees have indicated that the communities are local, intra-city networks. For example, extensive collaboration within the UCL Hospitals network and other London-based research organisations such as the Francis Crick Institute on single cell analysis was reported but no interactions are evident between the CRII funded capabilities. Annual networking meetings are arranged by Fluidigm, the manufacturer of CyTOF, as agreed with MRC during the initial negotiations to acquire six machines. These meeting have been funded and managed by Fluidigm to discuss new techniques developed by CyTOF users. Capability directors appear unaware of these meetings, indicating in their interviews that a UK wide network to share best practice could contribute to more effective use of the equipment. It is possible that SCC capability technical staff or users are participating in the Fluidigm network meetings, but any information or insight gained does not appear to be disseminating readily across the UK community.

MRC initiated the relationship with Fluidigm and negotiated a significant discount in price for each of the capabilities and other support provisions. However, the challenges arising from single-supplier technology have had implications for use and sustainability of the capabilities. The high cost of setting up an experiment precludes its use for students or early career researchers with limited consumables budgets. Additionally, the service contract cost requires an annual value-for-money assessment to determine whether to retain the equipment or purchase new technology. The interviews also touched on the difficulty of establishing a cost recovery system which incorporates the service contract costs but does not discourage exploration of new but potentially fruitful translational research paths.

As was anticipated at the time of funding, the vast quantities of data generated by the SCC capabilities have resulted in data storage and management challenges. Generally, these have been dealt with effectively but the availability of enough bioinformaticians to analyse the data continues to be a problem. The CRII funding highlighted the UK's commitment to world leading research with advanced research technologies in single cell analysis. The single cell research investment has raised UK global research profile and resulted in UK single cell researchers being targeted for key note conference speeches. The CyTOF was developed in Stanford in 2011 and launched by Fluidigm corporation in 2014. Evidence of the impact of the CRII investment in CyTOF is indicated in the rate of increase of CyTOF publications from UK research organisations receiving SCC capability awards vs those that have not (Figure 8 below). The number of CyTOF publications from UK research organisations that received CRII funding compares favourably with similar publications that have an involvement from Stanford University (in 2019 approximately 50 papers, compared to 70 from Stanford).

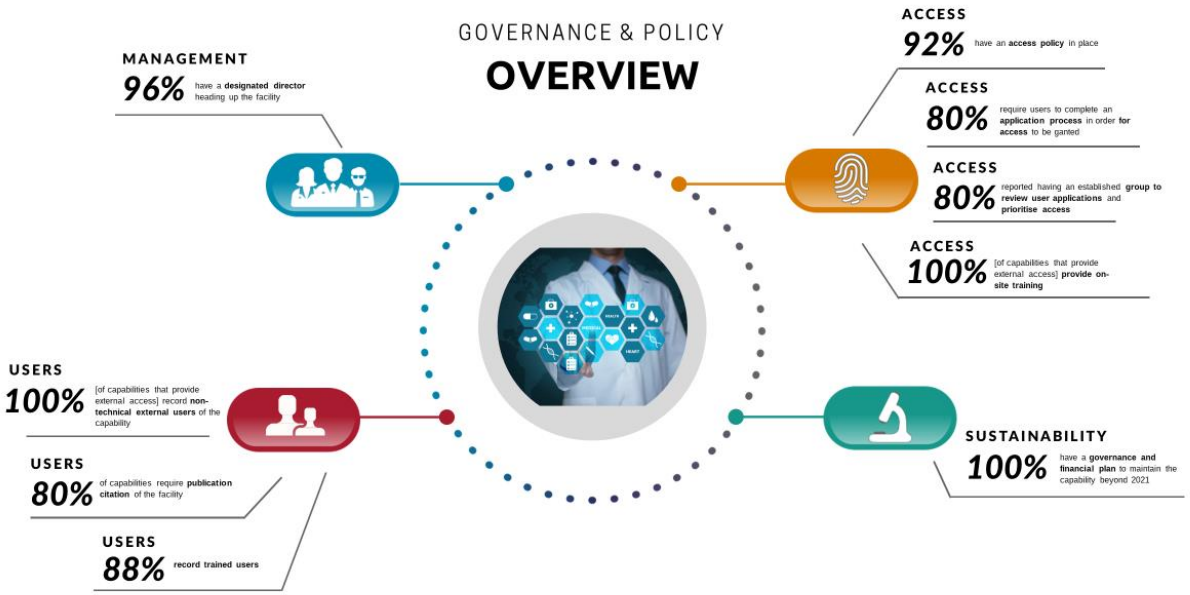
Figure 8 - Number of CyTOF publications from UK-based authors



Sustainability of facilities

This initiative was intended to establish capabilities that could continue to operate over the long-term. To that aim, the applicants were required to provide details of how the capability would be governed and plans for maintaining and enhancing the capability. In the 2019 survey, they reported on the structure and financial plans now in place to meet that obligation (Figure 9 below). The overwhelming majority of capabilities report having established clearly defined governance structure with a designated director or oversight committee, designated staff, controlled access procedure, facility user training procedures, and records of users and their publications. Although after four years of operation, many of the funded capabilities no longer have a presence which is externally distinguishable from their host facility, all capabilities appear to continue to function and to produce outputs[24].

Figure 9 – An overview of CRII capability governance and policy arrangements based on 2019 survey responses



In general, the capabilities were integrated into an existing facility enhancing its analytic capacity. A few programmes initiated establishment of new, stand-alone capabilities: the MR Linac Unit in the Royal Marsden NHS Foundation Trust, Phenome Centre Birmingham at University of Birmingham, Oxford Single Cell Biology Consortium, Cambridge Single Cell Analysis Clinical Core Facility and Queen's University Belfast Cellular Therapy Facility. However, all facilities were located within established research centres, where administrative support has been provided to run cost recovery systems and often bridging funding for capabilities running costs. NHS hospital trusts or NIHR BRCs have provided ongoing funding support for all but four of the capabilities (ANNEX 3) reflecting their clinical, in combination with academic, focus. In some cases, they are the host research centre. Figure 10 (below) shows the sustainability plans for the facilities, highlighting where each planned to meet their costs from users/awards (cost recovery), additional grants, and/or host institution support.

[24] From survey and researchfish returns

Plans for sustainable operation of the capabilities relied to varying degrees on recovering costs from users, securing additional infrastructure grants, and core/host organisation support (see Figure 5 and 10) Our evaluation did not determine details such as the total costs of running each capability or absolute income from users, but investigators reported that overall, approximately half[25] of the running costs of the capabilities were recovered from user access charges. This implies that many capabilities are dependent upon their running costs being underwritten by host institutions and securing further grant support.

With the rapid innovations in technology for these science areas, good financial plans should include support for upgrade of facilities as well as planned maintenance. This was reported in 77% of the capabilities that provided data and, in some cases, plans had already been activated to supply additional equipment to complement the existing capabilities or upgrade existing equipment. For example, the Manchester Single Cell Characterisation capability, which was split between the Manchester Academic Health Centre and The Division of Molecular and Cellular Function, reported upgrades to or duplication of five pieces of equipment in high demand[26]. However, it could not be determined whether these plans were likely to be able to keep pace with technology development. So, while capabilities have funds to operate now, are recovering a significant part of their running costs, and are underpinning research across a large grant investment, there is likely to be a need for further capital investments in the renewal of these capabilities and the establishment of new capabilities.

The capabilities which have translated findings into the clinic do not include upgrade in their sustainability plans. As clinical applications require a standardisation of equipment to hone implementation methodologies, upgrade to the latest technology may not be a useful driver for clinical implementation.

Figure 10 – Different approaches to funding sustainability plans across the CRII capabilities

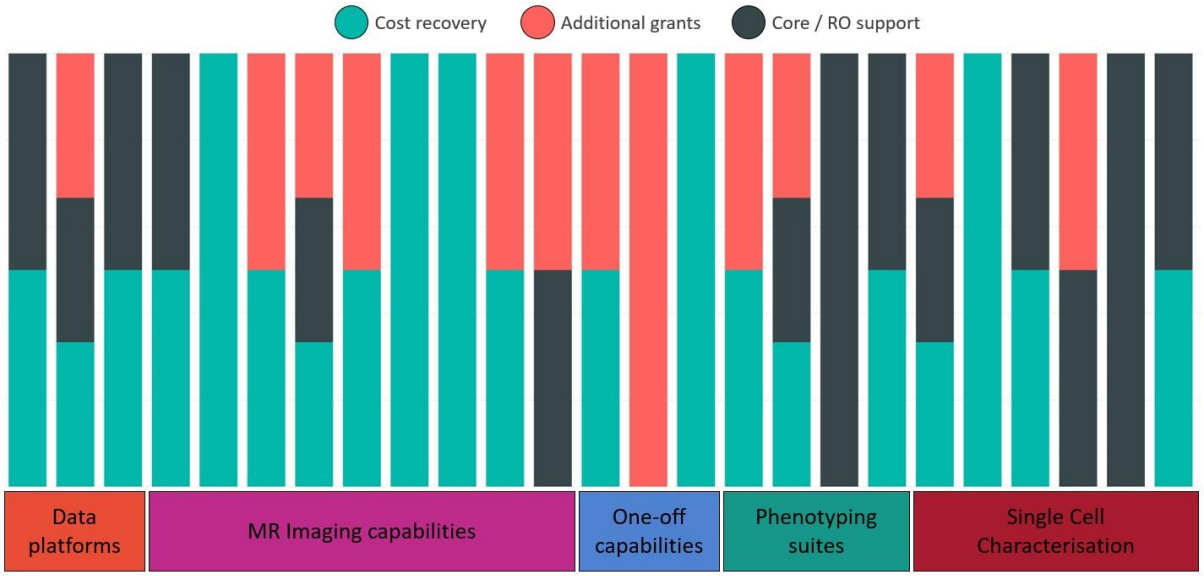


Figure note: The coloured bars represent the reported sustainability plans with one, two, or three income streams. The bars do not reflect the proportion of income from the three sources. The 25 bars indicate the plans for the 25 of 28 projects reporting (two of the 24 awards were split into 3 projects).

[25] Overall slightly more than 50% of the running costs of capabilities (excluding data platforms) were covered via user access charges
[26] From survey response and interview

The CRII capabilities employ on average 10 full time staff to support each capability. 76% of the core staff have dedicated time for methodology development or other research to improve the facility. This reveals an institutional commitment to continue development of the methodology and application of these cutting-edge technologies. Both survey and interview data reveal that the capabilities are active in training researchers. Excluding the data access platforms, 852 individuals across 19 capabilities were trained in 2018. Little funding for training was provided in the CRII awards; despite this, 23 of 24 facilities have established training programmes. The University of Birmingham was one of the few programmes with a funded training component and they report extremely high levels of uptake: 147 trained in 2018. Another SCC capability, at UCL, has independently established a remarkably active training programme.

The users of the capabilities are overwhelmingly academic researchers from the local community, except for the data platforms (Genomics England data access platform, DPUK imaging data sharing platform and the Genes & Health data from the *Phenotyping and experimental medicine Centre for naturally occurring gene knockouts in humans* award) and the Stoller Biomarker Discovery Centre at the University of Manchester to which CRII provided additional capability. The percentage of private sector capability users is generally 5% or less. About half the capabilities record significant (>20%) of clinical users. Concentrations of clinical interest peak in individual capabilities with the Biomarker Discovery Centre in Manchester reporting the highest percentage. The imaging capabilities as a group have the largest clinical population of users with the Cambridge imaging centre reporting 38% clinical users.

Section 6: Conclusions

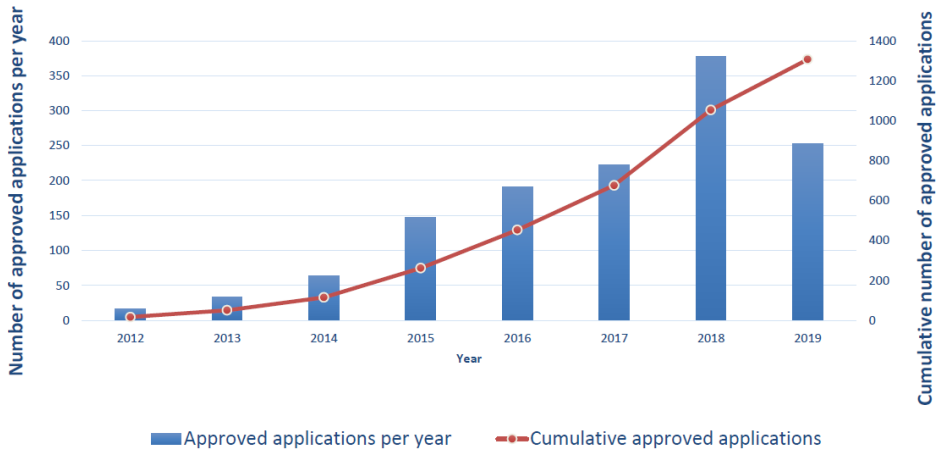
Many of the CRII programmes have made progress in establishing new technologies that enhance approaches available for translational research, and some have used the lift provided to develop clinical applications. They have generated interest from an expanding community of researchers in diverse health areas and made accessible methodologies useful for clinical therapeutics and prognostic development. This was an important set of infrastructure investments that has clearly helped keep the UK at the forefront of discovery science for clinical benefit.

It is important to recognise that it is difficult to generalise across this highly diverse group of capabilities when considering the factors influencing the extent of translational impact achieved. However, even at this early stage, it is evident that not all programmes have fulfilled or are likely to fulfil their research objectives while some will take longer than anticipated and it is worth reflecting on the possible reasons for this.

In reviewing the progress of the CRII programmes, it was logical that the maturity of existing work in the area and translational experience would largely affect the speed of translation into the clinic or extent of focused clinical research that we found in the evaluation. This can be seen by comparing the two awards given to progress hyperpolarised gas imaging techniques into clinical research. The project at Sheffield had been slowly addressing the challenges of translation for many years. The large CRII investment has been transformational in supporting the move from theory to practice within two years. This is in contrast to the less well-developed hyperpolarisation projects at Leeds and York where regulatory and methodological challenges remain to applying the technique to human scans. The large well-established programmes (DPUK, Oxford WIMM, Cambridge Wolfson Brain Imaging Centre, Manchester Stoller Biomarker Centre, Phenome Centre Birmingham) have integrated the CRII funded capabilities into the larger programme of work and have the greatest evidence of using the new technologies supported to expand translationally focused research outputs.

For some types of facility, the time taken to fully realise their objectives will be considerably longer than for others. For example, it is not unreasonable to expect that national facilities may take longer to demonstrate wider uptake, e.g. UK Biobank serves as a good example (Figure 11 below), applications to utilise UK Biobank data gradually increase from 2012 when the data first became available to researchers, as potential users secure funding to utilise the dataset and the dataset steadily becomes enriched with further information and thereby increasing attractive to users.

Figure 11 – UK Biobank approved applications from year of researcher access



The very limited time available for developing complex programme plans and identifying collaborations necessitated post-award revision and redesign in some projects. This delayed programme development and increased the cost of growing the capabilities to full capacity. The positive consequences of effective collaborative networks already being in place is evident in the DPUK outputs.

Limited availability of expertise in certain high skill areas, such as bioinformaticians, PET physicists, big data platform developers, is not a new issue. MRC has made efforts to address limited PET and informatics expertise in the past. However, the limited availability of high level bioinformatic expertise is seen as highly detrimental to UK science. One interviewee highlighted that the limited availability of senior high calibre bioinformaticians may have diminished UK researcher's ability to take advantage of the big UK data sets being created. He suggested that currently more analysis using the large UK databases were being done by bioinformatic institutes in the USA[27]. More broadly, interviews indicated that support for computational biology expertise should be a key priority in future investment into innovative technologies.

This initiative is novel in its density of funding for specific technologies. In particular, the CRII has had a clear transformational effect on the UK research landscape in SCC technologies and MR imaging capabilities.

[27] From interview

Section 7: ANNEXES

ANNEX I: CRII funded capabilities

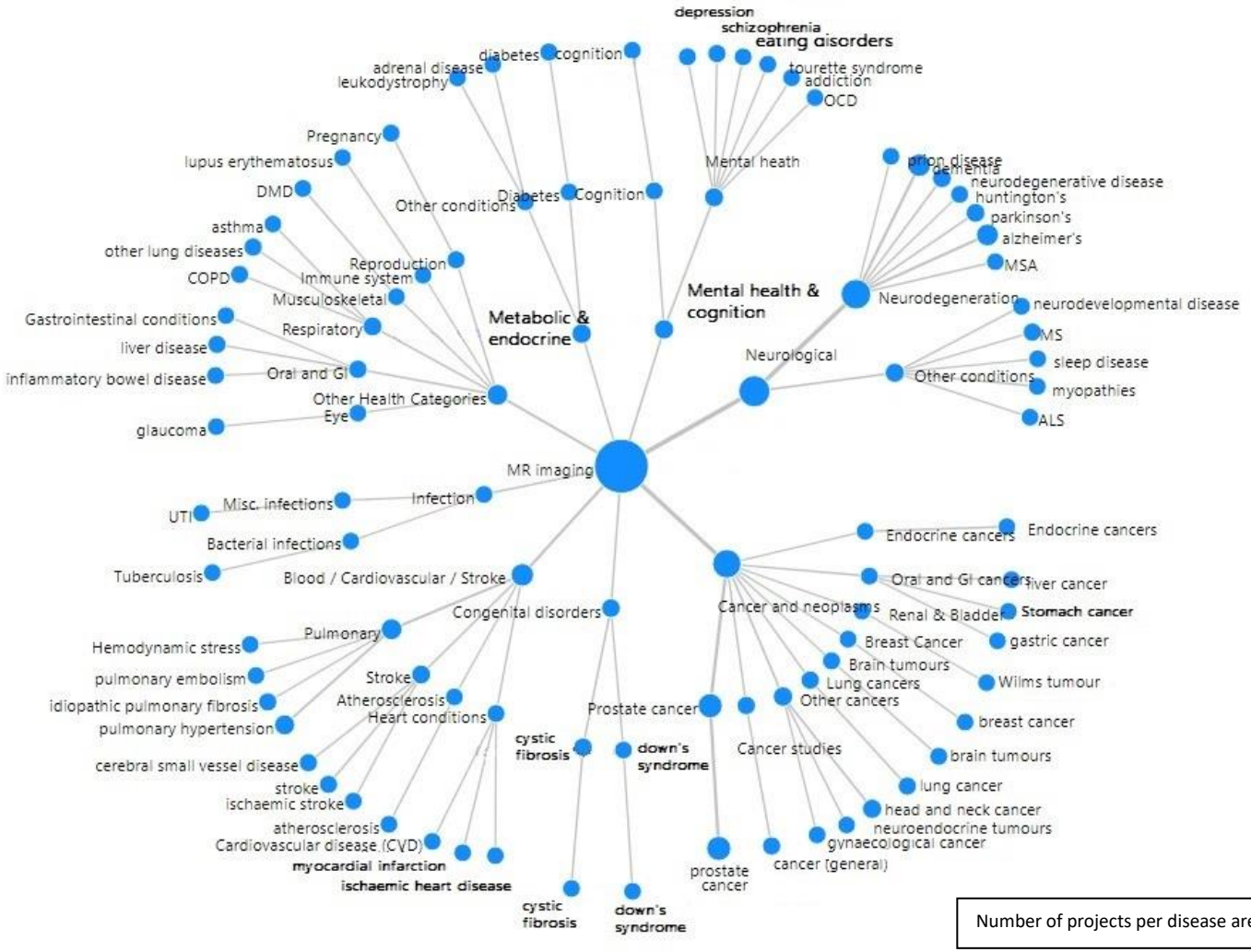
Science Area	Project title	Location	Award	Description	Equipment funded
14 Magnetic Resonance Imaging *9 awards contributing to the enhancement of 14 imaging capabilities*	Integrated DEmentiA research environment (IDEA)	Cambridge, Cardiff, Edinburgh, Imperial, Manchester, Newcastle	£22.2m	Imaging component of tripartite DPUK award distributed across six partners. Enhancement or establishment of UK PET/MRI capabilities co-localised with dementia cohort populations: five PET/MRI facilities fully or co-funded and multimodal imaging suites.	PET/MRI, 3T MRI, MEG, radiochemistry
	Innovative Technologies for Stratification and Experimental Medicine	Cambridge	£7.2m	The imaging component of Cambridge tripartite award expanding the capabilities of the Wolfson Brain Imaging Centre.	3T MRI / PET
	A new collaborative ultra-high field MRI facility for dementia and neuroscience research	Cambridge	£6.9m	Expanding the capabilities of the Wolfson Brain Imaging Centre.	7T MRI
	MICA: Ultra-High Field MRI: Advancing Clinical Neuroscientific Research in Experimental Medicine	Cardiff	£7.6m	Expanding the capabilities of the CUBRIC facility.	7T MRI
	A next-generation MRI brain imaging platform for dementia research: from microstructure to function	UCL	£1.2m	Expanding the capabilities of the Dementia Research Scanner Centre.	3T MRI
	Sir Peter Mansfield Imaging Centre	Nottingham	£7.7m	Expanding the capabilities of the Sir Peter Mansfield Imaging Centre.	3T MRI, hyperpolarisation, other imaging capability enhancement
	Development of MRI-guided radiation therapy	ICR	£10.1m	Establishing the MR Linac Unit in The Royal Marsden NHS Foundation Trust	MRI scanner and linear accelerator
	Expansion of state-of-the-art MR imaging infrastructure for pulmonary disease stratification: POLARIS	Sheffield	£7.4m	Expanding the POLARIS Centre	MRI, hyperpolarised xenon production facility
	A National Centre for Translational Hyperpolarised Magnetic Resonance	Leeds and York	£7.6m	Expanding the Advanced Imaging Centre	SABRE Hyperpolarisation MRI
	Centre for Image Guided Therapy - A Theranostic Approach to Patients with Cancer	UCL	£5.3m	Expanding the capabilities of UCL Centre for Advanced Biomedical Imaging	3T MRI, DNP hyperpolarisation

ANNEX 2: Diversity of health research areas addressed by the CRII-funded capabilities

Analysis of disease areas being investigated through the CRII funded capabilities showed 123 different specific diseases/conditions. Figure i and ii below depict the diversity of health conditions under study in MR imaging and Single Cell Characterisation capabilities.

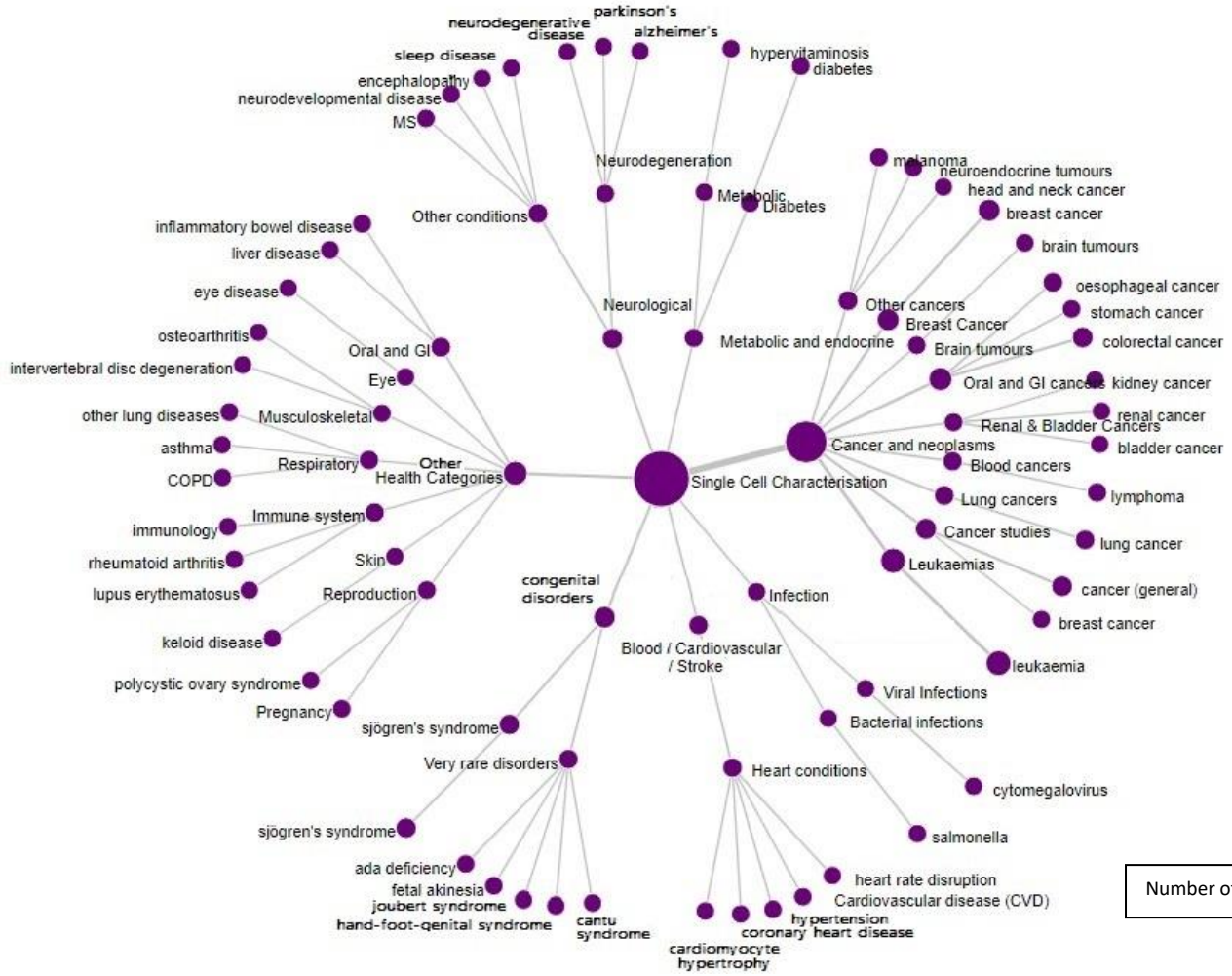
Original project proposals provided a list of the diseases of focus for the capabilities at the time of application. These were compared against the disease areas being investigated at the time of the evaluation, in 2019, as indicated in publications associated with the capability and ongoing projects described by award holders. We assessed publications attributed to each capability from both researchfish® submissions (796 unique publications) and publications referenced in the CRII survey (72 unique publications) as well as current projects using the capabilities as reported in the CRII survey (127 projects): 995 publications/projects in total. 552 publications (64% of total) and 112 projects had enough information to identify a specific disease focus. Methodological focused publications and projects were excluded from this analysis (175). MR imaging and Single Cell Characterisation capabilities produced the majority of attributed publications (73%). Of the seven MR imaging capability programmes for which we have data, four provided evidence of significant expansion of investigation into new disease areas. Of the seven SCC capability programmes which provided information, three provided evidence of significant expansion of investigation into new disease areas and two more showed early indications of expansion.

Annex 2 (figure i) – Distribution of health conditions under investigation using CRII MR imaging capabilities



Number of projects per disease area are reflected in size of bubble.

Annex 2 (figure ii) – Distribution of health conditions under investigation using the CRII Single Cell Characterisation capabilities



Number of projects per disease area are reflected in size of bubble.

ANNEX 3 - NIHR/NHS clinical links

Science Area	Research Organisation	Project Title	Clinical links
Multiple	DPUK	UK dementias platform	Many clinical links across the UK
MR Imaging	Cambridge	Innovative Technologies for Stratification and Experimental Medicine award (3T MRI / PET)	Funding support for staffing and other costs from Cambridge BRC; creating patient data linkage with the clinical research facilities
	Cambridge	A new collaborative ultra-high field MRI facility for dementia and neuroscience research	Funding support for staffing and other costs from Cambridge BRC
	Cardiff	MICA: Ultra-High Field MRI: Advancing Clinical Neuroscientific Research in Experimental Medicine	Clinical research studies in collaboration with CVUHB NHS
	UCL	A next-generation MRI brain imaging platform for dementia research: from microstructure to function	Funding support from NIHR UCLH BRC
	Nottingham	Sir Peter Mansfield Imaging Centre	Funding support from Queen's Medical Centre, research projects with Nottingham BRC
	ICR	Development of MRI-guided radiation therapy	Embedded in and supported by The Royal Marsden NHS foundation Trust
	Sheffield	Expansion of state-of-the-art MR imaging infrastructure for pulmonary disease stratification: POLARIS	Embedded in Northern General Hospital and Royal Hallamshire Hospital
	Leeds and York	A National Centre for Translational Hyperpolarised Magnetic Resonance	Integration with NHS and NIHR BRC facility
	UCL	Centre for Image Guided Therapy - A Theranostic Approach to Patients with Cancer	No evidence of direct links
Phenotyping suites	Liverpool	MICA: Applying innovative technologies to improve benefit-risk ratio of drugs: developing a national resource underpinned by the MRC Centre for Drug Safety Science	No evidence of direct links
	Manchester	Manchester Academic Health Science Centre Technology Hub: Clinical Proteomics Centre for Stratified Medicine	Funding support from NIHR BRC
	Cambridge	Innovative Technologies for Stratification and Experimental Medicine award (SMCL)	Funding for staffing from NIHR BRC

Science Area	Research Organisation	Project Title	Clinical links
Single Cell characterisation	Manchester	Advancing therapeutics by exploiting single cell functional analysis	Part embedded in NIHR Manchester Clinical Research Facilities
	Cambridge	Establishment of the Cambridge Single Cell Analysis Clinical Core Facility [SCACCF]	No evidence of direct links
	KCL	Single Cell-Level Functional Proteomics and Genomics exemplified in Cancer and Immunology	Funding support for staffing and other costs from Guys & St Thomas NHS TRUST BRC
	Oxford	The Oxford Single Cell Biology Consortium	WIMM and the director Professor Mead have strong clinical links there is no obvious BRC integration
	Birmingham	Integrating innovative technologies for genotyping and phenotyping in stratified medicine	Funding for staff and others by NIHR BRC
	UCL	Analysis of Cellular Heterogeneity for high resolution understanding of cancer	NIHR BRC funded additional equipment
	Newcastle	Newcastle University Single Cell Functional Genomics Unit (NUSCU)	No evidence of direct links
	Leeds	Developing a Facility for Sequential Isolation, Manipulation, Observation & Analysis of Single Cells	No evidence of direct links
Data platforms	QUML	UK Infrastructure for Large-scale Clinical Genomics Research	Integrated into DH&SC Genomics England
	Cambridge	Innovative Technologies for Stratification and Experimental Medicine award, (HPIH)	Supported by NIHR BRC
Other capabilities	QUB	A GMP cell therapy facility to test cell based therapies	Supported by NI HSC
	QMUL	Phenotyping and Experimental Medicine Centre for naturally occurring Gene Knock-Outs in Humans	Supported by NIHR BRC
	Exeter	Accelerated discovery of functional non-coding genomic variation using single molecule real-time (SMRT) sequencing	No evidence of direct links