Health Research Board

Review of clinical research infrastructure in Ireland

Final Report

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List of acronyms

CAMI	National Centre for Advanced Medical Imaging
CRCI	Clinical Research Coordination Ireland
CRDI	Clinical Research Development Ireland
CRF/C	Clinical Research Facility/Centre
CRI	clinical research infrastructure
CTI	Cancer Trials Ireland
CTN	Clinical Trial Network
DOH	Department of Health
FPFV	first patient first visit
GCLP	good clinical laboratory practice
GCP	good clinical practice
GMP	good manufacturing practice
GP	general practitioner
HIPE	Hospital Inpatient Enquiry
HPRA	Health Products Regulatory Authority
HRB	Health Research Board
HRCS	Health Research Classification System
HSE	Health Service Executive
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICORG	All-Ireland Cooperative Oncology Research Group
IMP	investigational medicinal product
IRNN	Irish Research Nurses Network
PI	principal investigator
PPI	public patient involvement
RCSI	Royal College of Surgeons in Ireland
TMRN	Trials Methodology Research Network
UCD	University College Dublin
UL	University of Limerick

Executive summary

The Health Research Board (HRB) is the lead agency supporting and funding health research in Ireland. The HRB seeks to improve people's health and wellbeing by funding cutting-edge research relevant to health and social gain.

Since 2007, the Irish government through the HRB has invested more than €160 million in the development of a national clinical research system with several components. These include investment in physical infrastructure on hospital sites for the purpose of conducting patient studies, support for disease-specific networks, funding for clinical trials and interventions, and access to appropriate services and supports in areas such as data management, methodology advice, and regulatory requirements.

Clinical research infrastructures are strategically valuable assets for Ireland. It is generally recognised that clinical research infrastructures enable the health research community to be at the forefront of high-quality clinical research activity, including clinical trials. This has a positive impact on the care and health outcomes of the population.

What is the report about?

In 2018, the HRB conducted a review of our investment in clinical research infrastructures.

The overall aim of the review was to generate appropriate evidence on current strengths, synergies, gaps, duplications, and needs in Ireland's clinical research infrastructures, either funded directly or peripherally by the HRB, in order to inform the HRB's strategic priorities for future investment in this area. Ultimately, the question being asked by the review was 'How and where should the HRB invest in clinical research infrastructures in the future?'

The review approach combined quantitative data supplemented by surveys, qualitative interviews (Amárach Research was commissioned by the HRB to conduct these interviews), and advice from an independent international panel of experts (International Advisory Committee).

When combined and validated by our International Advisory Committee, the two components of this review – quantitative data and qualitative interviews – along with the HRB's experience to date of managing and evaluating clinical research infrastructures offer important inputs into the HRB's considerations of, and approach to, our investment in clinical research infrastructures in the future.

The report presents the outcomes of the review and the HRB's conclusions including next steps.

What the review shows

This review provided valuable insights for the HRB into the current state of HRB-funded and associated clinical research infrastructures, how they are perceived by stakeholders and users, and how and where the HRB should invest in the future in this space.

The main quantitative findings of the review with respect to the current state of clinical research infrastructures in Ireland are as follows:

- The HRB invests approximately €8–10 million per year in clinical research infrastructures through various awards with end dates from 2021 to 2022.
- HRB-funded clinical research infrastructures in Ireland employ approximately 440 highly educated and skilled individuals with responsibility for managing the conduct of approximately 570 clinical trials/studies.
- Cancer is the main disease area for clinical research activity in HRB-funded and associated clinical research infrastructures, with 34% of current trial activity focusing on the area of cancer.
- Industry is the predominant funder of clinical trial activity in HRB-funded and associated clinical research infrastructures, with 58% of all active trials supported by industry and 27% supported by national funding agencies.

- International benchmarking shows that despite significant improvements in the clinical research infrastructure in Ireland in recent years, there is still a significant difference in our level of clinical trial activity (interventional studies) compared with our European counterparts. In 2018, there were approximately 370 clinical trials either open or recruiting in Ireland, compared with roughly 1,200 in Denmark, 700 in Norway, and 530 in Finland.
- Only Clinical Research Facilities/Centres (CRF/Cs) truly offer the full spectrum of supports for clinical trials, from study setup through to study closeout, on a regular basis, although some Clinical Trial Networks (CTNs) sought to offer services and supports that matched/duplicated those provided by the CRF/Cs.
- Clusters of specialised roles were noted across the HRB-funded and associated clinical research infrastructures (biostatistics, data management, pharmacovigilance, and quality and regulatory affairs); however, there was a noted lack of biostatistics expertise in the system, outside of the HRB-CRF Galway and the University College Dublin (UCD) CRC.
- In a survey of staff working in HRB-funded and associated clinical research infrastructures, 51% of respondents were on temporary contracts, with the majority funded by universities and/or grants of defined duration.

The main qualitative findings of the review with respect to clinical research infrastructures in Ireland and how they are perceived and used by the research community are as follows:

- Clinical research activity in Ireland is moving forward in a positive way; however improvements are being driven by individuals and institutions both of which operate in a degree of isolation.
- 'Skilled and passionate' clinicians are striving to improve patient outcomes, despite structural health research system barriers.
- The clinical research infrastructure, as depicted in the HRB clinical research infrastructure jigsaw (Figure 1.1), is perceived as a network of centres operating independently and not as part of a cohesive national research system. This means that:
    - Many stakeholders and infrastructure users perceive that there are barriers to accessing skills and services.
    - Duplication and resource inefficiencies exist within the clinical research system.
    - More collaboration and integration between all pieces of the HRB clinical research infrastructure jigsaw (see Figure 1.1) is required.
- Variability in funding across the different clinical research infrastructures is seen as something that is not sustainable in the long term and may, in fact, act as a barrier to collaboration/shared information.
- As research is not a fully integrated feature of the Irish healthcare system, significant barriers exist to the effective conduct of clinical research, such as an absence of defined career progression paths and funding uncertainty for personnel within the healthcare system.
- A number of barriers to the effective working of the clinical research infrastructure were identified:
    - Collaboration exists but is hampered by culture, competition, and different processes/standards, partly due to variability of funding and resources.
    - Duplication of skills and knowledge across the clinical research infrastructure is a key issue and represents an inefficient use of resources, particularly in the HRB CTNs.
    - A simplified infrastructure model is needed to improve information deficits and reduce resource inefficiencies.

- In terms of what is missing, some suggestions were made:
  - A clearly signposted central office/body is needed to facilitate the running of the infrastructures and improve communications and availability of information.
  - Centres of expertise (e.g. data management) would potentially help reduce duplication and ensure a more straightforward channel for accessing skills or resources.
- Views on the HRB's funding strategy focused on two core elements:
  - HRB funding emphasis should be on maintenance rather than expansion, so as not to lose the benefits of the investments already made.
  - The desire to have more certainty attached to funding, as the cyclical nature of funding (three- to five-year tranches) was believed to hamper long-term planning and development.
- Overall, there was a perceived lack of buy-in from the Health Service Executive (HSE) and Department of Health (DOH). In particular:
  - A cohesive national research system is needed to build upon the positives that currently exist within the clinical research infrastructure.
  - Funding is a central issue but it is accepted that increased funding on its own is not the solution to all problems within the clinical research infrastructure in Ireland.

Based on the qualitative and quantitative review findings and our own experience of managing and evaluating clinical research infrastructures, our key conclusions and suggestions for the future are as follows:

- Clinical research infrastructures are strategically valuable assets for Ireland.
- There is a need for better coordination of clinical research infrastructures in Ireland.
- The review considered the role of industry in supporting clinical research infrastructures into the future. Although the qualitative responses largely focused on clinical trial activity support, it was clear to the HRB that there is a need to consider the role of the enterprise agencies in providing support for the core clinical research infrastructure needed to maximise economic impact.
- Ireland needs to establish a Research and Development (R&D) Forum in health under the Sláintecare Implementation Strategy[1] in 2019 to address the current lack of coordination between different initiatives, research entities, and Government agencies in order to ensure that we achieve a more strategic national approach to investment in clinical research infrastructures in Ireland and the research they support.
- The health family i.e. the DOH, the HSE and the HRB and others need to invest more collectively in the clinical research infrastructure; for example, support for core posts in research nursing and data management would be a significant step towards the development of a more consistent and cohesive national system that values research and embeds clinical research into usual care.
- Overall, a cohesive national research system requires active engagement and collaboration within the health family in addition to the universities, enterprise agencies and industry.
- Principles for HRB's consideration in future investments in clinical research infrastructures include:
  - The need for a shared investment model.
  - HRB funding should only support the short- to medium-term development of infrastructure and is unsuitable for longer-term support. For this reason, any investment in infrastructure should be made with a clear exit strategy for the HRB, ideally with orderly transition towards full integration into the health system.

  - The HRB should consider appropriate opportunities to build capacity in specific areas where skill gaps were identified for health research.
  - Investments should be judged in an open and competitive process in order to select the best quality infrastructure.

- As a next step the HRB will use these principles to prepare an overall funding strategy and action plan for investment in this area, whilst working with members of the health family (and others) to develop a call for Clinical Research Facilities/Centres.

1 Background, aim, and objectives of the review

1.1 Background to the review

The Health Research Board (HRB) is the lead agency supporting and funding health research in Ireland. The HRB seeks to improve people's health and wellbeing by funding cutting-edge research relevant to health and social gain. To that end, the HRB manages a variety of funding schemes that support high-quality health research, build capacity for health research by supporting researchers' career development, and facilitate the conduct of world-class health research by providing vital research infrastructure and national networks of researchers.

The value of the HRB's current funding commitment is in the region of €180 million. As this is public money, there is an onus on the HRB to account to government and other stakeholders, including the public, for the funds it allocates, and the return accrued on this investment. There is also the need to inform the HRB's funding strategy with relevant review evidence. Within the HRB's Evaluation Strategy 2016–2020,[2] there is a commitment to undertake a review of its investment in clinical research infrastructures.

Since 2007, the Irish government, through the HRB, has invested in the development of a national clinical research system with several components (see Figure 1.1). These include investment in physical infrastructure at hospital sites in order to conduct patient studies, support for disease-specific networks, funding for trials and interventions, and the provision of access to appropriate services in areas such as data management, methodology advice, and regulatory requirements.

The overall aim of the HRB's investment in this space is to establish an environment conducive to clinical research and to develop Ireland as a high-quality location in which to conduct clinical research and trials.

The importance of clinical research to the boarder national social and economic agenda has been acknowledged in a number of Government strategies. Important DOH initiatives that have helped to underpin this environment include;

- Publication of the Action Plan for Health Research[3] in 2009 restating the importance of health research and finding the optimum opportunities for research and development between the academic research system and the healthcare system.
- Shaping the new direction of the HRB strategy 2016-2020 and the resultant organisational change to ensure it had a greater focus on research that benefits patients and the delivery and organisation of the healthcare system.
- Working with the State Claims Agency and the HRB to negotiate indemnity for all of those involved in clinical trials in hospitals/CRFs.
- Working to get research included in the text of Consultant's contracts.
- Establishing the DOH R&D Division in 2015 as part of its' commitment to take a greater leadership role in R&D and to ensure evidence-informed decision making in healthcare
    - One of the first actions of the new R&D Division was to secure sanction for a R&D Lead in the HSE and to explicitly refer to priorities for R&D in subsequent HSE National Service Plans.
- Securing a decision to join the European Clinical Research Infrastructure Network (ECRIN) in 2018.
- Ensuring that R&D is noted explicitly as an enabler of the goals set out in the Sláintecare Implementation Strategy with a specific action to establish a R&D Forum during 2019.

As the HRB has embarked on additional phases of funding for key clinical research infrastructures, with an emphasis on sustained integration into the healthcare system, it was considered timely to reflect on our investments to date to ensure that the need for future development and/or the strengthening of existing infrastructure and supports was identified, documented, and quantified.

In 2018, the HRB conducted a review of our own investment in clinical research infrastructures in order to inform our strategic priorities for future investment in this area. In addition, it was anticipated that the review would form valuable input into the next HRB strategy phase (2021–2025).

Figure 1.1: HRB clinical research infrastructure

1.2 Scope

The review focused on the HRB's investment in clinical research infrastructure, thus only HRB-funded and associated infrastructures, as depicted in Figure 1.1 (including the Irish Research Nurses Network (IRNN) and the Health Research Institute Clinical Research Support Unit at University Hospital Limerick), were examined.

It was not possible to examine all clinical research infrastructures in Ireland in this review, and the omission of infrastructures in no way reflects their contribution to the clinical research system in Ireland.

Additional information concerning the clinical research infrastructures reviewed is outlined in Chapter 3, Section 3.3.3.

1.3 Aim and objectives of review

The overall aim of the review was to generate appropriate evidence on current strengths, synergies, gaps, duplications, and needs in Ireland's clinical research infrastructure, funded either directly or peripherally by the HRB, in order to inform the HRB's strategic priorities for future investment in this area.

In this context, a review of the HRB-funded and associated clinical research infrastructures in Ireland included:

- Assessing the current funding status, level of integration with the healthcare system, activities, services, resources, capacity, and capabilities of existing clinical research infrastructures in Ireland in order to identify where strengths, synergies, gaps, and duplications exist in the system.
- Exploring the funding requirements and appropriate levels of integration of clinical research infrastructures within the healthcare system for future sustainability and growth.

Ultimately, the question being asked by this review was: 'How and where should the HRB invest in clinical research infrastructures in the future?'.

2 Overview of approach and methodology

This review of the HRB's investment in clinical research infrastructures used a mixed-model research methodology.

The methodologies used were as follows:

- Quantitative review (including surveys and a census of clinical trial activity)
- Qualitative in-depth interviews (Amárach Research was commissioned by the HRB to conduct these), and
- Advice from an independent international panel of experts (International Advisory Committee).

2.1 Quantitative review of clinical research infrastructures in Ireland

The HRB conducted a quantitative analysis of the current funding status, level of integration with the healthcare system, activities, services, resources, capacity, and capabilities of existing clinical research infrastructures in Ireland. The review used data gathered through existing HRB databases, supplemented by detailed surveys that included HRB and other clinical research infrastructures identified for the purpose of this review.

Two customised surveys were developed on SmartSurvey: an infrastructure survey and a staff survey. An online link to the surveys was distributed to all the clinical research infrastructures involved, and the programme manager or equivalent person within each clinical research infrastructure distributed the staff survey link to their staff members. The infrastructure manager completed the infrastructure survey (see Appendices A and B for the infrastructure and staff survey templates).

In addition to the surveys, a census of clinical trial activity was conducted to determine the level of activity across clinical research infrastructures, including the context and funding sources of activity, to present a national census of clinical trial activity in Ireland as of 31 May 2018 (see Appendix C for the clinical trial activity template).

The key outputs of the quantitative review are outlined in Chapters 3 and 4 of this report.

2.2 Qualitative in-depth interviews

As part of the review of clinical research infrastructure in Ireland, Amárach Research was commissioned by the HRB to conduct the qualitative element of this review project.

Amárach Research conducted a series of semi-structured qualitative interviews between July and September 2018 (see Appendices D and E for stakeholder and service user discussion guides). The HRB provided lists of those who were willing to share their contact details.

In total, 28 interviews were conducted as detailed below:

- Twenty individuals were linked with clinical research infrastructures, including CRFs, Clinical Research Centres (CRCs), networks, universities, and Hospital Groups, and
- Eight individuals were infrastructure users – either current users, potential users, or those with industry perspectives.

Written consent was obtained from all interviewees, and the interviews were recorded. Interviews were then transcribed, and all transcriptions were analysed using NVivo 12 software. Qualitative analysis was conducted using thematic analysis (Braun and Clarke, 2006[4]).

The qualitative findings presented in this report are the perceptions of those interviewed and must be read as such. They are not meant to represent a factual representation of the clinical research infrastructure in Ireland but present the opinions of infrastructure users and those linked with the clinical research infrastructures.

The qualitative findings are outlined in Chapters 5, 6, and 7 of this report.

2.3 International Advisory Committee

The HRB worked with an International Advisory Committee (see Appendix F for membership details) during the review in order to ensure that it was achieving the objectives set out for the review. The objectives were to inform priorities and/or opportunities for future investment in clinical research infrastructures, and in doing so to address the needs of Ireland's clinical research system.

The role of the International Advisory Committee was to provide advice and guidance to the HRB at key stages during the review:

- An initial meeting was convened at the HRB offices in June 2018 to review the survey instruments and discussion guides in order to ensure that they were suited to delivering the aims and objectives of the review.
- A final meeting was held in November 2018 to review the preliminary results from both the quantitative and qualitative reviews and to seek advice on future investment in clinical research infrastructures.

When combined and validated by our International Advisory Committee, the two components of this review – quantitative data and qualitative interviews - along with the HRB's experience to date of managing and evaluating clinical research infrastructures offer important inputs into the HRB's considerations of, and approach to, our investment in clinical research infrastructures in the future.

This report summarises the findings from the review and the HRB's conclusions including next steps.

3 Mapping of clinical research infrastructure and performance in Ireland

3.1 Introduction

This chapter outlines the current state of HRB-funded and associated clinical research infrastructures in Ireland and describes the outcome of an infrastructure survey and census of clinical trial activity from the clinical research infrastructures reviewed.

The HRB-funded clinical research infrastructures were the priority for the review, with the inclusion of some aligned infrastructures. It was not possible to examine all clinical research infrastructures in Ireland in this review, and the omission of infrastructures in no way reflects their contribution to the clinical research system in Ireland.

The purpose of the infrastructure survey and the census of clinical trial activity was to assess the capabilities, activities, services, and integration with the healthcare system in existing HRB-funded and associated clinical research infrastructures in Ireland in order to identify where strengths, synergies, gaps, and duplications exist in the system.

3.2 Key findings

The key findings from the review of the current state of clinical research infrastructures and their performance in Ireland are as follows:

- Clinical research infrastructures in Ireland are predominantly based in a hospital setting supported by their partner universities.
- Only three of the current seven Clinical Research Facilities/Centres (CRF/Cs) are funded directly by the HRB.
- Only CRF/Cs truly offer the full spectrum of supports, from study setup through to study closeout, on a regular basis.
    - Some CTNs sought to offer services and supports that matched/duplicated those provided by the CRF/Cs.
- There is a lack of capability for Phase I clinical trials in Ireland.
- There were 570 ongoing studies across 11 clinical research infrastructures in Ireland as of 31 May 2018:
    - Cancer is the main disease area for clinical trials and studies.
    - The majority of the ongoing trials are Phase II and Phase III studies.
    - Clinical trial funding is sourced predominantly from industry, followed by national funding agencies.

3.3 Mapping of clinical research infrastructure in Ireland

3.3.1 What are clinical research infrastructures?

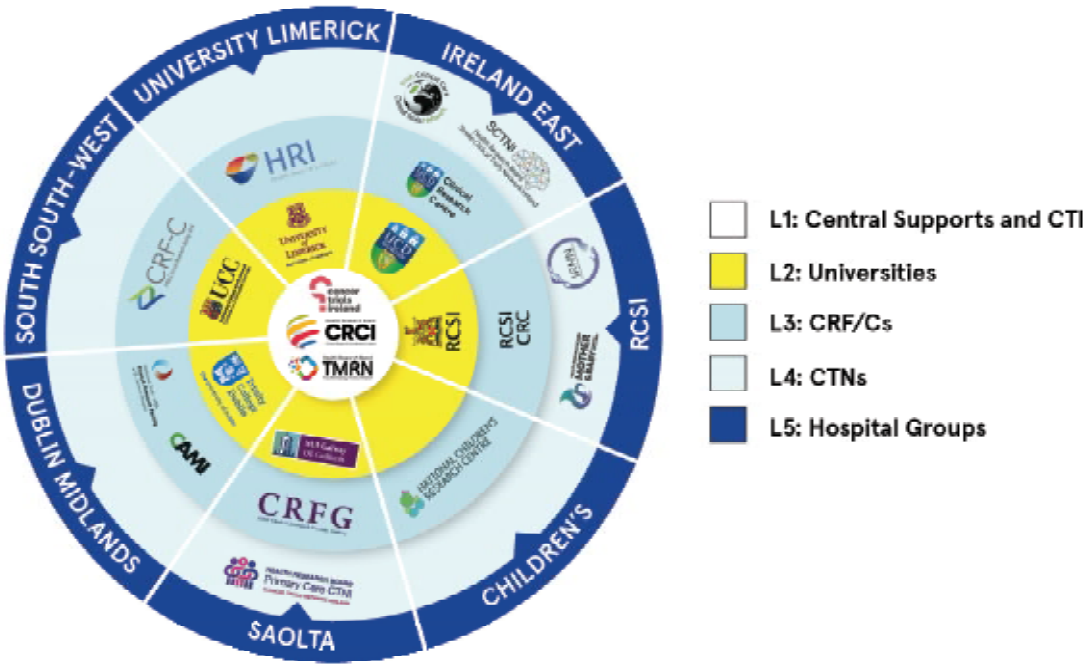
In alignment with the *HRB Strategy 2016–2020*,[5] clinical research infrastructures are defined as the physical facilities, equipment, coordination, research supports, and networks used by the research community to conduct clinical research nationally. They provide a single point of access to resources, knowledge, and skills, and are a key part of the national research landscape.

3.3.2 Where are clinical research infrastructures in Ireland?

Clinical research infrastructures in Ireland come in many forms and sizes and are established either in a university or a hospital setting. With the exception of the HRB Primary Care Clinical Trials Network

Ireland, no clinical research infrastructure is located or focused within the community setting (see Figure 3.1).

Figure 3.1: Mapping of clinical research infrastructures with their associated host institution and/or academic partner and Hospital Group



Note: *Cancer Trials Ireland (CTI) is included in this image alongside central supports since, despite being referenced as a CTN as part of the HRB clinical research infrastructure (Figure 1.1), Cancer Trials Ireland has strong similarities to a distributed CRF specialising in cancer. One of the unique features of Cancer Trials Ireland is that it can act as a sponsor for cancer clinical trials*.

Figure 3.2: Mapping of clinical research infrastructures geographically

Figure 3.2 shows that the majority of clinical research infrastructures are based in Dublin, although they work on a national basis.

3.3.3 Which clinical research infrastructures were evaluated?

The clinical research infrastructures assessed during this review, as depicted in Figure 1.1, include the following:

3.3.3.1 Clinical Research Facilities/Centres

Clinical Research Facilities/Centres (CRF/Cs), which are located on the sites of hospitals, provide the infrastructure, physical space and facilities, experienced research and specialist support staff, and the necessary quality and oversight programmes that are critical for the successful conduct of world-class clinical research. They are hosted with the support of each hospital's academic partner.

There are seven CRF/Cs on the island of Ireland, at different stages of development and with varying funding models in operation. Three of these are funded directly by the HRB through a four-year award, while the other four CRCs receive indirect funding from the HRB through HRB CRCI to support feasibility requests.

The three HRB-funded CRF/Cs are located at:

1. Wellcome Trust – HRB-CRF at St. James's Hospital in Dublin (hosted by Trinity College Dublin)
2. HRB-CRF Cork at the Mercy University Hospital (hosted by University College Cork), and
3. HRB-CRF Galway at University Hospital Galway (hosted by the National University of Ireland Galway).

The other CRF/Cs in Ireland include:

4. UCD CRCs at Mater Misericordiae University Hospital and St. Vincent's University Hospital (hosted by UCD)
5. Royal College of Surgeons in Ireland (RCSI) CRC at Beaumont Hospital (hosted by Royal College of Surgeons in Ireland)

6. National Children's Research Centre at Our Lady's Children's Hospital, Crumlin, and
7. The Health Research Institute Clinical Research Support Unit at University Hospital Limerick.

3.3.3.2 HRB Clinical Research Coordination Ireland

HRB Clinical Research Coordination Ireland (HRB CRCI) is a national, integrated network of all the CRF/Cs in Ireland to enable and support multicentre clinical trials. The overall aim of HRB CRCI is to grow clinical research in Ireland by offering a seamless, integrated, and coherent system of support for multicentre clinical research, undertaken by individual investigators and/or industry in Ireland.

HRB CRCI provides a central point of contact for industry and academics who want to conduct multicentre trials. It offers support for the study feasibility process, which helps to identify suitable sites, provide information on potential recruitment, and advises on regulatory and ethical requirements.

3.3.3.3 HRB Trials Methodology Research Network

HRB Trials Methodology Research Network (HRB-TMRN) was established in 2014 to develop national capacity in trial methodology and reporting in Ireland by providing the clinical trials community with the appropriate support, training, and education. HRB-TMRN is based in the National University of Ireland Galway but includes partners from across the island of Ireland, including Northern Ireland.

3.3.3.4 HRB Clinical Trial Networks (CTNs) including Cancer Trials Ireland

HRB CTNs bring together clinicians, health professionals, health researchers, and clinical research staff to develop a research strategy in a specific disease or health area, and provide the critical mass needed to conduct multicentre clinical trials.

The HRB currently funds five CTNs in the following areas:

1. Cancer (Cancer Trials Ireland, formerly ICORG)
2. Stroke (HRB Stroke Clinical Trials Network Ireland)
3. Mother and Baby (HRB Mother and Baby Clinical Trials Network Ireland)
4. Critical care (HRB Irish Critical Care Clinical Trials Network), and
5. Primary care (HRB Primary Care Clinical Trials Network Ireland).

Cancer Trials Ireland is the most established network, with a HRB investment of more than €60 million since 2002 to build and enhance the capacity across 11 hospital sites in Ireland[6] to conduct high-quality clinical trials of cancer therapies on an all-island basis. Cancer Trials Ireland is significantly larger than the other four HRB CTNs and is operated on a separate funding model.

The other four disease-specific HRB CTNs were established in 2015 at a cost of €2.5 million per award for a period of five years. The funding to each HRB CTN supports both network activities (e.g. developing a comprehensive research strategy and programme, supporting the writing of grant applications, and engaging with potential academic and industry partners) and conducting trial activities (at least one definitive interventional multicentre trial).

3.3.3.5 Irish Research Nurses Network

The Irish Research Nurses Network (IRNN) was established in 2008 to support the educational and professional needs of clinical research nurses in Ireland. Since 2017, the IRNN has received funding from the HRB for the specific purpose of supporting IRNN objectives and activities. It is an important vehicle for professional development and recognition of research nurses in the context of growing clinical research activity in Ireland.

3.3.3.6 National Centre for Advanced Medical Imaging

The National Centre for Advanced Medical Imaging (CAMI) was established in 2008 to develop research using magnetic resonance imaging (MRI) in Ireland. The mission of CAMI is to act as a

unified research imaging centre spanning basic and clinical studies. CAMI provides MRI infrastructure for patient-focused research studies and clinical trials aimed at improving understanding and diagnosis of disease.

3.4 Services and supports provided by clinical research infrastructure

An online infrastructure survey (see Appendix A for more details) was sent to the HRB-funded and associated clinical research infrastructures (16 in total) and asked about the facilities they have and the clinical research supports and services they provide to the clinical research community. Of the 16 clinical research infrastructures that were sent the survey, 14 responded, although not all respondents replied consistently.

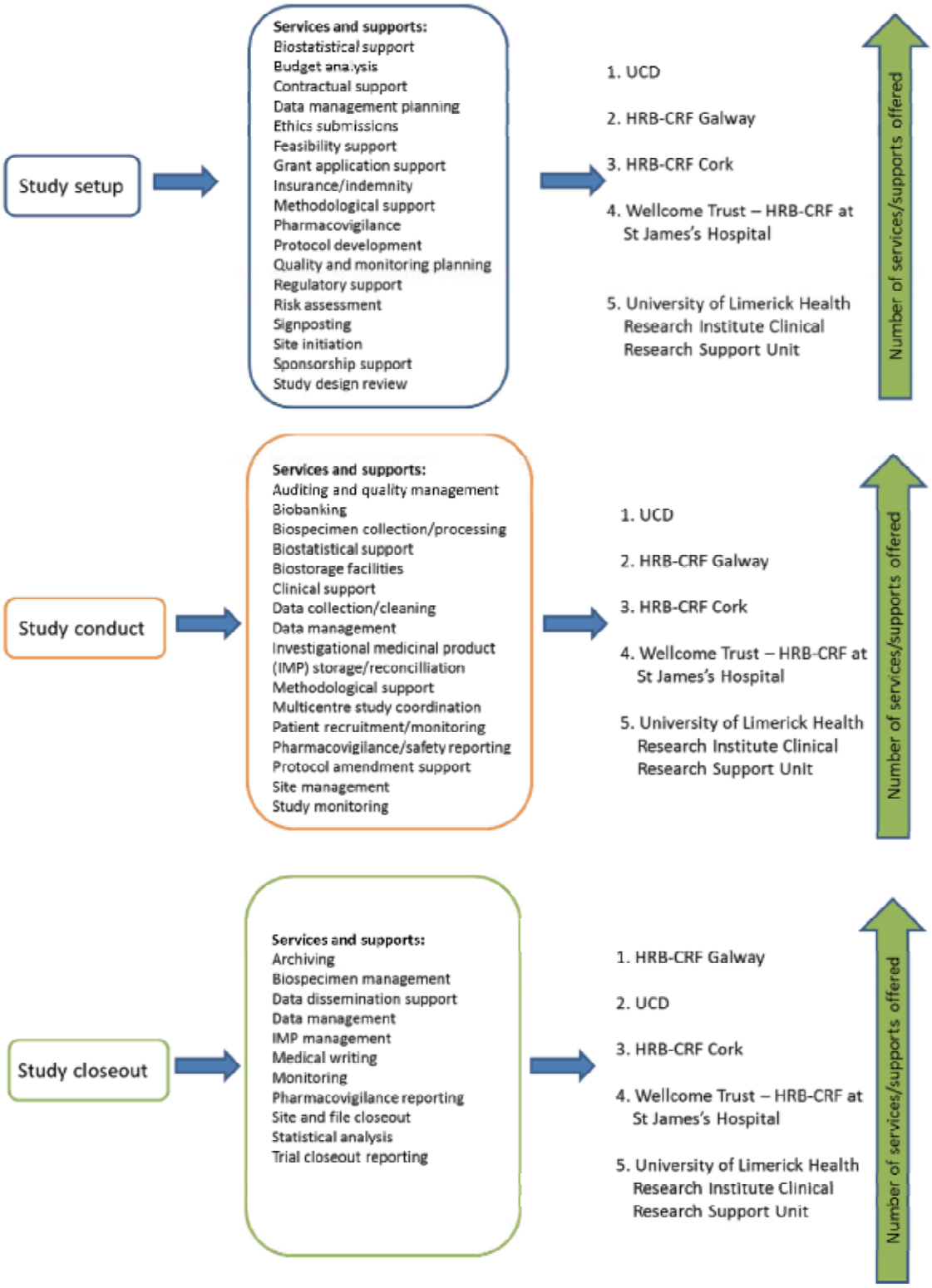
From the information reported by respondents, there was a clear distinction in the services and supports offered for trial delivery between the main CRF/Cs and the smaller CTNs. The majority of CTNs reported that they provided services and supports at all stages of clinical trial delivery from study setup through study conduct and to study closeout. However, only the CRF/Cs provided weekly (reflecting greater frequency) services and supports in all three phases of trial conduct (setup, conduct, and closeout).

Across the CRF/Cs there were some differences in the number of services and supports they offered on a weekly basis, largely reflecting the differing scale and perhaps capacity of the clinical research infrastructures. These are summarised in Figure 3.3 showing the ranked order of facilities providing weekly infrastructure services and supports for study setup, study conduct and study closeout.

The clinical research infrastructures were asked whether they outsourced any of their study supports and services by using expertise from outside their own infrastructure. The most common supports and services outsourced included:

- Biostatistical and data management
- Contractual
- Insurance/indemnity
- Methodological, and
- Pharmacovigilance supports and services.

Figure 3.3: Top five facilities providing weekly infrastructure services and supports



3.5 Census of national clinical research infrastructure trial activity

3.5.1 Introduction to clinical research

For the purpose of this review, we used the HRB definition of clinical research – that is, "research with the goal of improving the diagnosis and treatment of disease and injury and of improving the health and quality of life of individuals as they pass through normal life stages. Clinical research is conducted on or for the treatment of patients".[7]

Clinical trials are a form of clinical research designed to evaluate and test new or existing interventions and their effects on health outcomes. Interventions include but are not restricted to drugs; cells and other biological products; surgical procedures; radiological procedures; devices; behavioural treatments; process-of-care changes; and preventive care.

Clinical trials conducted to support licensing or regulatory approval of therapies or diagnostic methods are referred to as regulated studies.[8] Studies that do not fall under specific legislative frameworks are referred to as non-regulated studies.[9]

Clinical trials can be conducted by commercial entities and/or independent clinical investigators and researchers. Commercial studies, including pharmaceutical companies and/or contract research organisations, typically have a financial interest in the intervention being tested, and these trials are often conducted to support licensing or regulatory approval of the intervention.

Investigator-initiated or investigator-led trials are often conducted in order to test therapies and generate clinical evidence to inform health-related decisions that improve the safety and quality of healthcare. The HRB is the leading funder in Ireland for such studies, with a dedicated funding stream, known as the Definitive Interventions and Feasibility Awards,[10] to support such activity.

A well-designed clinical trial is the gold standard for proving that a treatment or medical approach works. Clinical trials differ in terms of why they are conducted and what type of evidence they are designed to generate. Clinical trials are often conducted in four phases (see Table 3.1). The trials have a different purpose at each phase and help researchers answer different questions.

Table 3.1: Clinical trial purpose at each phase

Phase	Purpose
Phase I	The purpose is to test an intervention in a small group of people for the first time. Researchers evaluate the intervention's safety, determine a safe dosage range, and identify side-effects. There are typically fewer than 100 study participants.
Phase II	The purpose is to evaluate whether an intervention does what it is intended to do. Researchers continue monitoring for side-effects and gather information that goes into designing a larger Phase III trial. The intervention is given to a larger group of people to see if it is effective and to further evaluate its safety.
Phase III	Researchers confirm its effectiveness, monitor side-effects, compare it to commonly used treatments, and collect information that will allow the intervention to be used safely. The intervention is given to large groups of people, i.e. a broader and more representative patient population.
Phase IV	The purpose is to monitor the long-term effects of interventions on the general population after they have been introduced to practice and/or approved by the regulatory body. These studies provide additional information, including intervention risks, benefits, and best uses.

3.5.2 Clinical trial activity across the clinical research infrastructures

In order to present a national census of clinical trial activity in Ireland as of 31 May 2018, a census of clinical trial activity was carried out during this review to determine the level of clinical trial activity across clinical research infrastructures, including the context and funding sources of activity.

Data on clinical trial activity were collected, standardised, and consolidated from 11 clinical research infrastructures in Ireland (see Appendix B for the clinical trial activity template), namely:

1. HRB Mother and Baby Clinical Trials Network Ireland
2. HRB Stroke Clinical Trials Network Ireland
3. HRB Irish Critical Care Clinical Trials Network Ireland
4. HRB Primary Care Clinical Trials Network Ireland
5. Cancer Trials Ireland
6. HRB-CRF Cork
7. Wellcome Trust – HRB-CRF at St. James's Hospital
8. HRB-CRF Galway
9. UCD CRC
10. Centre for Advanced Medical Imaging, and
11. Health Research Institute Clinical Research Support Unit at University Hospital Limerick.

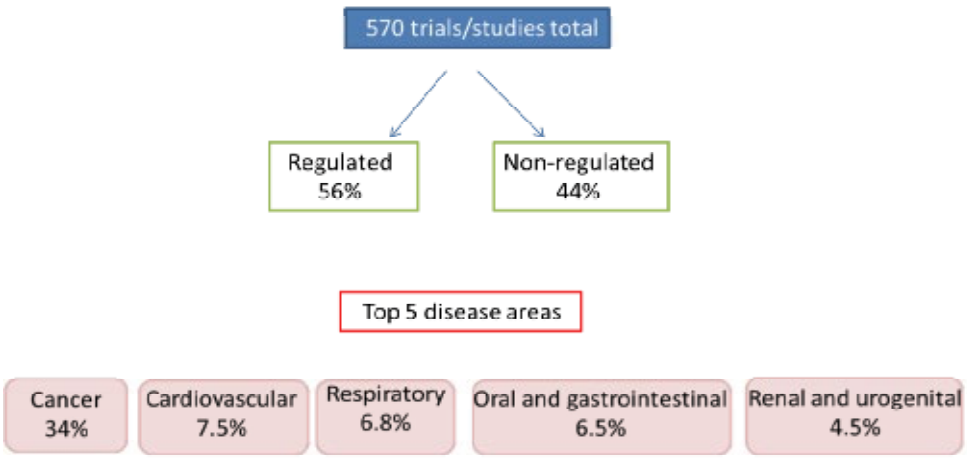
Note: *Only 11 of the 13 clinical research infrastructures (responsible for conducting clinical trials) responded and not all clinical research infrastructures replied consistently with their information. Clinical research infrastructures reported on all clinical research studies rather than on clinical trials, so the information reported relates to clinical research studies.*

Clinical research infrastructures did not provide data on whether patient recruitment was on target, or on the numbers of days to 'first patient first visit' (FPFV). As a result, no analysis is included on these indicators for trial activity performance or quality across clinical research infrastructures in Ireland.

Figure 3.4 shows the breakdown of clinical research activity (570 trials/studies) across 11 clinical research infrastructures in Ireland as of 31 May 2018. Of these, 56% were regulated studies and 44% were non-regulated studies.

The top five disease areas being researched are cancer, cardiovascular, respiratory, oral and gastrointestinal, and renal and urogenital. Cancer is the main disease area, with 34% of all reported trials/studies focusing on this disease area.

Figure 3.4: Breakdown of clinical research activity across 11 clinical research infrastructures in Ireland as of 31 May 2018



In order to benchmark Ireland's activity against other European countries, data were extracted from ClinicalTrials.gov (as of 31 May 2018) for European countries with similar populations to Ireland. In 2018, there were approximately 377 clinical trials either open or recruiting in Ireland, compared with

1,191 in Denmark, 710 in Norway, and 528 in Finland. Table 3.2 demonstrates that despite significant investment in clinical research infrastructure in recent years, and Ireland's improved clinical trial activity, there is still a significant difference in our level of clinical trial activity (interventional studies) compared with our European counterparts.

Table 3.2: Clinical trials (interventional studies) across European countries as of 31 May 2018

European country	Number of ongoing interventional studies
Denmark	1191
Norway	710
Finland	528
Ireland	**377**
Croatia	182

3.5.3 Distribution of clinical research phase/type

As mentioned in Section 2.1, the census requested information on clinical trial activity across the clinical research infrastructures. However, a number of clinical research infrastructures also reported on observational studies. Where information was provided on clinical trials, the trial phase and status were analysed, and results are shown in Figure 3.5 and Figure 3.6.

Figure 3.5: Number of trials in a particular phase and type of study

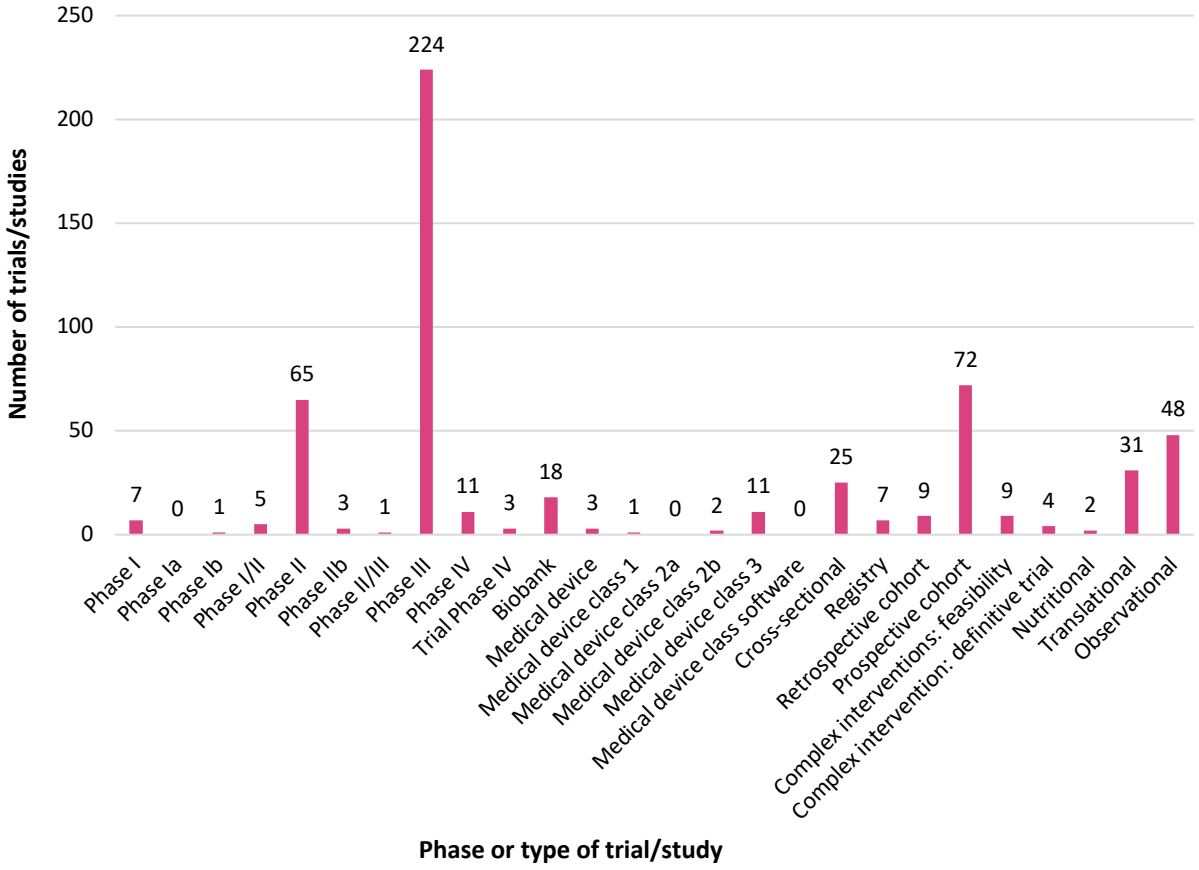


Figure 3.5 highlights that more than 40% of ongoing studies are classified as Phase III studies, which assess the effectiveness of an intervention in a broader and more representative patient population. The low number of Phase I trials reflects the lack of capability for Phase I trials within the clinical

research infrastructures, as only one clinical research infrastructure reported having the capability to conduct Phase I studies in Ireland. There are 154 (27%) ongoing international multicentre trials.

3.5.4 Distribution of clinical research study status

Figure 3.6 highlights that the majority of trials/studies reported are either in the setup or recruiting stage. As no direct questions were asked concerning the status of these trials/studies, we can only assume that the status reported represents the natural order of trial progress as opposed to depicting issues with the progression of trials/studies. However, given the number of ongoing trials/studies reported, it appears unusual that such a large portion are in setup and recruiting compared with in follow-up, analysis, and/or reporting. This could potentially highlight factors impacting the progression of trial activity at the early stages of research, such as issues or delays with contracts, insurance/indemnity, ethical approvals, and/or factors associated with the implementation of General Data Protection Regulation (GDPR).

Figure 3.6: Status of current trials/studies

3.5.5 Distribution of funding source for clinical research activity

The census of clinical trial activity asked for the funding source for each clinical study. The information in Figure 3.7 includes both clinical trials and clinical research studies in the analysis. As funding source data were not reported for every study, the results in Figure 3.7 represent only 335 trials/studies (59% of total studies reported).

Figure 3.7: Distribution of funding source of 335 trials/studies reported across clinical research infrastructures

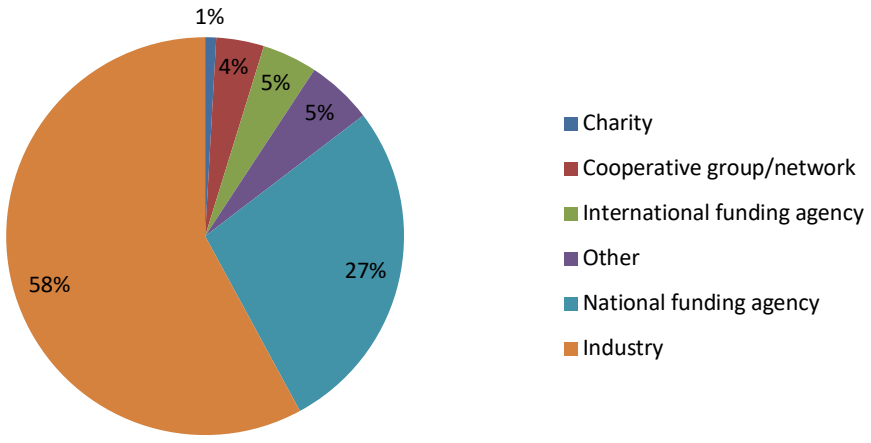


Figure 3.7 demonstrates that 58% of funding for the clinical research activity reported was supported by industry and 27% by national funding agencies. International funding agencies, cooperative groups, and charities represent smaller alternative funding sources of clinical research activity support.

4 Mapping of resources and competencies in clinical research infrastructure personnel

4.1 Introduction

This chapter describes the outcome of a staff survey of personnel working in, or affiliated with, HRB-funded and associated clinical research infrastructures in Ireland. The purpose of the staff survey was to obtain a wide and clear perspective of the clinical research workforce engaged in the conduct and support of clinical research within the clinical research infrastructures. It includes information about the position types, employment contracts, qualifications and expertise, and perspectives around career progression in their roles. The survey instrument used to collect these data is described in Appendix C

4.2 Key findings

The key findings from the review of staffing in the HRB-funded and associated clinical research infrastructure system in Ireland are as follows:

- Approximately 440 personnel are working in clinical research across the HRB-funded clinical research infrastructures in Ireland.
- Eighty per cent of all clinical research infrastructure staff reported are female, and 20% are male.
- The top clinical research position of academic study/trial coordinator/manager was often filled by nurses.
- Cancer Trials Ireland and CRF/Cs are the main employers of clinical research infrastructure personnel.
- Clusters of specialised roles were noted across the clinical research infrastructures, as well as a lack of biostatistics expertise in most clinical research infrastructures, with the exception of HRB-CRF Galway and the UCD CRC.
- The majority of respondents had a primary degree in nursing with further training to master's level.
- Fifty-one per cent of respondents were on temporary contracts, with the majority funded by universities and/or grants of defined duration.
- Career progression opportunities were few, with 52% of respondents stating that they had no career progression opportunities.

4.3 Distribution of personnel across clinical research infrastructures in Ireland

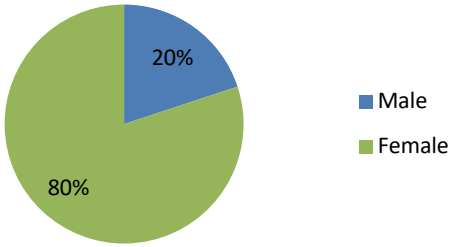
A total of 278 personnel completed the staff survey and, after the removal of non-consenting responses and responses from infrastructures outside the scope of this review, 266 responses were available for further analysis.

With 278 personnel responding across 16 clinical research infrastructures, and including data from existing HRB databases, we found that approximately 440 personnel are engaged in the conduct and support of clinical research within the clinical research infrastructures in Ireland.

4.3.1 Gender breakdown

Figure 4.1 shows that the gender of all respondents to the staff survey across the clinical research infrastructures was 80% female and 20% male. However, the breakdown of gender by academic and clinical research position highlighted that those in senior positions such as professor, associate professor, and medical consultant were predominantly male.

Figure 4.1: Gender breakdown of all respondents across clinical research infrastructures



4.3.2 Top clinical research positions across clinical research infrastructures

Figure 4.2: Research positions held by the 266 respondents to the staff survey

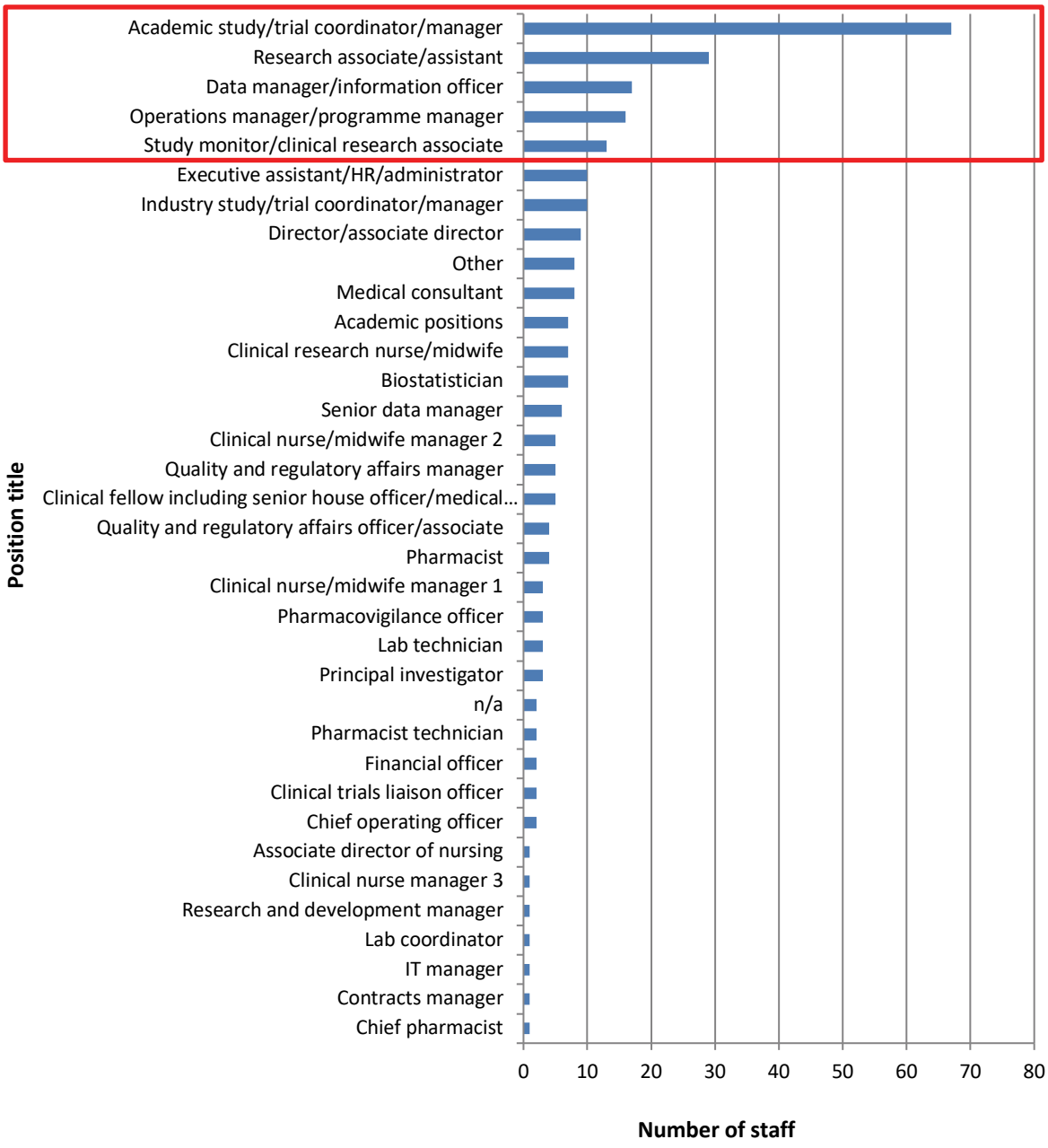


Figure 4.2 shows that, of the 266 respondents, the top five clinical research positions reported across all clinical research infrastructures were:

1. Academic study/trial coordinator/manager
2. Research associate/assistant
3. Data manager/information officer
4. Operations manager/programme manager, and
5. Study monitor/clinical research associate.

Figure 4.3 shows the distribution of the top three reported positions across the clinical research infrastructures as a percentage of the total number of staff in each clinical research infrastructure, namely the number of academic study/trial coordinators/managers (A), research associates/assistants (B), and data managers/information officers (C) per clinical research infrastructure. Data are not shown for operations managers/programme managers or study monitors/clinical research associates across each clinical research infrastructure, as the numbers were too small. From Figure 4.3, it can be seen that Cancer Trials Ireland is one of the main employers for all three top positions, followed by the CRF/Cs.

Figure 4.3 (A): Academic study/trial coordinators/managers across clinical research infrastructure (%)

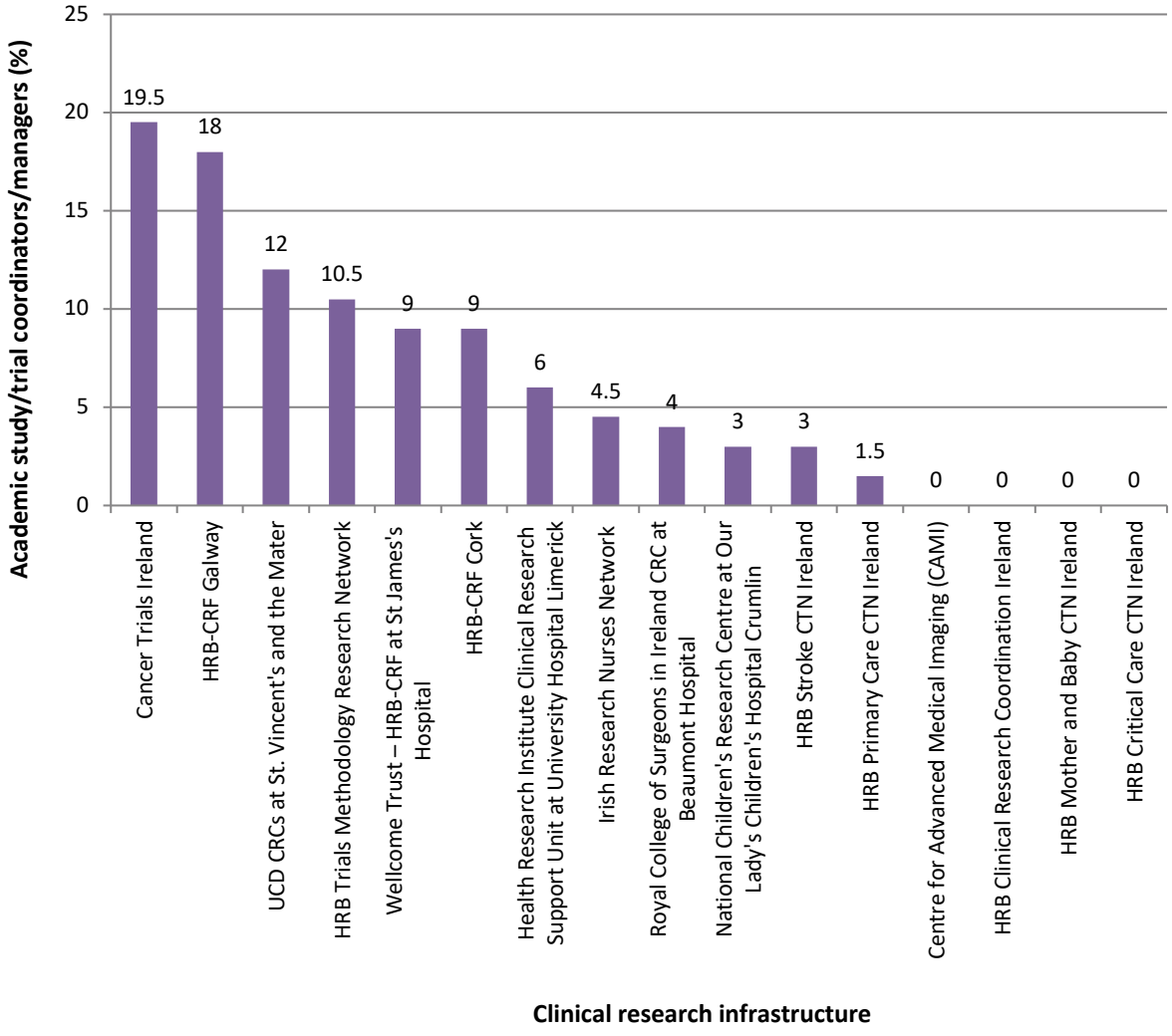


Figure 4.3 (B): Research associates/assistants across clinical research infrastructure (%)

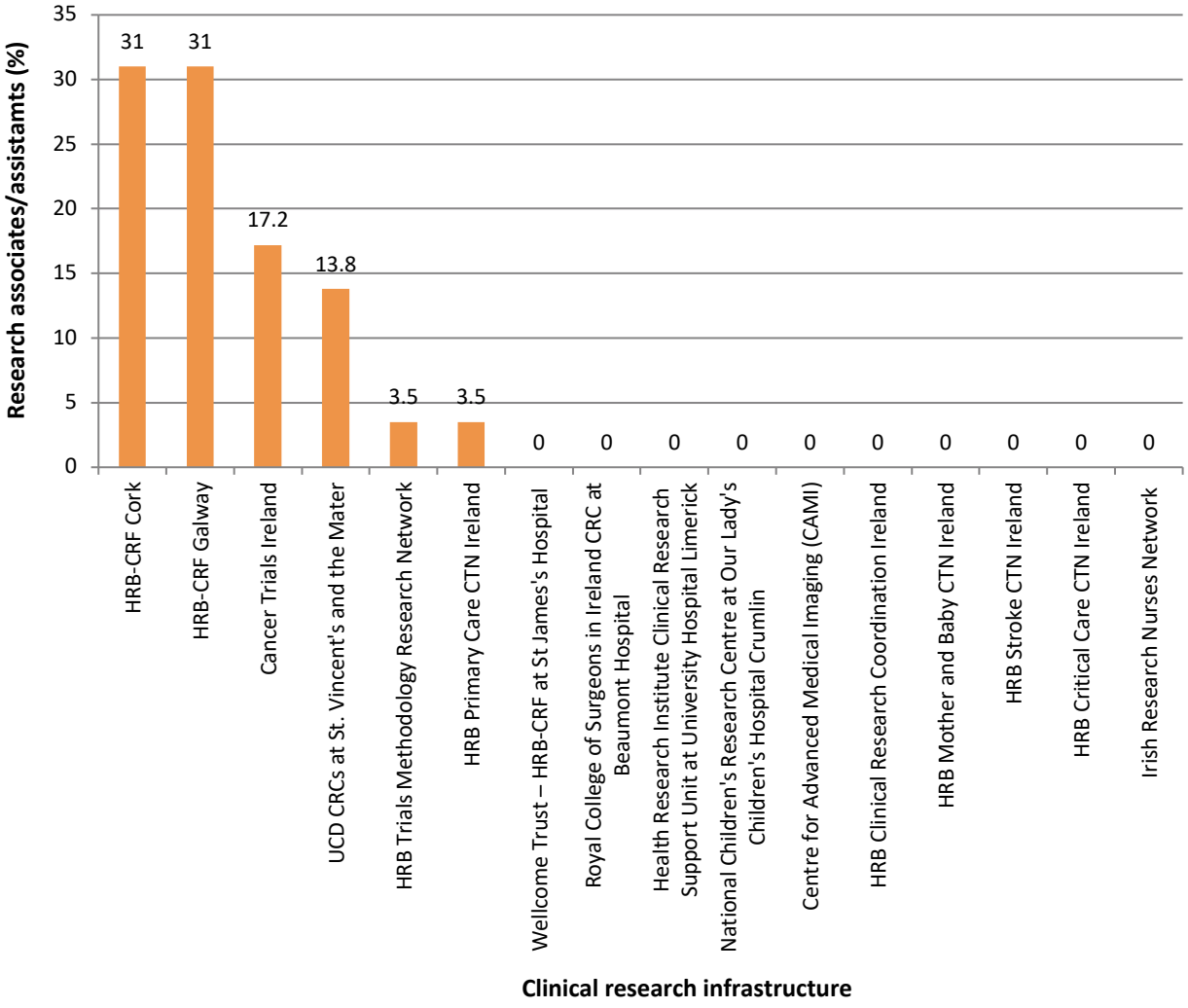
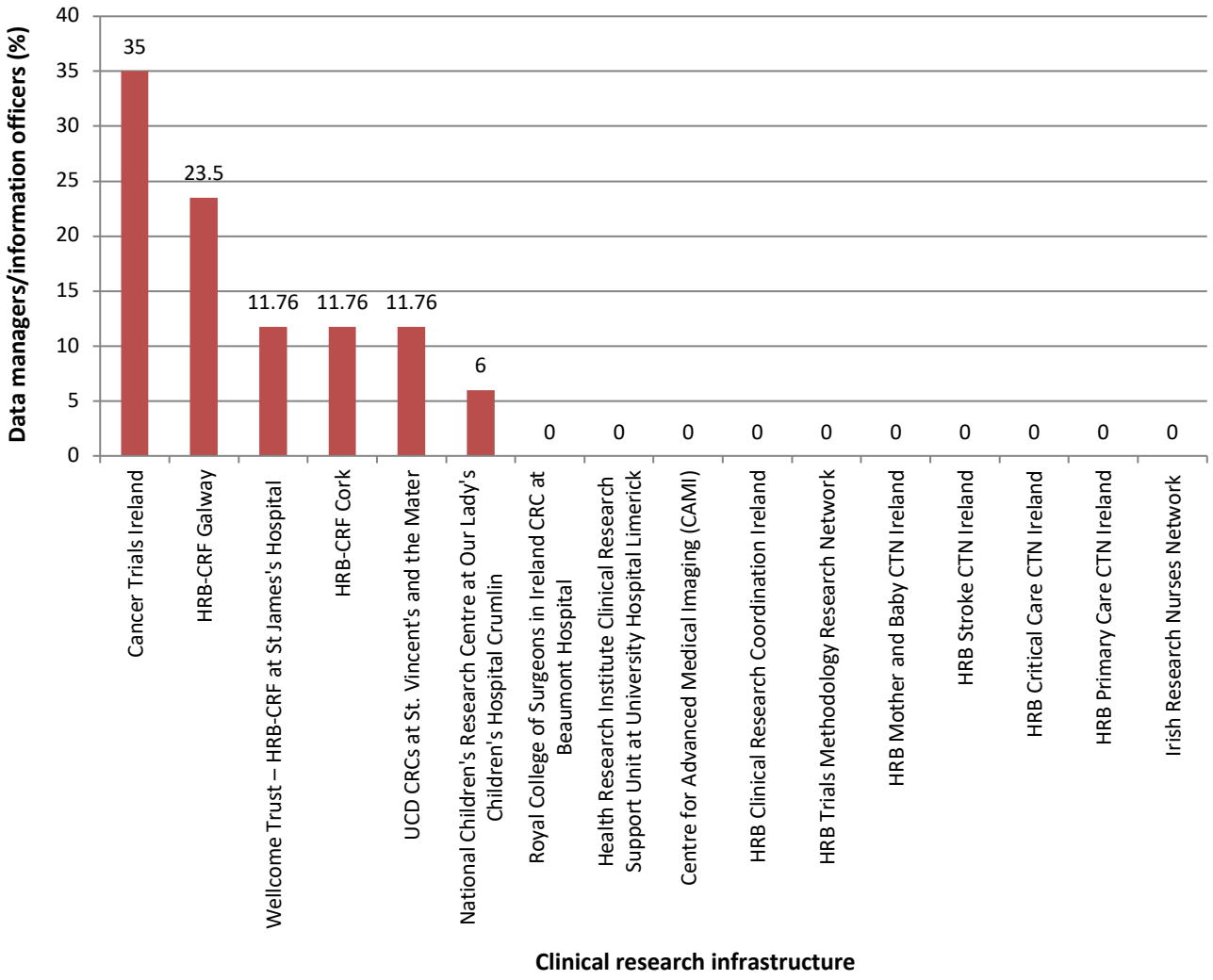


Figure 4.3 (C): Data managers/information officers across clinical research infrastructure (%)



4.3.3 Distribution of clinical research nurses across clinical research infrastructures

The number and roles of nurses across clinical research infrastructures were also examined in the staff survey and are shown in Table 4.1. Survey respondents reported that 75 clinical research nurses worked across the clinical research infrastructures and that a large percentage of the top position of academic study/trial coordinator/manager was performed by nurses.

Table 4.1: Overview of the number of nurses in the clinical research infrastructure and the percentage of these that are the academic study/trial coordinator/manager in their respective clinical research infrastructure

Clinical research infrastructure	Number of nurses	% as academic study/trial coordinator/manager
Wellcome Trust – HRB-CRF at St. James's Hospital	14	50%
HRB-CRF Galway	12	58%
Cancer Trials Ireland	12	58%
UCD CRC	10	80%

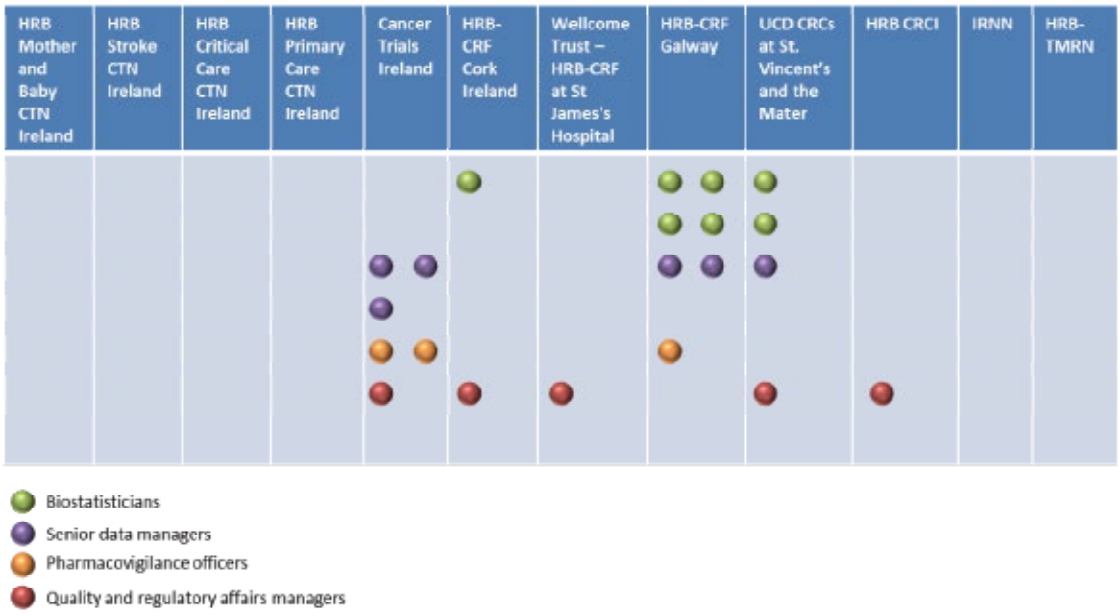
HRB-CRF Cork	9	66%
IRNN	6	83%
HRB Stroke CTN Ireland	6	83%
RCSI CRC	3	66%
Health Research Institute Clinical Research Support Unit at University Hospital Limerick	3	100%

4.3.4 Distribution of clusters of specialised support positions across clinical research infrastructures

The reported number and distribution of specialist support staff across clinical research infrastructures varied, demonstrating very low numbers of specialist roles such as biostatisticians, senior data managers, pharmacovigilance officers, and quality and regulatory affairs managers.

Figure 4.4 visually highlights these clusters of expertise, as reported.

Figure 4.4: Clusters of specialised support positions across clinical research infrastructures

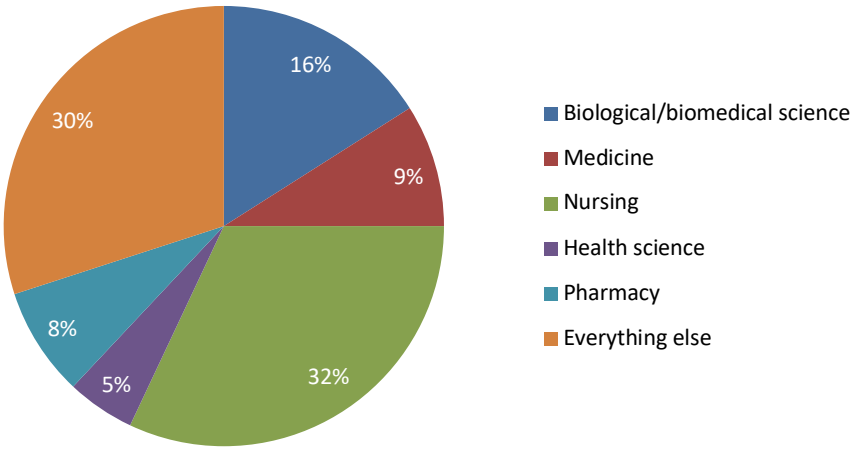


4.4 Skills and competencies of personnel across clinical research infrastructures

4.4.1 Primary degree

All respondents reported that they had obtained a primary degree. Figure 4.5 shows that the majority of respondents (32%) obtained their primary degree in nursing, 16% in biological/biomedical science, 9% in medicine, 8% in pharmacy, 5% in health science, and 30% in other areas.

Figure 4.5: The primary degree subject area of all respondents as a percentage of total responses



4.4.2 Further training towards a clinical research career

As shown in Figure 4.6, the results of the staff survey indicated that in terms of further research training, 53% of respondents have a master's qualification and 23% have a PhD.

Figure 4.6: Percentage of respondents with a master's qualification (A) and with a PhD (B)

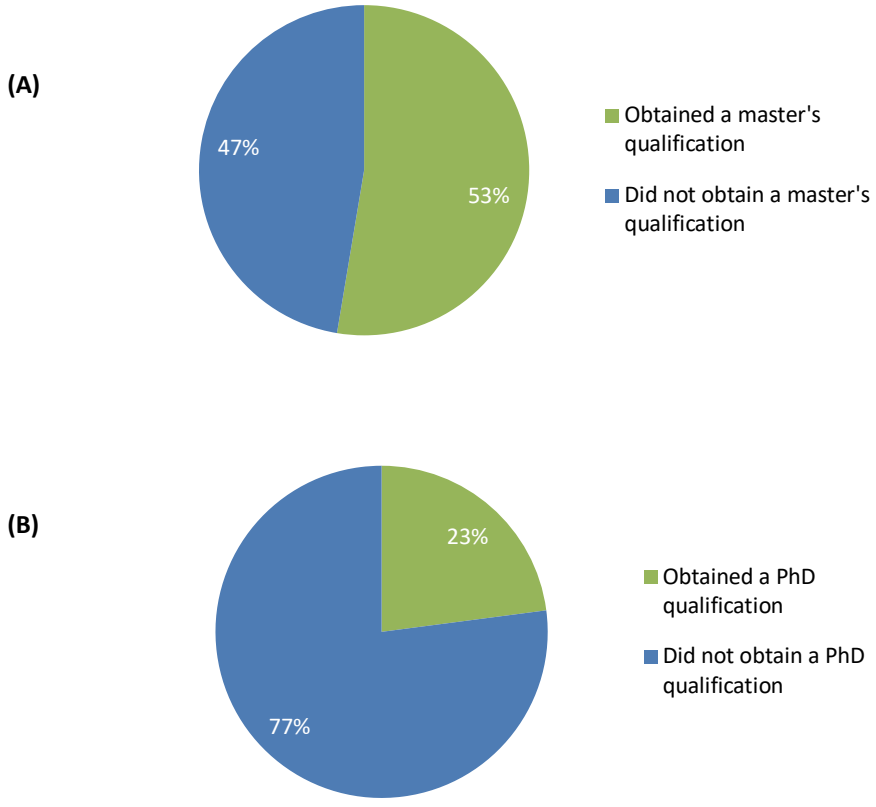


Figure 4.7: Master's degree subject areas

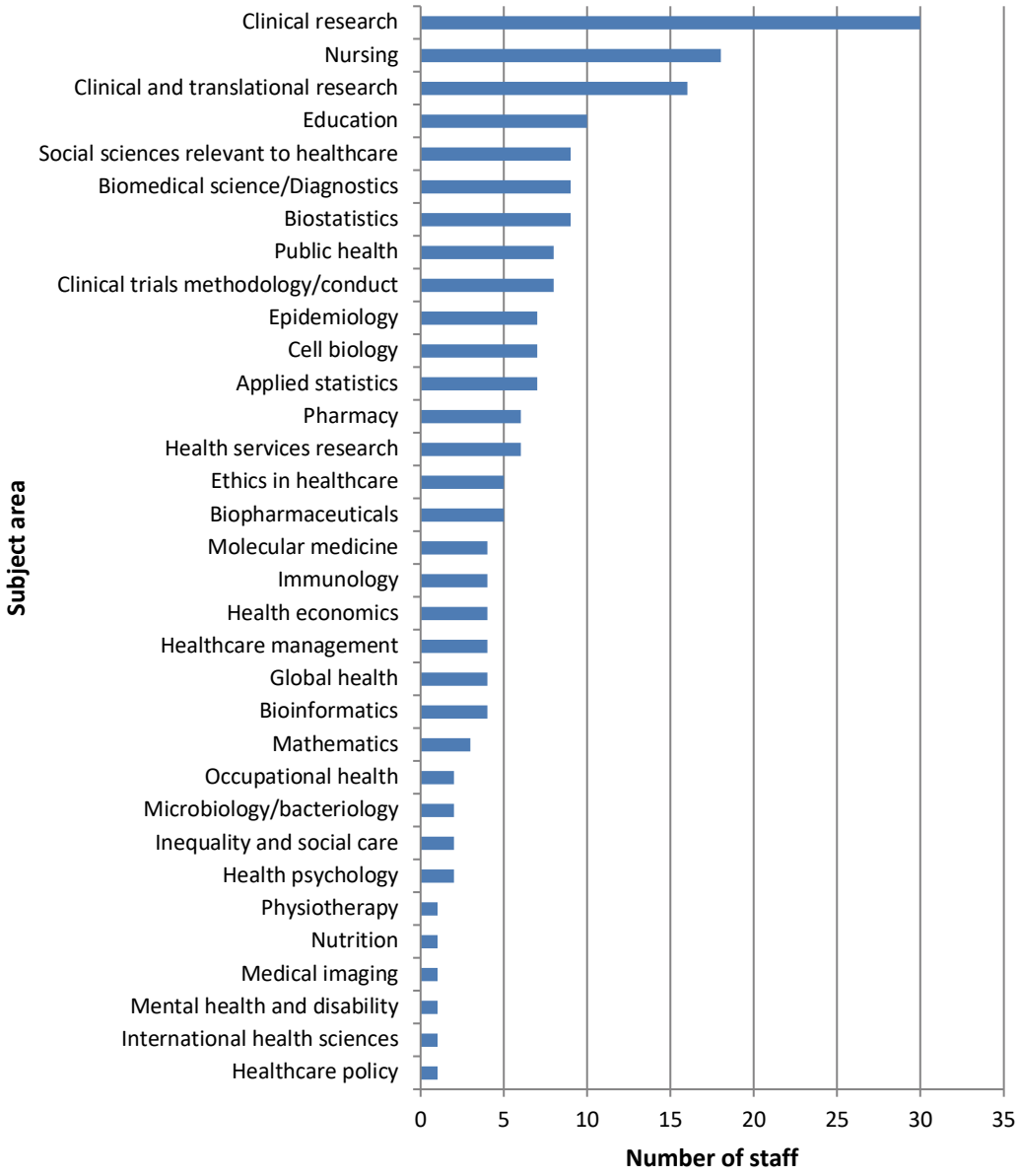


Figure 4.7 shows the subject area in which respondents obtained their master's degrees. Master's training in clinical research, nursing, clinical and translational research, and education accounted for the majority of reported subject areas.

Figure 4.8: PhD subject areas

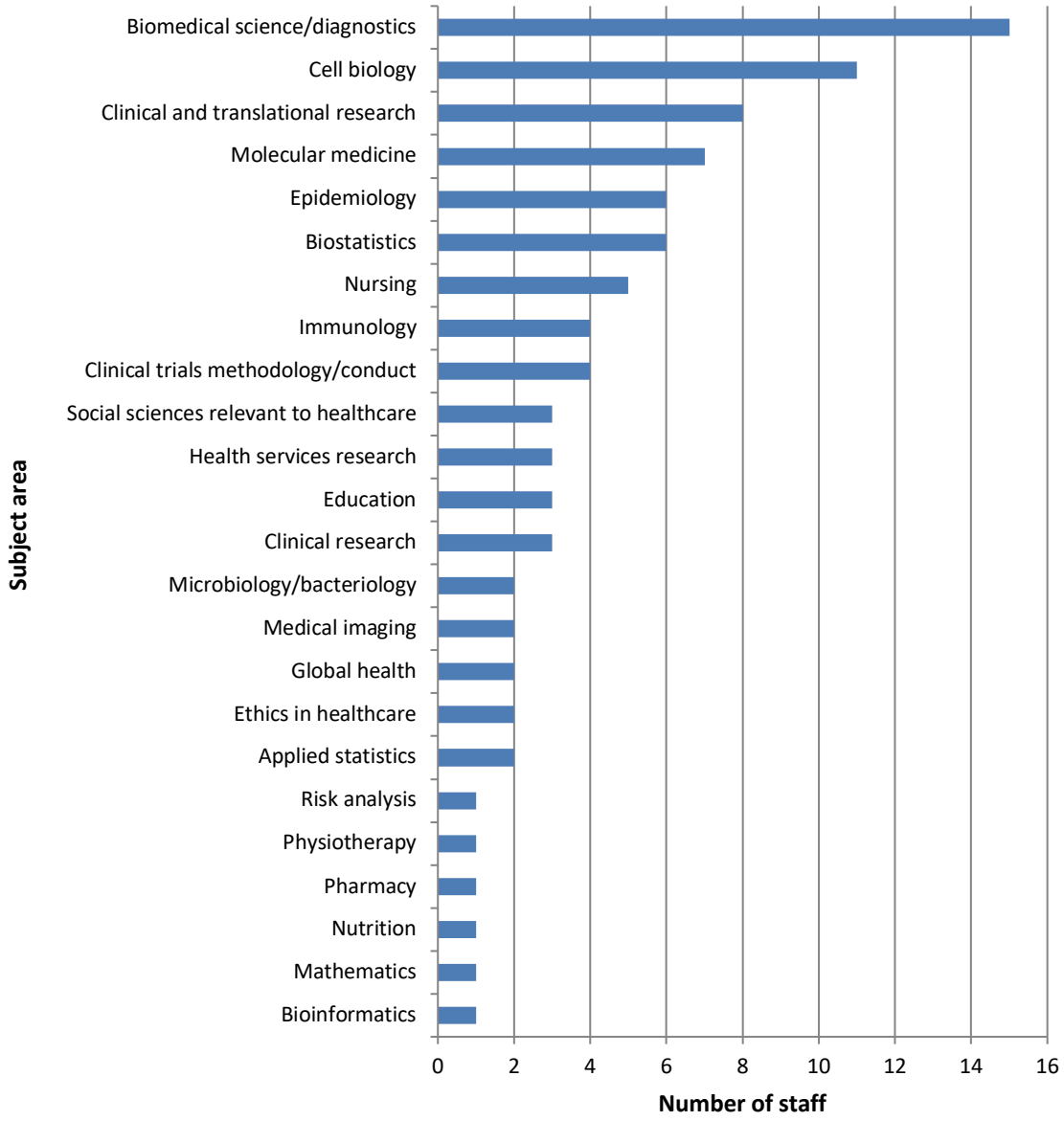


Figure 4.8 shows the subject area in which respondents obtained PhDs. PhD training in biomedical science/diagnostics, cell biology, clinical and translational research and molecular medicine accounted for the majority of reported subject areas.

4.4.3 Additional training

In addition to primary degree and master's or PhD qualifications, staff were asked if they obtained any diplomas or certificates for further training; the results of which are shown in Table 4.2.

The majority of respondents (75%) obtained further training in the International Council for Harmonisation of Good Clinical Practice (ICH-GCP), including refresher courses, followed by data protection, ICH-GCP for medical devices, and general project management as the most common areas of further training.

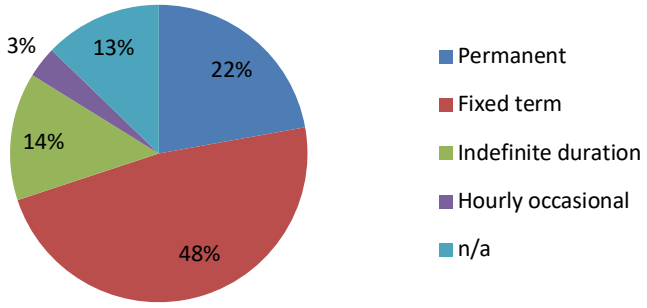
Table 4.2: Additional training beyond a master's degree or PhD

Course	Number of respondents	% of respondents
ICH-GCP	192	75
Data protection	45	18
ICH-GCP for medical devices	39	15
General project management	32	13
Trial methodology	22	9
Pharmacovigilance	18	7
Clinical and translational research course	18	7
Good clinical laboratory practice (GCLP)	16	6
Risk-based monitoring	16	6
Public patient involvement (PPI) training	15	6
Clinical project management	15	6
Ethics	15	6
Biostatistics	14	5
Research integrity	11	4
Cochrane training	11	4
Risk management in clinical research	10	4
Medical writing and data presentation	9	4
Meta-analysis	8	3
Medical device regulation training	7	3
Good manufacturing process (GMP)	5	2
Journalology	5	2
Bioinformatics	3	1

4.5 Contract types and salary source

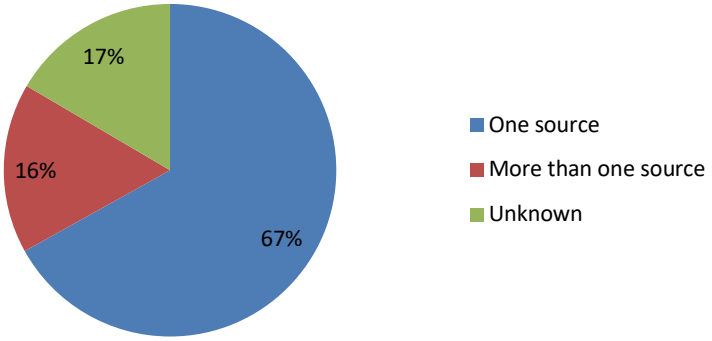
The staff survey asked what employment contract type respondents had. Figure 4.9 shows the contract types of all respondents, with 51% of respondents on temporary contracts (fixed term or hourly occasional).

Figure 4.9: Contract types of all respondents

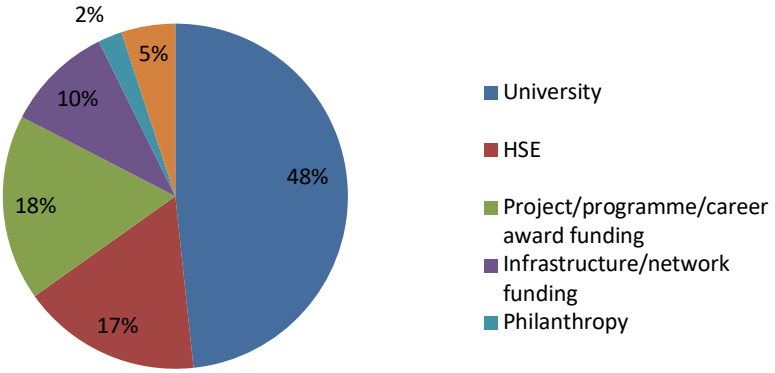


The staff survey followed up on the contract type to understand how respondents' salaries were funded: from either a single source of funding or from more than one source (Figure 4.10 (A)). The source of single-source funding is shown in Figure 4.10 (B).

Figure 4.10: Source of contract funding (A), and breakdown of single-source funding (B)



(A) Source of contract funding



(B) Breakdown of single-source funding

Figure 4.10 (A) shows that 67% of people stated that their salary was funded from a single source, 16% stated that it was from more than one source, and 17% did not know the funding source.

Figure 4.10 (B) shows the breakdown of the sources of single-source funding, highlighting that the majority (48%) of funding was from universities, 28% was from both project/programme/career award funding and infrastructure/network funding (grants of defined duration), 17% was from the HSE, 5% was from industry, and 2% was from philanthropy.

4.6 Career progression structure and promotion opportunities

All respondents were asked if they thought there was an opportunity for career progression in their current clinical research position. Figure 4.11 shows that 42% of respondents said that there were career progression opportunities, 53% said there were not, and 5% did not say.

Figure 4.11: Availability of career progression structure and promotion opportunities

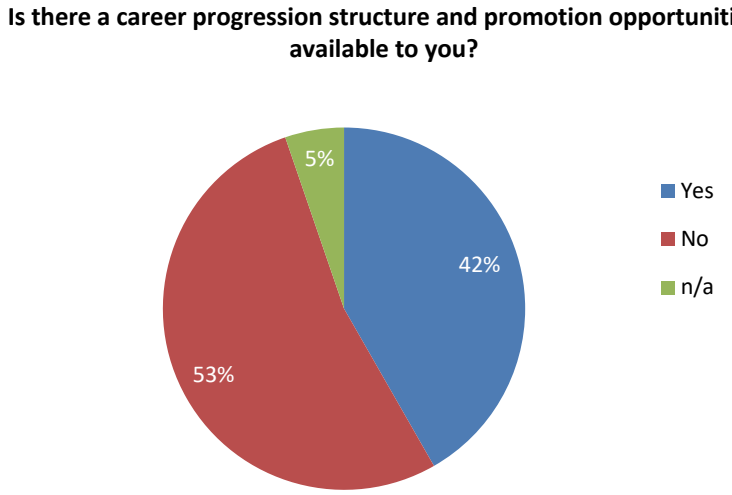


Table 4.3 shows that the majority of respondents' main reason for a lack of career progression and opportunities was that they felt there was either no career path for their profession or that there was a lack of available positions within their clinical research infrastructure.

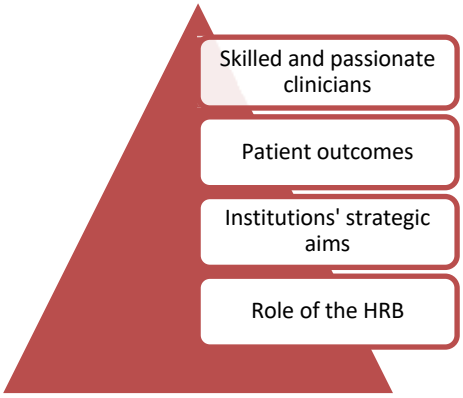
Table 4.3: Reasons for no career progression

Reasons for no career progression	Number of respondents
No career path for your profession	50
Lack of available positions	42
No opportunities for increased responsibility in your role	21
Have reached the peak of career path	16
Other	12

5 Perceived drivers of clinical research in Ireland

5.1 Introduction

This chapter outlines the findings from the qualitative in-depth interviews conducted by Amárach Research with infrastructure stakeholders and service users. The primary focus of this chapter is on what is seen to be driving clinical research in Ireland, namely patient outcomes, the skilled and passionate clinicians working within clinical research, the strategic priorities of institutions in terms of clinical research, and the role of the HRB.



5.2 Key findings

- Clinical research activity in Ireland is moving forward in a positive way.
    - However, improvements are being driven by individuals and institutions, both of which operate in a degree of isolation, and not as part of a cohesive national research system.
- 'Skilled and passionate' clinicians are striving to improve patient outcomes despite structural health system barriers.
- The strategic priorities of institutions are driving a culture and/or long-term strategy of clinical research.
- The HRB is a key support for clinical research infrastructure, but this is at the developmental stage and has funding constraints, which indicates more funding support is needed.
- Overall, there was a perceived lack of support and buy-in from the Health Service Executive (HSE)/Department of Health (DOH).
    - A cohesive national research system is needed to build upon the positives that currently exist within the clinical research infrastructures.

5.3 Skilled and passionate clinicians focusing on patient outcomes

A focus on improving patient outcomes is seen as one of the key drivers of clinical research in Ireland. Within the clinical research infrastructures, many believe that improvements in patient outcomes must begin with a focus on addressing a research question. Answering that research question and determining how this can positively affect patients is the focus for researchers and clinicians. In order to continue to improve clinical research in Ireland, it is important that the patient becomes the central focus. Driving clinical research forward by focusing on patient outcomes enables clinicians to provide better healthcare and enables hospitals to become centres of excellence. This brings efficiencies and long-term health and economic benefits to the country.

"It is always an interest in the specific research question. How it would affect their patients."

"You have a research system and you have a hospital system and we've got some of the best clinicians in the world committed to getting the best outcomes for their patients."

"It's about patients' experience from the beginning to the very end, all aspects of it. From waiting times to outcomes of their treatment."

Many respondents noted the importance of individuals within the healthcare system and their role in clinical research infrastructures. The skilled and passionate clinicians working within the healthcare system were seen by many to be a key driving factor of clinical research across all aspects of the clinical research infrastructures, but in some cases, it was in spite of structural barriers that may exist. The passion of clinicians themselves is fundamentally linked to the desire to improve patient outcomes. However, it was felt that these clinicians were operating in a degree of isolation and not as part of a cohesive healthcare system focused on clinical research.

"Key drivers are the individuals who have an ambition to contribute and make a difference in terms of the clinical outcomes for patients."

"Within the health service, [I] don't get the impression at all that there's a drive towards research, I think it's just the individuals wanting to deliver research."

5.4 The strategic importance of clinical research

Clinical research in Ireland is also seen to be driven forward at an institutional level. Some institutions, primarily universities, have a strong focus on clinical research as part of their strategy. These institutions aim to become centres of excellence in particular research fields. These strategic aims stimulate a culture of research in the institutions, meaning that they are fully committed to conducting research over the long term. This culture is seen to be a key factor in providing the necessary support for the principal investigators (PIs) conducting clinical trials. While a research strategy advances the institution's scientific interests, it also plays a key role in driving the strategic priorities of the institution in terms of funding and revenue raising. However, the strength of research strategies varies across the clinical research infrastructures and is not part of an overarching culture.

"The most important driver of success is the institution. If it cares, it will make sure to recruit investigators who have an interest and will be sure they protect the time of those investigators and they will make sure they are supported."

"There are strategic implications as well. The university and the hospital here have a strong position on med tech, so given where we're based with a strong med tech focus and that's (research) another driver to kind of support the strategic aims of institutions."

5.5 The HRB's role in driving clinical research

The general consensus is that the HRB took on an important and central role in driving investment in clinical research. The contributions of the HRB, in terms of financial support and infrastructure, have positively impacted on clinical research infrastructure in Ireland. However, many recognise that the HRB's work on the clinical research infrastructure is at the developmental stage, with the HRB itself having funding constraints.

"The HRB has been transformative in terms of the infrastructure and the changes to the landscape. They've had funding limitations and their ambitions have had to be curtailed, and the ambitions of the community because of that."

In an overall health spending context, the HRB's budget is seen as "miniscule" in comparison with the total health spend.[11] The principal view is that the HRB needs additional funding support: "[They] cannot do it all on their own." The agency is viewed as a "positive force" in terms of research investment, yet it was acknowledged that the role of the HRB is not to drive research at a broad national level – this is the responsibility of the DOH and the HSE.

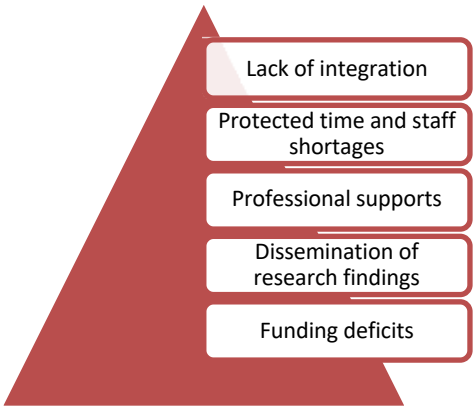
"There's been fantastic initial steps taken and the work of the HRB in developing the clinical research facilities, the development [of] the CRCI, the trials, the networks."

"Within the budget available, the HRB has taken very clever steps and done a very good job. I just think that the task is bigger than those small steps."

6 Perceived barriers to clinical research in Ireland

6.1 Introduction

This chapter outlines the findings from the qualitative in-depth interviews conducted by Amárach Research with infrastructure stakeholders and service users. The focus of this chapter is on the perceived barriers to conducting clinical research in Ireland, including a lack of integration of research into healthcare provision in Ireland, a lack of protected time for clinicians, staffing shortages (particularly research nurses and clinical research professional supports, i.e. regulatory support), a lack of dissemination of research findings at a public and governmental level, and funding deficits.



6.2 Key findings

- Clinical research is recognised as not being a fully integrated aspect of the healthcare system in Ireland.
  - Lack of integration is seen as the principal barrier to effectively conducting clinical research in Ireland.
  - This is illustrated by the underutilisation of general practitioners (GPs).
- Clinicians are lacking protected time within hospitals, meaning that time dedicated to research suffers – particularly given resource constraints within hospitals.
  - This can lead to some clinicians losing their focus on/passion for research.
- Lack of integration also creates resource constraints with regard to research nurses and professional supports (such as regulatory support).
  - A definite career pathway is not available to research nurses, which significantly impedes recruitment.
  - Appropriate professional supports to assist in the proposing and running of clinical trials is needed and is seen as an investment in the clinician.
- The benefits of clinical research to healthcare are not thought to be fully understood and recognised by the general population or the HSE/DOH.
  - In order to potentially advance HSE/DOH buy-in and reduce the constraints caused by the lack of integration, clinical research activity and impact communications need to be improved.
    - Patient outcomes and the tangible benefits of clinical research to the health service and to citizens' health in general needs to be the driving message.
- Funding levels will always be a core issue. However, there is acknowledgement that increased funding on its own is not the solution to all problems facing clinical research activity in Ireland.

- Current funding is seen as too fragmented, inequitable, and not sufficient; funding for core staffing supports should be a focus.

6.3 Integrating clinical research into the healthcare system

The view is that there is a lack of emphasis on research within the healthcare system, resulting in it not being a fully integrated component of healthcare provision in Ireland. This is considered one of the primary barriers to conducting clinical research in Ireland. The lack of integration means that a culture of clinical research is not present within most hospitals, creating constraints across a range of areas within the hospital, with principal investigators (PIs) struggling to adequately allocate and manage time and resources.

"The role of research is fairly limited from a HSE perspective. The fact they have such a limited role is deeply regretted."

A further example of this is the underutilisation of GPs, who many believe have no incentive to get involved in research. This is viewed as an inefficient use of resources, as GPs are the largest medical discipline. Many see opportunities to do more clinical research within the primary care environment. Given the extensive reach of the GP network, both in terms of location and the number of people who use the service every year, even a small degree of clinical research within the system would have a wide impact. Conducting clinical research through primary care settings could also potentially free up resources in pressured clinical settings.

Furthermore, going to the patients in the community means that participation in clinical research is much more practical and attractive to patients. However, the structures to conduct good clinical research through the primary care network are currently somewhat underdeveloped, with a misalignment of primary care and the Hospital Groups, meaning that the capacity and skills that might be available within primary care are not being fully exploited.

"Clinical research in primary care is set up to a degree but not perhaps sufficient. I think it does need to evolve as Sláintecare does. Galway have quite a good GP network and Trinity have a good GP network, but I think those need to develop more."

"Community-based research is probably under-resourced and not really brought to the fore. But I think it is an area that we're looking at."

The belief is that integration should be driven at a governmental/policy level (HSE/DOH). There is a desire for research to become core to clinical practice within hospitals and to incorporate a role for GPs. This integration enables research career pathways, which is seen as a key factor that will drive a culture of research across the Irish healthcare system.

"The HSE need to buy into the fact if we want a good health service it needs to have research embedded into it."

6.4 Protected time and staffing shortages

At an individual level, clinicians feel that they lack the protected time needed for research. Firstly, significant time is needed to procure funding in terms of formulating proposals. Secondly, and most obviously, protected time is needed to conduct the research when a proposal is successful. Given the lack of a research culture within the healthcare system, if clinician time is not protected, creating the necessary time during working hours proves difficult.

"Protecting the time of the clinicians is the key issue and then making sure the protected time is being used productively, not for routine stuff that others could do."

Given that research is not seen as core to clinical roles, workloads within hospitals mean that research is not viewed as a priority. When there are vacant consultant posts, long waiting lists, and people waiting on trolleys, it is hard to ensure that research is given the required time and attention. Senior clinicians are spending most of their working hours dealing with the present issues and hospital emergencies. This can lead to some clinicians losing their focus and/or passion for research.

"The more you can do to facilitate those investigators to kind of reinvigorate their interest in clinical research the better."

"Senior people are dealing with firefighting on trolleys and mounting costs and worrying about whether their clinicians can do research is very far down their line."

Staffing shortages are seen to act as a key barrier to conducting clinical research in Ireland. A range of key staff are needed in order to conduct clinical research. This includes, most importantly, research nurses, but also includes a range of other supporting staff. In general, these staff are not present.

In cases where the staff are present (supported by HRB funding), their availability is low and does not sufficiently cover the requirements of conducting clinical research. There are also recruitment pressures coming from industry, meaning that staff who have been trained within the clinical research infrastructures are being lost to industry.

"The hospital doesn't employ the requisite staff. They won't have a research team, such as research nurses, data managers, clinical project managers, quality and regulatory affairs and coordinators, which are all needed."

"You can't get funding for a project manager, or a research nurse on the ground. That's what they need. It is the funding for those kind of people who are trained in good clinical practice."

"There are huge pharma companies starting new clinical trials locally and now they are starting to poach the really well-trained staff that we have grown here through investment and research."

A lack of research nurses in particular stands out as a significant barrier to conducting clinical research. A key factor constraining the recruitment and retention of research nurses is the lack of a definite career pathway, with indefinite contracts (for the duration of the research programme only) acting as a barrier to recruitment.

The prevalence of indefinite contracts also means that skilled and experienced research nurses, who have spent a number of years working in a research-focused environment, are lost to general nursing when research funding comes to an end. There is a strong recognition that research nurses are key drivers of the day-to-day running of clinical research trials. Their importance cannot be overstated and as long as there are shortages, there will be difficulties in running clinical trials efficiently and effectively going forward.

"Clinical research isn't integrated into the HSE. Nurses have to leave secure posts to come into it. If that money runs out, then they're not guaranteed a job at the end of it. That's what sometimes drives people back into clinical practice."

6.5 Building an infrastructure of professional supports

Linked to staffing shortages, a lack of infrastructure supporting clinical trials is seen as another barrier to conducting research across the clinical research infrastructures. Many respondents feel that there is a lack of appropriate professional supports available to assist the proposing and running of clinical trials. There is the view that clinician time is valuable, and that professional and administrative research support is needed in order to ensure that clinician time is being used most efficiently. Supports are seen as an investment in the clinician and their research idea; however, supports are currently believed to be severely lacking. The pharmaceutical industry is seen to have superior infrastructure and processes supporting clinical research. Professional knowledge and supports are built around scientific knowledge, enabling clinicians to better focus on answering the research question.

"The premise is that a clinician will provide clinical skills and the ideas. Then the clinical research facility will provide the technical expertise, the staff, the resources."

While more roles and supports are wanted, there is also a desire for a clearer definition of roles, meaning that the work parameters of each member of the research team are more specific. This enables a greater focus on the clinical trial and means that staff are not tied up with other hospital duties that may arise.

Support is believed to be especially needed on the regulatory side of clinical trials. Not only is this needed in order to improve time management efficiencies, but clinical trial regulation is a hugely complex area where clinicians or PIs are not necessarily best placed to provide the expertise. Furthermore, some believe that Ireland is somewhat behind other countries in terms of its regulatory standards. A centralised body overseeing standardised regulations and procedures is recommended by many. This would reduce the time burden on clinicians (or research team members), while also ensuring a uniformly high standard across all clinical trials conducted in Ireland.

"There is no joined-up system of regulatory oversight, proper support for the clinicians and cohort of trained research nurses across the county. We are starting from a low base."

"We need to build up a cohort of people who can manage the regulatory side, the monitoring side, the paperwork side. The clinician's time is extremely valuable."

Electronic hospital records are also seen as an area where support is needed. Irish hospitals are seen to be very behind in this regard.

"Ninety-eight per cent of general practice records are completely computerised. It's a largely computerised system. We're frustrated with the inability of hospitals to move along on that."

6.6 Dissemination of research findings and increasing awareness

Many believe that there is a lack of dissemination of findings from clinical trials. This can act as a barrier to conducting clinical research in Ireland. If clinical research is to become a core element of healthcare provision in Ireland, it is crucial that policy-makers and decision-makers realise its value. Patient outcomes and the overall value to the healthcare system should be a key focus for educating the public and healthcare professionals. If the tangible impact of clinical research can be illustrated to the HSE/DOH collectively, there is a sense that pockets of leveraged funding may become more available. But, more importantly, it will potentially help build the case for a more integrated approach to clinical research in Ireland.

"It needs to be at a government level when you start realising the value of clinical research. The research is there to say clinical research improves patients' health. It equips health outcomes in hospitals and it improves retention of staff."

"We need to tell the public that this is what your money is being spent on and so you can trust that, you know, the Government, the DOH, the HRB, all the academic institutions and the hospitals. They want to make things better for mothers and babies."

"We have some amazing stories of world-class excellence in our Irish hospitals and just the message gets lost, you know."

6.7 Funding and core support deficits

Across the board, funding is seen to be the biggest issue facing all aspects of the clinical research infrastructure. However, most acknowledge that increased funding on its own will not be the solution to all problems facing clinical research activity in Ireland.

"The answer to research problems is always funding, but if you have an inadequate health system and you're trying to do excellent research, it is not going to work."

There is a sense that the HRB plays an important role by investing in clinical research infrastructure, but due to limited funds some felt that the HRB trying to fund infrastructure and primary research over the long term would be difficult.

For the most part, CRF/Cs have not found a way to be fully self-sustainable and most feel that they could not exist without a degree of core supports, even those not currently funded by the HRB.

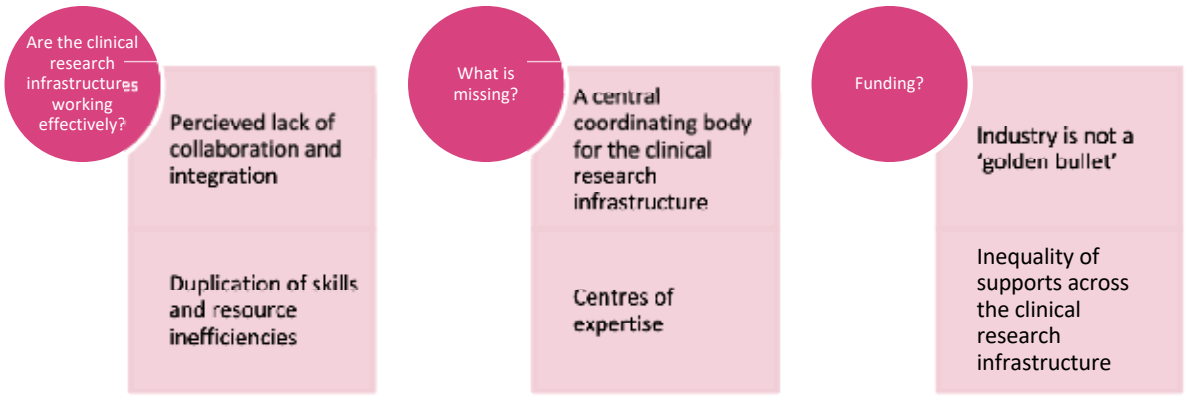
"I think there needs to be a commitment and the recognition that ongoing support and centralised support is necessary. That the research facilities are never going to pay for themselves."

"They've then put money into networks that are not adequately resourced. So, what's that going to do?"

7 Perceptions of the HRB's clinical research infrastructure supports

7.1 Introduction

This chapter explores perceptions of the clinical research infrastructure in Ireland from the perspectives of stakeholders and service users. The stakeholder interviews – conducted by Amárach Research – focused on funding, integration with the healthcare system, the growth of the clinical research infrastructures, and sustainability of the infrastructures into the future. Service user interviews focused on core functions supplied by the clinical research infrastructures, participation and clinical research infrastructures' relationships, ease of access, and the role of industry.



7.2 Key findings

- The clinical research infrastructures as depicted in Figure 1.1 are seen as a physical network of centres, operating in a degree of isolation and not as part of a unified infrastructure.
  - This means that many do not know how to tap into the range of skills and services available.
  - More collaboration and integration between all pieces of the HRB clinical research infrastructure is required.
- Are the clinical research infrastructures working effectively?
  - Collaboration exists but is hampered by culture, competition, and different processes/standards, partly due to inequity of funding and resources.
  - Duplication of skills and knowledge across the clinical research infrastructure is an inefficient use of resources and a key issue – particularly across the CTNs.
  - A simplified infrastructure model is needed in order to improve information deficits and reduce resource inefficiencies.
- What is missing?
  - A clearly signposted central office/body is needed to facilitate the running of the infrastructure and to improve communications and the availability of information.
  - Centres of expertise (e.g. data management) would potentially help reduce duplication and ensure a more straightforward channel for accessing skills or resources.
- The preference for a long-term HRB funding strategy focuses on two core elements:

- The HRB funding emphasis should be on maintenance rather than expansion, and on not losing the benefits of the investments already made.
- There is a desire to have more certainty attached to clinical research infrastructure funding; the cyclical nature of funding (awarded in three- to five-year tranches) is believed to hamper long-term planning and development.

7.3 Are the clinical research infrastructures working effectively?

The current clinical research infrastructures are seen to have improved in recent years, primarily driven by more money and resources. Many believe this is the first iteration of creating a clinical research infrastructure in Ireland, and that it will naturally improve over time. But so far, the improvements have not gone far enough. Many feel that the clinical research infrastructure jigsaw depicted in Figure 1.1 is a "good start" and that it helps visualise the elements of the clinical research infrastructure. However, it understandably failed to capture what is an inherently complex system.

"It accurately depicts clinical research infrastructure funded by the HRB. But, of course, the HRB is one cog in the wheel. I do think that the HRB have done an amazing job at funding the infrastructure."

"I think the HRB has put the foundations in place, but the landscape is a bit more complex than just this."

7.3.1 Lack of collaboration and integration

The clinical research infrastructures are viewed by many as a physical network of centres. These centres are seen to be operating, to a certain extent, in isolation and not necessarily as part of an integrated system of clinical research activity. Most notably, many see a disconnection between the CRF/Cs and the CTNs, with little dialogue between the two. In order to achieve a fully functioning infrastructure, there needs to be more collaboration and integration between all parts of the system. Many feel that the clinical research infrastructure, in its current structure, would never work effectively unless all centres operate following the same processes and to the same standards.

Infrastructure users felt positive about their dealings with the CRF/Cs as individual units. However, most do not see an overarching coordination across the network. Proximity seems to be a driving factor in the good relationships between CRF/Cs and some infrastructure users. This meant that many researchers were not tapping into the whole clinical research infrastructure. When they did contact other pieces of the clinical research infrastructure, they experienced differing standards or ways of doing things.

"The biggest challenge is predictability. You can walk into the system and you don't necessarily know what you're going to get out of it."

"The CTNs are not working very well with the CRFs. I think there should be more dialogue between those networks on the left, with the CRFs on the right, and I know from experience that doesn't happen very much."

The respondents' views are mixed in terms of whether the clinical research infrastructure was working effectively or was fit for purpose, with two main contrasting views. Firstly, many held the view that the clinical research infrastructure promotes collaboration and allows users to access the skills and supports of the CRF/Cs. Individual units are seen to be working well, but not the clinical research infrastructure as a whole.

"I think CRCI as a collaborative vehicle is really, really important."

"The CRCI is very strong in bringing us together and increasing the efficiency of activities that would be done across the board."

Conversely, others believe that competition and different processes and standards – created by inequity of funding and supports from the HRB and the universities – means that the clinical research infrastructure is not a fully integrated system, nor would it ever be. This leads to many skills and

supports that are available across the network not being fully utilised. This can be a particular issue for service users in terms of different ways of doing things.

"At the moment it's not a level playing field. Because some of the research centres have that resource, where they have funded posts, and others don't, and yet we're all part of the infrastructure."

7.3.2 Duplication of skills and resource inefficiencies

The view that inefficiencies exist across the Irish clinical research infrastructures is a common theme that emerges, most notably in terms of the duplication of skills and knowledge. Given the current difficulties in conducting clinical research from a funding and resource point of view, this duplication is not seen as an efficient use of funding or people. Across the CTNs, in particular, there is a worry that funding networks may partially duplicate roles that could be better utilised across other research programmes in the infrastructure.

"You could argue that the country only needs one or two data management centres. One or two bio repositories. One or two centres providing pharmacovigilance. But it probably doesn't need all seven Hospital Groups providing all of those services."

"Across the CTNs there is a degree of replication. They all have a common set of functions at the core such as programme management, regulatory affairs, etc., and I wonder could we be a bit cleverer about providing some of those services centrally."

Many feel that there is a possibility to better maximise the HRB's investment and the skills available within the clinical research infrastructure in order to benefit from the growing expertise across a range of areas, to collaborate more, and to appoint centres to provide core expertise, which could potentially reduce duplication and inefficiencies.

"I feel in our CTN, they are doing a lot of great work, but there is a lot of duplication of what is happening there or what is happening in the CRFs. It's unclear from a client perspective what should be done by the CRF that could support the CTN."

Furthermore, having specifically appointed centres may make it easier to access services across the clinical research infrastructures, allowing for better utilisation of skills and resources across the whole clinical research infrastructure. There is a sense that accessing skills or services can be difficult due to poor communication regarding what is available and poor signposting of the services. There is a preference for a simplified infrastructure model, whereby one centre will act as a "one-stop shop to access, for example, biostatistics support for clinical trials – this being the most commonly cited example".

"Galway have a fantastic biostatistical resource. But we can only utilise some of it and we would love to utilise more of it."

"But I've no idea how to tell my clinicians to work with Galway. If I don't know that and I'm in the system. You see, I see all these little pieces that's not joined together at all."

7.4 What is missing?

Across the stakeholder and service user interviews, there was a view that the clinical research infrastructure was missing a number of "pieces of the jigsaw", namely a clearly signposted central coordinating body, as well as education and training aspects.

7.4.1 A central coordinating body for the clinical research infrastructure

The role of HRB CRCI attracted some confusion and somewhat diverse opinions. Firstly, the use of the abbreviation leads to confusion with Clinical Research Development Ireland (CRDI) but, overall, some are unsure of HRB CRCI's function and questioned what specific role it plays in the Irish clinical research infrastructure. Some thought its functions were similar to CRDI's,[12] and infrastructure users in particular had experienced a lack of communication between departments in their dealings with HRB CRCI.

"It seems to me like CRDI has become very similar to what CRCI is and I just think there's a greyness there."

There is, however, a clear view that HRB CRCI acts as a centre point for increasing collaboration across the clinical research infrastructure. It is seen as a space for a collective of individuals who usually compete for funding to come together with their shared vision.

"The HRB is key in setting up the infrastructure and enabling structures. It has encouraged the sharing of knowledge at a national level. It means people are sitting and having those discussions. We just need to accelerate it."

However, into the future there is a desire for HRB CRCI to have more of a central role in communications and developing the collaborative approach many believe is missing across the clinical research infrastructure. Many want to see HRB CRCI act as a central point of contact and information for infrastructure users and members.

"The CRCI should have a role in coordinating one kind of central message; I would have seen them as the point of contact and have an overarching and signposting role."

Overall, there is a strong sense that the clinical research infrastructure is missing a central office/body facilitating the running of the infrastructure. Some felt that HRB CRCI and CRDI may be moving towards this function, but the common view was that neither took on the central role of coordinating such activities – likely driven by confusion over the functions of each body.

"I think you could have a trial approved here and you could have a separate perspective on it in another region and I don't think that's as drawn up as it needs to be."

A more simplified support infrastructure is desired, whereby one point of contact coordinates a range of supports and information. A centralised approach may help reduce resource pressures faced when conducting clinical trial activities, with the potential to unburden staff within hospitals, meaning that hospital staff time would be used more efficiently. It would support a standardisation of procedures and processes across the clinical research infrastructure. It is believed that this structure could increase transparency and information sharing, thus facilitating increased collaboration across regions and institutions.

"I have personal experiences now of Cork, Galway and Trinity and they all seem to have slightly different angles on things when we ask questions and when we deal with the people. I think it will take a while [before] everybody is on the same page."

"From an ethics point of view, I think everything is there. Though it could be improved by centralising ethics and regulatory approval. So that it all just went to one portal."

Some of the suggested functions for this centralised office are as follows:

- A national ethics committee or agreement on ethical approval
- A national approach to biobanking
- Agreement on governance and data
- Agreed contracts, and
- A national approach to clinical trial regulation.

There is a sense that many operating within the clinical research infrastructure and infrastructure users were not fully aware of how to tap into the range of skills and services available. Although this was not a direct criticism of the clinical research infrastructure, there does seem to be a need to increase information and awareness. More information is needed about supports that are available and how to access them.

For many, a key barrier to increased awareness and information was confusion about who/where to contact and that there was no well-defined point of contact for information. A centralised

centre/body with the role of educating/informing researchers about supports is seen as something that is missing from the clinical research infrastructure overall.

While the knowledge/information is available, it needs to be better and more clearly integrated within the clinical research infrastructure and with greater communications supporting it. Centralised information is needed in order to ensure that clinicians are aware of supports, what is feasible, and what should be costed into grants. With a substantial number of clinicians having research experience within other, better-resourced healthcare systems, there needs to be a better understanding of the realities and pragmatics of conducting clinical research in Ireland.

"We have a lot of work to do in educating our research community. That if you're going to sign up to be part of a regulated trial you need to actually cost in the full cost of doing that at the highest level."

7.4.2 Education and training

Education and training are core features missing from the clinical research infrastructure. Similar to other areas, while education and training opportunities are available within the clinical research infrastructure, there are information deficits and awareness is limited. A centralised centre for education and training would remove some of the perceived access barriers. Education and training for data management/statistical skills, research methodology, and grant costing/feasibility in particular is required. Furthermore, there are perceptions that clinicians may lack some of the project management skills and training required to run a clinical trial.

While some believed there was a lack of emphasis on training within the clinical research infrastructure overall, there was a recognition that clinicians/PIs may not have the interest or time to undertake training and education.

"Maybe the infrastructure is missing more emphasis on training. But then, of course, you can bring a horse to water but how do you make them drink. You can provide the training but how do you get PIs to appreciate that they need the training."

CRDI and the HRB Trials Methodology Research Network (HRB-TMRN) were acknowledged as having education as part of their offerings, but for some their expertise and focus were too narrow. Overall, these bodies were mentioned infrequently, suggesting an information deficit on the part of many about what is actually available in the clinical research infrastructures and what they perceive to be available.

"I know the Trial Methodology Research Group has a remit in training and education. But that really is around trial technology, not basic clinical research, not GCP training, even though our centres do that. So, I think there is definitely a piece there that we are missing."

"There is the HRB Trials Methodology Network, and that's very specific, very good, but very specific."

7.5 Funding

Funding was naturally viewed as a core issue across all interviews. Many feel that industry should only be used to supplement core funding, while the inequity in funding can be damaging to collaboration. In order to sustain the current infrastructure it was believed that the primary focus should be on maintenance, with more certainty attached to funding.

7.5.1 Industry is not a 'golden bullet'

While industry is seen as a popular potential source of funding in theory, there is an acknowledgement of the limits to the amount of funding that might be leveraged and the cost/benefit of securing the funding. The perception is that a high level of investment is required in order to secure and undertake industry-sponsored clinical trials, while the financial rewards are considered somewhat low, especially given the time and skills needed, particularly in terms of regulation standards.

"The experience we have, and I think it's shared by the others, is that industry want the stuff done at the highest quality for the lowest cost. Which is problematic."

However, many do not see securing industry funding as a certainty, with the standard of clinical research in Ireland needing to improve if it is to successfully compete with other countries. Firstly, the CRF/Cs would need to produce higher-quality trial activity and be more consistent in hitting participant recruitment targets before seeking industry investment. Secondly, a lack of standardisation across processes and regulations was believed by some to hinder Ireland's potential to be a high-quality location to conduct clinical trials.

"We are not delivering on the trials in terms of recruitment and time to deliver. Time for contract and sign-off and getting the studies up and running is very slow. But before we start charging for the luxury of coming to Ireland to do our clinical research, we need to be offering luxury service and we are not."

"A lot of countries get money from industry-led clinical trials, but they won't get them unless they are top of the range. I don't believe there is any easy money from industry. It's massively competitive."

Looking forward, funding of clinical trial activity in Ireland could not be purely dependent on commercial or industry-focused research. The belief is that the long-term strategy should focus on investigator-led clinical trial activity. While industry can provide a degree of funding, this should be used to supplement core staff funding, which is a requirement that cannot be overlooked or supplied from elsewhere.

"Core support for research and core support for the infrastructures long term [is lacking]. Core funding as opposed to programmatic funding is a real problem. Particularly with income with the retention of staff."

"We have a very small core staff, we have a programme manager and a half-time administrator; that's our core funding for staff and it is not enough."

7.5.2 Inequity of supports across the clinical research infrastructure

As noted previously in Section 5.4, the strategic importance of clinical research varies across universities, with differing levels of financial support given by the institutions towards clinical research. Some make substantial financial contributions, while others see the time used by joint appointment on clinical research as a core support.

Given the funding structure of the clinical research infrastructure and the varying levels of support the HRB provides across it, the inequity in funding is queried by many. Inequity in funding is seen as something that would not be pragmatic in the long term and may, in fact, act as a barrier to collaboration for some. The institutions/facilities with higher levels of support are seen to have better skills, more resources, and more time available to them.

"The HRB is funding clinical research services in some universities and not others and that creates complexity in the system because clinical research is by definition collaborative. You have different funding models which put more pressure on some sites versus others, that creates difficulties by itself."

"At the moment it's not a level playing field because some of the research centres have that resource, where they have funded posts and others don't. Yet we're all part of the infrastructure."

"Some of the things that are in the infrastructure aren't HRB funded. They're part of a network but are struggling by themselves. Some of the centres are struggling for resources more than others."

However, many believe that since each Hospital Group has an affiliated academic institution, it may be more useful to view both as a collective. Collaborating with Hospital Groups to leverage funding and ensure it is attributed to the corresponding facility seems like the best way to ensure that both academic and healthcare system money could contribute to clinical research. There is recognition that many third-level institutions are themselves constrained by funding issues and pressures, especially in terms of hiring teachers/lecturers.

"I believe the cleanest is to work with the Hospital Groups, each of which has an academic partner, and figure out what kind of core funding they can put into the hospitals and health system, to fund research."

7.5.3 Looking forward: certainty of funding and maintaining the current infrastructure

Looking forward, many feel that the next tranche of HRB funding should be focused on consolidation and ensuring that the current clinical research infrastructure is maintained. It is important for many that the HRB does not spread itself too thinly by moving investment to new areas, with a feeling that rather than potentially losing the good of the investments already made, the emphasis should be on maintenance over expansion. The feeling is that the HRB funding strategy should be a long-term vision to maximise investment, solidify the current infrastructure, and produce more consistent results.

"But the HRB have been hugely supportive and have invested a lot in this area. So, it would be good to see an appreciation of … by other funders in supporting clinical research to the same extent as well."

"I think they need to make sure that they solidify the infrastructure that they have in place. That it gets so that it becomes more consistent at delivering the long term. I think what it has invested in is good."

In line with a long-term funding strategy, there is a desire from many to have certainty attached to their funding and for it not to be cyclical – especially for CTNs. Having to apply for funding in tranches creates uncertainty about the future of the individual centres and the associated jobs. Indefinite funding and the end of some research programmes means the research system may lose talented and skilled individuals, particularly research nurses.

"To keep us is operation, it is on a three-year cycle or a five-year cycle of funding. We need to quit that and say this is [a] permanent facility, it's part of the hospital."

"Good clinical research is going to cost money. It is not pretending that three years of research, of support will create an infrastructure which is then self-sustaining."

8 Conclusions

8.1 Clinical research infrastructure in Ireland: the present state

This report presented a review of the current clinical research infrastructures in Ireland. As highlighted, the review prioritised HRB-funded and associated clinical research infrastructures, which are part of a wider and more diverse landscape of clinical research infrastructures in Ireland.

Since 2007, the Irish government, through the HRB, has invested more than €160 million in the development of a national clinical research system with several components. On an annual basis, the HRB continues to invest approximately €8–10 million in clinical research infrastructures. The current round of contracts for HRB-funded clinical research infrastructures comes to an end from 2021 to 2022. The purpose of this review was to inform the HRB's strategic priorities for future investment in this area.

Understanding the diversity, synergies, and capabilities of our clinical research infrastructures is important to our consideration of future investments in this area. The review looked at the current funding status, level of integration with the healthcare system, activities, services, resources, capacity, and capabilities of existing HRB-funded and associated clinical research infrastructures in Ireland, in order to identify where strengths, synergies, gaps, and duplications exist in the system.

8.1.1 What the review shows

The review highlights the diversity in the size, type, services, and supports that each HRB-funded and associated clinical research infrastructure is providing to the health research community. Only CRF/Cs truly offer the full spectrum of supports from study setup through to study closeout on a regular basis, although some CTNs sought to offer services and supports that matched/duplicated those provided by the CRF/Cs. Clusters of specialised roles were noted across the HRB-funded and associated clinical research infrastructures (biostatistics, data management, pharmacovigilance, and quality and regulatory affairs); however, there was a noted lack of biostatistics expertise in the system, outside of the HRB-CRF Galway and the UCD CRC.

Many see clinical research in Ireland moving in a positive direction, driven forward by enthusiastic individuals and strategically minded institutions. In May 2018, HRB-funded clinical research infrastructures employed approximately 440 highly educated and skilled individuals with responsibility for managing the conduct of approximately 570 clinical trials/studies.

International benchmarking shows that despite significant improvements in the clinical research infrastructure in Ireland in recent years, there is still a significant difference in our level of clinical trial activity (interventional studies) compared with our European counterparts. In 2018, there were approximately 370 clinical trials either open or recruiting in Ireland, compared with roughly 1,200 in Denmark, 700 in Norway, and 530 in Finland.

Cancer is the main disease area for clinical research activity in HRB-funded and associated clinical research infrastructures, with 34% of current trial activity focusing on the area of cancer.

Industry is the predominant funder of clinical trial activity in HRB-funded and associated clinical research infrastructures, with 58% of all active trials supported by industry and 27% supported by national funding agencies.

Overall, clinical research activity is happening in isolated pockets, and not as part of a cohesive national research system. As a result, the clinical research infrastructures are seen more as a network of independent centres rather than as a cohesive infrastructure. For many stakeholders and infrastructure users this means that there are barriers to accessing skills and services, and that duplication and resource inefficiencies exist within the clinical research system.

There is a need for better coordination of clinical research infrastructures in Ireland.

The variability in funding across the different clinical research infrastructures is seen as something that is not sustainable in the long term and may, in fact, act as a barrier to collaboration/shared information.

Because research is not a fully integrated feature of the Irish healthcare system, significant barriers exist to the effective conduct of clinical research, such as an absence of defined career progression paths and funding uncertainty for personnel within the healthcare system.

Clinical research staff within the HRB-funded and associated clinical research infrastructures are funded through grants from universities and funding agencies such as the HRB (more than 51% of respondents to the staff survey were on temporary contracts). This leads to a number of resource constraints, particularly for research nurses and professional support staff, as temporary positions are unattractive to highly skilled staff and thus are difficult to fill.

Understandably, funding is a central issue, but it is accepted that increased funding on its own is not the solution to all problems within the clinical research infrastructure in Ireland.

8.2 Clinical research infrastructure in Ireland: suggestions for the national system

Clinical research infrastructures are strategically valuable assets for Ireland. It is generally recognised that clinical research infrastructures enable the health research community to be at the forefront of high-quality clinical research activity, including clinical trials, which has a positive impact on the care and health outcomes of the population.

The review considered the role of industry in supporting clinical research infrastructures into the future. Although the interview responses largely focused on clinical trial activity support, it was clear to the HRB that there is a need to consider the role of the enterprise agencies in providing support for the core clinical research infrastructures needed to maximise economic impact.

Overall, a cohesive national research system requires active engagement and collaboration within the health family i.e. the DOH, the HSE and the HRB, in addition to the universities, enterprise agencies and industry.

8.2.1 Awareness raising

Patient outcomes and the tangible benefits of clinical research need to be the central message in communications about clinical research activity. This shift in focus away from more academic outputs could potentially advance HSE/DOH ability to showcase the positive impacts of clinical research and enhance their ability to secure increased resources at governmental level to enable them to participate more in supporting research within the healthcare system.

To this end, an evaluation of public investment in clinical research focused on the return on investment and broader economic and societal impact (for the system and for patients) would be an important way to provide robust evidence to underpin this message. Such a study should be considered as part of a national approach to clinical research activity.

8.2.2 Strategic national approach

A more strategic national approach to clinical research infrastructures in Ireland is needed in order to ensure that as a country we continue to reap the benefits of the infrastructures we already support, as well as those of the future.

The qualitative responses noted that “it is not the HRB’s role as a funding agency to drive research policy at a broad national level and that this is the responsibility of the DOH and the HSE”. Although the DOH is the setter of national policy, the HRB (and the HSE R&D team) has a key role in guiding and working with the DOH to develop national research policy.

Internationally, a strategic roadmap is the accepted approach to planning for investments in national research infrastructures. In 2007, Ireland published a national roadmap for research infrastructures.[13] At the time, most of the current clinical research infrastructures were yet to be commissioned.

Therefore, the HRB welcomes the establishment of the planned Sláintecare Health R&D Forum in 2019 to address the current lack of coordination between different initiatives, research entities, and Government agencies in order to ensure that we achieve a more strategic national approach to investment in clinical research infrastructure in Ireland and the research it supports.

8.2.3 Supporting clinical research infrastructure (human capital) within an integrated healthcare system

Human capital, that is, the highly skilled and educated workforce that enables clinical research activity within clinical research infrastructures, is a critical and essential component of the clinical research infrastructure landscape.

Clinical research infrastructures require a highly specialised skill base in a wide range of disciplines, including but not limited to research nurses, data managers, statisticians, and methodologists. These skill sets are highly sought after by others, including industry, highlighting the challenge of retaining staff.

However, retaining staff is not just about financial incentives. Secure employment is an important factor. Unfortunately, the current mechanism of funding, which is uncertain and results in short-term contracts (typically lasting three to five years), means inevitable insecurity for key personnel. This also makes it more difficult to manage and operate clinical research infrastructures. Greater certainty attached to tenure is desired, as the cyclical nature of funding may hinder longer-term strategic planning and development.

Another common issue reported in this review was the lack of career progression for clinical research personnel, particularly research nurses. This is mainly within the remit of the HSE (e.g. alignment of clinical research nursing posts and career progression with the normal nursing career pathway), and integration of research expertise into the grading when a nurse reverts to a service post is crucial. The same principle should apply to other healthcare practitioners.

It is widely acknowledged that clinical research should be a core activity within the healthcare system, with healthcare professionals having the protected time to pursue research. We acknowledge that newly appointed cancer consultants and advanced nurse practitioners have protected time for research. However, while protected time for research can be incorporated into new employment contracts, it needs the appropriate supports in order to ensure that it is also a reality on the ground, and the mechanisms needed to make this happen still need to be delivered on.

Having the health family and others invest more collectively in the clinical research infrastructure, for example, through support for core posts in research nursing and data management, would be a significant step towards the development of a more consistent and cohesive national system that values research and embeds clinical research into usual care. This would mean that providing Irish patients with access to clinical trials and other benefits of research would be the norm rather than the exception.

8.3 Clinical research infrastructures in Ireland: Principles for HRB's consideration in future investments

As the lead agency supporting and funding health research in Ireland, the HRB acknowledges that our primary remit is to support health research activity. Since 2007, we have broadened our investment beyond research activity to building an enabling environment for health research in Ireland through investment in clinical research infrastructures that can support excellence, build critical mass, and improve coordination across the system.

We will continue to invest in clinical research infrastructures, but with a clear understanding that our role should be to initiate clinical research activity and "pump prime" the system. In time, the HRB's investment in clinical research infrastructures should be scaled back to enable support to be diverted to other strategic areas.

The following principles will be considered by the HRB as we reflect on our strategic direction for future investments in this area.

8.3.1 Shared investment model

For any future investment in clinical research infrastructures, a shared investment model is critical, not only to leverage additional resources, but also to ensure the step change needed to achieve sustained integration of research within the healthcare system.

Any shared investment models need to be considered in the context of Sláintecare and the new regional integrated hospital-community structures in order to ensure that clinical research infrastructures are future-proofed in line with the future structure of the healthcare system.

Currently, the HRB provides the only dedicated funding stream (i.e. Definitive Interventions and Feasibility Awards) for clinical trials and interventions available to the research community. However, as we are also the lead funder of core staff in the clinical research infrastructures, our capacity to invest in actual clinical research activity is limited.

Moving to a shared investment model for all clinical research infrastructure investment will enable the HRB to divert its resources for infrastructures support to new investments in clinical research activity.

8.3.2 Duration of investment

There was a persistent desire expressed during the review for more certainty attached to funding, since the current cyclical nature of funding may hinder long-term planning and development of clinical research infrastructures.

As a funder, it is difficult for the HRB to move away from this mechanism of cyclical funding, which speaks to the need to be clearer about our role in supporting clinical research infrastructures. HRB funding should only support the short- and medium-term development of infrastructures and is not suitable for provision of longer-term support. For this reason, any investment in infrastructure should be made with a clear exit strategy for the HRB, ideally with an orderly transition towards full integration into the healthcare system.

Consistent longer-term core supports need to be met at a national level. Through the R&D Forum under Sláintecare, the HRB would like to address this with other research entities and Government agencies in order to ensure a more strategic and sustainable national approach to investment in clinical research infrastructures and the research they support.

8.3.3 Skills gap

As noted, clinical research infrastructures require a highly specialised skill base in a wide range of disciplines in order to enable clinical research activity. The appropriate skill mix is a critical and essential element of the clinical research infrastructure. A notable skills gap was reported in the area of biostatistics expertise within the system.

In alignment with the *HRB Strategy 2016–2020*, a highly skilled workforce is key to the successful delivery of each of our objectives. Therefore, through our framework for the development of health research careers[14] – which is aimed at training and supporting health researchers at different levels throughout their career, from early stages to leading health research – the HRB should consider appropriate opportunities to build capacity in this specific area for health research.

8.3.4 Approach to investments

Echoing the advice of our International Advisory Committee and in line with the aforementioned principles, the HRB's future investment in clinical research infrastructures should be based on a shared investment model and judged in an open and competitive process to select the best quality infrastructures.

The quality of clinical research infrastructures should be based on:

- Inclusiveness
- Visibility/awareness
- Accessibility
- Performance
- Utilisation, and
- Relevance for the academic and healthcare practitioner research community.

8.4 Next steps

This review provided valuable insights for the HRB into the current state of the HRB-funded and associated clinical research infrastructures in Ireland and how these are perceived and used by the research community

Combined with HRB's experience of managing and evaluating clinical research infrastructures it provided important inputs to crystalise key principles for the HRB's consideration in future investments in this space.

As a next step the HRB will use these principles to prepare an overall funding strategy and action plan for investment in this area, whilst working with members of the health family (and others) to develop a call for Clinical Research Facilities/Centres.

Appendices

Appendix A Infrastructure survey template

Clinical Research Infrastructure

Infrastructure Survey

Introduction

Thank you for agreeing to take part in this survey. This survey will be used by the Health Research Board (HRB) to assess and review the current clinical research infrastructures in Ireland. The information that you provide will be used to inform the future investments of the HRB in this area.

The survey should only take 5–10 minutes to complete and all answers will be kept strictly confidential.

Background

Over the past decade, the HRB has invested more than €100 million to develop a national clinical research system. The goal of this investment was to create the right environment and build capacity to do clinical research in Ireland and to establish Ireland as a high-quality location to conduct clinical research and trials.

Now, as the HRB begins to develop its next strategy of funding, it is important to assess these existing infrastructures and to generate sufficient evidence on current gaps/synergies, duplications, and needs of the clinical research infrastructure in Ireland.

Please click “next page” to begin.

Physical Infrastructure

1. Does your facility have full-service Phase I capability?

- [ ] Yes
- [ ] No

2. If no, please specify a reason:

- [ ] 0. n/a
- [ ] 1. Insufficient trained and experience staff
- [ ] 2. Insufficient emergency equipment and infrastructure
- [ ] Other (please specify):

3. Enter the current number of inpatient beds available for clinical research participants in your facility:

Approximately what percentage of these inpatient beds are used on a daily basis?

4. Enter the current number of outpatient beds available for clinical research participants in your facility:

Approximately what percentage of these outpatient beds are used on a daily basis?

Rooms/suites

5. Select “dedicated” if your infrastructure provides any of the following facilities and they are solely dedicated to clinical research. Select “non-dedicated” if your infrastructure provides any of the following facilities but they are not solely dedicated to clinical research. If this section is not relevant to your infrastructure, click “next page” at the bottom of the page.

	Dedicated	Non-dedicated
1. Aseptic rooms/suites	☐	☐
2. Catheter labs	☐	☐
3. Consultation and examination rooms/suites	☐	☐
4. Dietetics kitchens	☐	☐
5. Echocardiology rooms/suites	☐	☐
6. EEG rooms/suites	☐	☐
7. Endoscopy rooms/suites	☐	☐
8. Exercise physiology rooms/suites	☐	☐
9. GMP facilities	☐	☐
10. Isolation rooms/suites	☐	☐
11. Pharmacy rooms/suites	☐	☐
12. Phlebotomy rooms/suites	☐	☐
13. Procedure rooms/suites	☐	☐

6. Select “infrastructure” if these facilities are located and primarily accessed within the clinical research infrastructure. Select “hospital” if these facilities are located and primarily accessed within the hospital wards but outside of the clinical research infrastructure. Select “community” if these facilities are located and primarily accessed within the community.

	Infrastructure	Hospital	Community
1. Aseptic rooms/suites	☐	☐	☐
2. Catheter labs	☐	☐	☐
3. Consultation and examination rooms/suites	☐	☐	☐
4. Dietetics kitchens	☐	☐	☐
5. Echocardiology rooms/suites	☐	☐	☐
6. EEG rooms/suites	☐	☐	☐
7. Endoscopy rooms/suites	☐	☐	☐
8. Exercise physiology rooms/suites	☐	☐	☐
9. GMP facilities	☐	☐	☐
10. Isolation rooms/suites	☐	☐	☐

	Infrastructure	Hospital	Community
11. Pharmacy rooms/suites	☐	☐	☐
12. Phlebotomy rooms/suites	☐	☐	☐
13. Procedure rooms/suites	☐	☐	☐

Laboratories

7. Select "dedicated" if your infrastructure provides any of the following laboratory facilities and they are solely dedicated to clinical research. Select "non-dedicated" if your infrastructure provides any of the following facilities but they are not solely dedicated to clinical research. If this section is not relevant to your infrastructure, click "next page" at the bottom of the page.

	Dedicated	Non-dedicated
1. Analytic labs	☐	☐
2. Aseptic labs	☐	☐
3. Biochemistry	☐	☐
4. Haematology	☐	☐
5. Imaging labs	☐	☐
6. Immunology	☐	☐
7. Microbiology	☐	☐
8. Neuropathology	☐	☐
9. Pharmacokinetic (PK) labs	☐	☐
10. Pre-analytical processing labs	☐	☐

8. Select "infrastructure" if these laboratories are located and primarily accessed within the clinical research infrastructure. Select "hospital" if these laboratories are located and primarily accessed within the hospital wards but outside of the clinical research infrastructure. Select "community" if these laboratories are located and primarily accessed within the community.

	Infrastructure	Hospital	Community
1. Analytic labs	☐	☐	☐
2. Aseptic labs	☐	☐	☐
3. Biochemistry	☐	☐	☐
4. Haematology	☐	☐	☐
5. Imaging labs	☐	☐	☐
6. Immunology	☐	☐	☐

	Infrastructure	Hospital	Community
7. Microbiology	☐	☐	☐
8. Neuropathology	☐	☐	☐
9. Pharmacokinetic (PK) labs	☐	☐	☐
10. Pre-analytical processing labs	☐	☐	☐

Administrative space

9. Select "dedicated" if your infrastructure has any of the following administrative spaces and they are solely dedicated to clinical research. Select "non-dedicated" if your infrastructure has any of the following administrative spaces but they are not solely dedicated to clinical research. If this section is not relevant to your infrastructure, click "next page" at the bottom of the page.

	Dedicated	Non-dedicated
1. Offices	☐	☐
2. Meeting rooms	☐	☐
3. Monitor rooms	☐	☐

Of the office space, please indicate the occupancy and capacity of each room. e.g. #1: 5 desks occupied out of 6.

10. Select "infrastructure" if these administrative spaces are located and primarily accessed within the clinical research infrastructure. Select "hospital" if these administrative spaces are located and primarily accessed within the hospital wards but outside of the clinical research infrastructure. Select "community" if these administrative spaces are located and primarily accessed within the community.

	Infrastructure	Hospital	Community
1. Offices	☐	☐	☐
2. Meeting rooms	☐	☐	☐
3. Monitor rooms	☐	☐	☐

IT systems

11. Select the clinical information system/s that you use.

☐ 0. n/a

☐ 1. CRF Manager

☐ 2. Maternal & Newborn Clinical Management System

- [ ] 3. iSoft Patient Administration System
- [ ] 4. iSoft Clinical Manager System (iCM)
- [ ] 5. MediData Rave
- [ ] 6. MACRO
- [ ] 7. OpenClinica
- [ ] 8. IBM Clinical Development
- [ ] 9. EDGE
- [ ] Other (please specify):

12. Do you have a dedicated website?

- [ ] Yes
- [ ] No

13. If yes, please enter the URL:

Study setup supports and services

14. Study set-up - Select the frequency – "weekly", "monthly", or "yearly" – at which the following supports and services are provided by your infrastructure. If this section is not relevant to your infrastructure, please click "next page" at the bottom of the page.

	Weekly	Monthly	Yearly
1. Biostatistical support	☐	☐	☐
2. Budget analysis	☐	☐	☐
3. Contractual support	☐	☐	☐
4. Data management planning	☐	☐	☐
5. Ethics submissions	☐	☐	☐
6. Feasibility support	☐	☐	☐
7. Grant application support	☐	☐	☐
8. Insurance/indemnity	☐	☐	☐
9. Methodological support	☐	☐	☐

	Weekly	Monthly	Yearly
10. Pharmacovigilance	☐	☐	☐
11. Protocol development	☐	☐	☐
12. Quality and monitoring planning	☐	☐	☐
13. Regulatory support	☐	☐	☐
14. Risk assessment	☐	☐	☐
15. Signposting	☐	☐	☐
16. Site initiation	☐	☐	☐
17. Sponsorship support	☐	☐	☐
18. Study design review	☐	☐	☐

15. Select “in-house” if these supports and services are primarily provided by your infrastructure. Select “outsourced” if these supports and services are primarily provided using expertise from outside your infrastructure.

	In-house	Outsourced
0. n/a	☐	☐
1. Biostatistical support	☐	☐
2. Budget analysis	☐	☐
3. Contractual support	☐	☐
4. Data management planning	☐	☐
5. Ethics submissions	☐	☐
6. Feasibility support	☐	☐
7. Grant application support	☐	☐
8. Insurance/indemnity	☐	☐
9. Methodological support	☐	☐
10. Pharmacovigilance	☐	☐
11. Protocol development	☐	☐
12. Quality and monitoring planning	☐	☐
13. Regulatory support	☐	☐
14. Risk assessment	☐	☐

	In-house	Outsourced
15. Signposting	☐	☐
16. Site initiation	☐	☐
17. Sponsorship support	☐	☐
18. Study design review	☐	☐

Study conduct supports and services

16. Study conduct Select the frequency – "weekly", "monthly", or "yearly" – at which the following supports and services are provided by your facility. If this section is not relevant to your infrastructure, please select "next page" at the bottom of the page.

	Weekly	Monthly	Yearly
0. n/a	☐	☐	☐
1. Auditing and quality management	☐	☐	☐
2. Biobanking	☐	☐	☐
3. Biospecimen collection and processing	☐	☐	☐
4. Biostatistical support	☐	☐	☐
5. Biostorage facilities	☐	☐	☐
6. Clinical support	☐	☐	☐
7. Data collection/cleaning	☐	☐	☐
8. Data management	☐	☐	☐
9. IMP storage/reconciliation	☐	☐	☐
10. Methodological support	☐	☐	☐
11. Multicentre study coordination	☐	☐	☐
12. Patient recruitment/monitoring	☐	☐	☐
13. Pharmacovigilance/safety reporting	☐	☐	☐
14. Protocol amendment support	☐	☐	☐
15. Site management	☐	☐	☐
16. Study monitoring	☐	☐	☐

17. Study conduct Select “in-house” if these supports and services are primarily provided within your infrastructure. Select “outsourced” if these supports and services are primarily provided using expertise from outside your infrastructure.

	In-house	Outsourced
0. n/a	☐	☐
1. Auditing and quality management	☐	☐
2. Biobanking	☐	☐
3. Biospecimen collection and processing	☐	☐
4. Biostatistical support	☐	☐
5. Biostorage facilities	☐	☐
6. Clinical support	☐	☐
7. Data collection/cleaning	☐	☐
8. Data management	☐	☐
9. IMP storage/reconciliation	☐	☐
10. Methodological support	☐	☐
11. Multicentre study coordination	☐	☐
12. Patient recruitment/monitoring	☐	☐
13. Pharmacovigilance/safety reporting	☐	☐
14. Protocol amendment support	☐	☐
15. Site management	☐	☐
16. Study monitoring	☐	☐

Study closeout supports and services

18. Study closeout Select the frequency – “weekly”, “monthly”, or “yearly” – at which the following supports and services are provided by your infrastructure. If this section is not relevant to your infrastructure please click “next page” at the bottom of the page.

	Weekly	Monthly	Yearly
0. n/a	☐	☐	☐
1. Archiving	☐	☐	☐
2. Biospecimen management	☐	☐	☐
3. Data dissemination support	☐	☐	☐

	Weekly	Monthly	Yearly
4. Data management	☐	☐	☐
5. IMP management	☐	☐	☐
6. Medical writing	☐	☐	☐
7. Monitoring	☐	☐	☐
8. Pharmacovigilance reporting/reconciliation	☐	☐	☐
9. Site and file closeout	☐	☐	☐
10. Statistical analysis	☐	☐	☐
11. Trial closeout reporting	☐	☐	☐

19. Study closeout Select “in-house” if these supports and services are primarily provided within your infrastructure. Select “outsourced” if these supports and services are primarily provided using expertise from outside your infrastructure.

	In-house	Outsourced
0. n/a	☐	☐
1. Archiving	☐	☐
2. Biospecimen management	☐	☐
3. Data dissemination support	☐	☐
4. Data management	☐	☐
5. IMP management	☐	☐
6. Medical writing	☐	☐
7. Monitoring	☐	☐
8. Pharmacovigilance reporting/reconciliation	☐	☐
9. Site and file closeout	☐	☐
10. Statistical analysis	☐	☐
11. Trial closeout reporting	☐	☐

20. Which clinical research infrastructure are you reporting from?

- [ ] 1. Wellcome Trust – HRB CRF at St. James's Hospital
- [ ] 2. HRB-CRF University College Cork
- [ ] 3. HRB-CRF National University of Ireland in Galway
- [ ] 4. Royal College of Surgeons in Ireland Clinical Research Centre (CRC) at Beaumont Hospital
- [ ] 5. University College Dublin CRC at St. Vincent's and the Mater
- [ ] 6. University of Limerick Health Research Institute Clinical Research Support Unit
- [ ] 7. National Children's Research Centre at Our Lady's Children's Hospital, Crumlin
- [ ] 8. Centre for Advanced Medical Imaging (CAMI)
- [ ] 9. HRB Clinical Research Coordination Ireland
- [ ] 10. HRB Trials Methodology Research Network
- [ ] 11. Cancer Trials Ireland
- [ ] 12. HRB Mother and Baby CTN Ireland
- [ ] 13. HRB Stroke CTN Ireland
- [ ] 14. HRB Irish Critical Care CTN
- [ ] 15. HRB Primary Care CTN Ireland
- [ ] 16. Irish Research Nurses Network

Appendix B Clinical trial activity template

Study acronym	Status	Regulated	Study type	Multicentre	International	Funding source	HRCS	HIPE	Total Patients	Recruitment to target?	# days FPFV

Appendix C Staff survey template

Clinical Research Infrastructure:

Staff survey

Introduction

Thank you for agreeing to take part in this survey. This survey will be used by the Health Research Board (HRB) to assess and review the current clinical research infrastructures in Ireland. The information that you provide will be used to inform the future investments of the HRB in this area.

This survey should be completed by all staff working in clinical research infrastructures in Ireland. This survey should only take 5–10 minutes to complete and all answers will be kept strictly confidential.

Please note: At the end of this survey you will be asked to give consent in line with the General Data Protection Regulation (GDPR).

Background

Over the past decade, the HRB has invested more than €100 million to develop a national clinical research system. The goal of this investment was to create the right environment and build capacity to do clinical research in Ireland and to establish Ireland as a high-quality location to conduct clinical research and trials.

Now, as the HRB begins to develop its next strategy of funding, it is important to assess these existing infrastructures and to generate sufficient evidence on current gaps/synergies, duplications, and needs of the clinical research infrastructure in Ireland.

Please click “next page” to begin.

1. Please indicate the gender you identify most with.

- [ ] 1. Male
- [ ] 2. Female
- [ ] 3. Prefer not to say
- [ ] 4. Prefer to use my own term

If you prefer to use your own term, please specify:

2. Choose the option that most closely reflects your current academic research position:

- [ ] 0. n/a
- [ ] 1. Undergraduate student
- [ ] 2. Master student
- [ ] 3. Studentship
- [ ] 4. PhD student
- [ ] 5. Post-doctoral researcher (1–5 years)
- [ ] 6. Post-doctoral researcher (+5 years)
- [ ] 7. Research fellow
- [ ] 8. Senior research fellow
- [ ] 9. Lecturer (below the bar)
- [ ] 10. Lecturer (above the bar)
- [ ] 11. Senior lecturer
- [ ] 12. Associate professor
- [ ] 13. Professor
- [ ] Other (please specify):

3. If you are a nurse, choose the option that most closely reflects your current position:

- [ ] 0. n/a
- [ ] 1. Clinical research nurse/midwife
- [ ] 2. Clinical nurse/midwife manager 1
- [ ] 3. Clinical nurse/midwife manager 2
- [ ] 4. Clinical instructor
- [ ] 5. Clinical nurse manager 3
- [ ] 6. Associate director of nursing
- [ ] 7. Director of nursing
- [ ] Other (please specify):

4. Choose the option that most closely reflects your current clinical research position:

- [ ] 0. n/a
- [ ] 1. Academic study/trial coordinator/manager
- [ ] 2. Biostatistician
- [ ] 3. Chief operating officer
- [ ] 4. Chief pharmacist
- [ ] 5. Clinical fellow including senior house officer/medical officer
- [ ] 6. Clinical therapist
- [ ] 7. Clinical trials liaison officer
- [ ] 8. Communications officer
- [ ] 9. Contracts manager
- [ ] 10. Data manager/information officer
- [ ] 11. Database developer

- [ ] 12. Director/associate director
- [ ] 13. Executive assistant/HR/administrator
- [ ] 14. Financial analyst
- [ ] 15. Financial officer
- [ ] 16. Health economist
- [ ] 17. Industry study/trial coordinator/manager
- [ ] 18. IT manager
- [ ] 19. Lab coordinator
- [ ] 20. Lab technician
- [ ] 21. Medical consultant
- [ ] 22. Operations manager/programme manager
- [ ] 23. Pharmacist
- [ ] 24. Pharmacist technician
- [ ] 25. Pharmacovigilance officer
- [ ] 26. Quality and regulatory affairs director
- [ ] 27. Quality and regulatory affairs manager
- [ ] 28. Quality and regulatory affairs officer/associate
- [ ] 29. Research and development manager
- [ ] 30. Research associate/assistant
- [ ] 31. Senior data manager
- [ ] 32. Study monitor/clinical research associate
- [ ] Other (please specify):

5. Which clinical research infrastructure are you most closely affiliated with?

- [ ] 1. Wellcome Trust – HRB CRF at St. James's Hospital
- [ ] 2. HRB-CRF University College Cork
- [ ] 3. HRB-CRF National University of Ireland in Galway
- [ ] 4. Royal College of Surgeons in Ireland Clinical Research Centre (CRC) at Beaumont Hospital
- [ ] 5. University College Dublin CRC at St. Vincent's and the Mater
- [ ] 6. University of Limerick Health Research Institute Clinical Research Support Unit
- [ ] 7. National Children's Research Centre at Our Lady's Children's Hospital, Crumlin
- [ ] 8. Centre for Advanced Medical Imaging (CAMI)
- [ ] 9. HRB Clinical Research Coordination Ireland
- [ ] 10. HRB Trials Methodology Research Network
- [ ] 11. Cancer Trials Ireland
- [ ] 12. HRB Mother and Baby CTN Ireland
- [ ] 13. HRB Stroke CTN Ireland
- [ ] 14. HRB Irish Critical Care CTN
- [ ] 15. HRB Primary Care CTN Ireland
- [ ] 16. Irish Research Nurses Network
- [ ] Other (please specify):

6. What FTE of your current contract is dedicated to clinical research? (note: this must be a numeric value from 0.0–1.0)

7. What is your employment contract type?

- [ ] 1. Permanent
- [ ] 2. Contract of indefinite duration
- [ ] 3. Fixed-term contract
- [ ] 4. Hourly occasional
- [ ] Other (please specify):

8. Is your salary funded by one source only? If so, please specify the source.

- [ ] 0. n/a
- [ ] 1. University
- [ ] 2. HSE
- [ ] 3. Project/programme/career award funding
- [ ] 4. Infrastructure/network funding
- [ ] 5. Philanthropy
- [ ] 6. Industry
- [ ] Other (please specify):

9. Is your salary funded by more than one source? If so, please specify all sources.

- [ ] 0. n/a
- [ ] 1. University
- [ ] 2. HSE
- [ ] 3. Project/programme/career award funding
- [ ] 4. Infrastructure/network funding
- [ ] 5. Philanthropy
- [ ] 6. Industry
- [ ] Other (please specify):

Please indicate the percentage split of your salary, if known:

10. Do you hold a joint appointment with a university and a hospital?

- [ ] 0. n/a
- [ ] 1. Yes
- [ ] 2. No

11. In what subject area did you undertake your primary degree/qualification?

- [ ] 0. n/a
- [ ] 1. Biological/biomedical sciences
- [ ] 2. Business studies
- [ ] 3. Chemistry
- [ ] 4. Commerce
- [ ] 5. Computer science
- [ ] 6. Dental studies
- [ ] 7. Economics
- [ ] 8. Education
- [ ] 9. Engineering
- [ ] 10. Environmental science
- [ ] 11. European studies
- [ ] 12. General science
- [ ] 13. Genetics
- [ ] 14. Health science
- [ ] 15. Humanities
- [ ] 16. Languages
- [ ] 17. Law
- [ ] 18. Management
- [ ] 19. Mathematics/statistics
- [ ] 20. Medicine

- [ ] 21. Microbiology
- [ ] 22. Nursing
- [ ] 23. Nutrition science
- [ ] 24. Pharmacy/pharmacology
- [ ] 25. Physics
- [ ] 26. Politics
- [ ] 27. Psychology
- [ ] 28. Social sciences
- [ ] 29. Therapies
- [ ] Other (please specify):

12. In what areas have you received further formal qualifications? Tick master's or PhD, if relevant.

	MSc	PhD
0. n/a	☐	☐
1. Applied statistics	☐	☐
2. Bioinformatics	☐	☐
3. Biostatistics	☐	☐
4. Biomedical science/diagnostics	☐	☐
5. Biopharmaceuticals	☐	☐
6. Cell biology	☐	☐
7. Child health	☐	☐
8. Clinical research	☐	☐
9. Clinical and translational research	☐	☐
10. Clinical trials methodology/conduct	☐	☐
11. Education	☐	☐
12. Epidemiology	☐	☐
13. Ethics in healthcare	☐	☐
14. Global health	☐	☐

	MSc	PhD
15. Healthcare policy	☐	☐
16. Healthcare management	☐	☐
17. Health economics	☐	☐
18. Health psychology	☐	☐
19. Health services research	☐	☐
20. Health technology assessment	☐	☐
21. Inequality and social care	☐	☐
22. International health sciences	☐	☐
23. Immunology	☐	☐
24. Mathematics	☐	☐
25. Medical anthropology	☐	☐
26. Mental health and disability	☐	☐
27. Medical imaging	☐	☐
28. Microbiology/bacteriology	☐	☐
29. Modelling in healthcare	☐	☐
30. Molecular medicine	☐	☐
31. Nursing	☐	☐
32. Nutrition	☐	☐
33. Occupational health	☐	☐
34. Pharmacy	☐	☐
35. Physiotherapy	☐	☐
36. Primary care	☐	☐
37. Public health	☐	☐
38. Risk analysis	☐	☐
39. Social sciences relevant to healthcare	☐	☐

13. Have you obtained any diplomas or certificates of further training? Please tick all that apply.

- [ ] 0. n/a
- [ ] 1. Biostatistics
- [ ] 2. Bioinformatics
- [ ] 3. Clinical project management
- [ ] 4. Clinical and translational research course
- [ ] 5. Cochrane training, including evidence synthesis training
- [ ] 6. Data protection
- [ ] 7. Ethics
- [ ] 8. General project management
- [ ] 9. Good Clinical Laboratory Practice (GCLP)
- [ ] 10. Good Laboratory Practice (GLP)
- [ ] 11. Good Manufacturing Process (GMP)
- [ ] 12. ICH-Good Clinical Practice (GCP) including refresher courses and incorporating E6(R2) Addendum
- [ ] 13. ICH-Good Clinical Practice for medical devices
- [ ] 14. Journalology
- [ ] 15. Medical device regulation training
- [ ] 16. Medical writing and data presentation
- [ ] 17. Meta-analysis
- [ ] 18. Pharmacovigilance
- [ ] 19. Public Patient Involvement (PPI) training
- [ ] 20. Research integrity
- [ ] 21. Risk-based monitoring
- [ ] 22. Risk management in clinical research
- [ ] 23. Trial methodology
- [ ] Other (please specify):

14. Is there a career progression structure and promotion opportunities available to you?

- [ ] 0. n/a
- [ ] 1. Yes
- [ ] 2. No

15. If yes, why?

- [ ] Clear career path and promotion steps in your profession
- [ ] Clear opportunities for increased responsibility in your role
- [ ] Expert and professional training provided to allow growth and development
- [ ] Senior positions available
- [ ] Other (please specify):

16. If no, why?

- [ ] No career path for your profession
- [ ] No opportunities for increased responsibility in your role
- [ ] Lack of available positions
- [ ] Have reached the peak of career path
- [ ] Other (please specify):

17. Do you consent to the information you supplied in this survey up to this point being used for research purposes by the HRB and commissioned third party Amárach Research? The data supplied will be anonymised, analysed, and aggregated in a report.

- [ ] 1. Yes
- [ ] 2. No

To validate the data and since there is no national data set with clinical research staff, we are hoping to develop a national network of contacts. To facilitate this we encourage you to share your details:

Title	
First name	
Surname	
Job title	
Email address	

18. Please choose all that apply to you. Do you consent to let the HRB store your information to:

- ☐ Share the published report with you?
- ☐ Invite you to complete additional surveys about your research activity and support needs?
- ☐ None of the above?
- ☐ NOTE: The HRB will not share your contact details with any third party and will hold the data until the analysis is complete and no longer than one year, after which time they will be deleted.

Appendix D Stakeholders discussion guide

HRB clinical research infrastructure review
Interview Guide
05.07.18

1. Introduction

Interviewer
Amárach
Scope of review:
- Looking at the CRFs and CRI jigsaw to inform future investments in this area

Confidentiality
Recording

Key points to address in interviews:
- Funding
- Healthcare system (HSE) integration
- Growth, and
- Sustainability.

2. Overview (7 minutes)

- Tell me a little bit about your role and responsibilities.

- Tell me about your organisation – CRI or university or hospital.
  - What are the key drivers of clinical research in your organisation?
    - Probe: Personnel, funding, existing collaborative relationships, patient outcomes, etc.
  - What are the barriers to you supporting clinical research?
    - Probe: Clinician's time/buy-out, facilities, integration into health system, dedicated funding for research activity.

Note: Avoid labouring these points as they are well-known.

3. Clinical research infrastructure in Ireland (10 minutes)

Sent over previously a jigsaw of the clinical research infrastructure in Ireland [Figure 1.1].

- To what extent do you think that the infrastructures are fit for purpose?

- In your opinion:
  - Do you see key aspects that are missing?
  - Do you think any of these pieces overlap?
  - Do you work collaboratively with other 'pieces of the jigsaw'?
    - Probe: Are there key synergies? Duplications? New CRIs? Ease of access to all?

- Ideally, what would the integration of your CRI with the healthcare system look like?
  - Probe: Governance structures between university and/or HSE, type of staffing contract, insurance, indemnity.

4. Funding (10 minutes)

- In your opinion, what is the level of funding required for your CRI?
    - Probe: Personnel, facilities, IT systems, etc.

- Where/what organisation funds your clinical research infrastructure?
    - Is there a shortfall?
    - Where is the most critical shortfall?
        - Probe: Physical infrastructure, core funding for staff, duration of funding contracts.

- In your opinion, is there sufficient funding available for academic investigator-led clinical research activity in your CRI?

- Can you think of any international models which work in funding clinical infrastructure?
    - What are they?
    - Is there a key element of any international model that could be applied?

5. Going forward (7 minutes)

- Can you think of any ways to ensure sustainability in CRIs into the future?

- Are there other sources of funding that you think should be used to fund clinical research infrastructure?
    - Probe: Industry, universities, Hospital Groups?
        - Should they be playing a bigger role?

- Thinking of clinical research, what CRIs are needed going forward in Ireland?
    - Going forward, more healthcare will be provided in the community or at primary care; do you think we are currently set up to do research in that context?
        - Probe: What (else) would be needed?

- In summary, in your opinion, what/where do you think the HRB should invest to maximise the impact of clinical research infrastructure in Ireland?

Appendix E Service users discussion guide

HRB clinical research infrastructure review

Interview guide – accessing and perceptions of infrastructure

30.08.18

1. Introduction

Interviewer
Amárach
Scope of review:
- Looking at the CRFs and CRI jigsaw to inform future investments in this area

Confidentiality
Recording

Key points to address in interviews:
- Core functions of CRIs
- Participation and use
- Ease of access to infrastructures, and
- Industry's role in supporting national CRI.

2. Overview (7 minutes)

- Tell me a little bit about your role and research.

- Tell me about your organisation – CRI or university or industry.
  - What are the key drivers of clinical research in your organisation?
    - Probe: Personnel, funding, existing collaborative relationships, patient outcomes, etc.
  - What are the barriers to you conducting clinical research?
    - Probe: Clinician's time/buy-out, facilities, integration into health system, dedicated funding for research activity.

Note: Avoid labouring these points as they are well-known.

3. Clinical research infrastructure in Ireland (10 minutes)

Sent over previously a jigsaw of the clinical research infrastructure in Ireland [Figure 1.1].

- To what extent do you think that the infrastructures are fit for purpose?

- What is your perception of the jigsaw?
  - Probe: Would you have been aware of the various pieces?

- In your opinion:
  - Do you see key aspects that are missing?
  - Do you think any of these pieces overlap?

- Have you engaged with any aspects of the jigsaw?
  - Probe: CTNs, CRCI, TMRN, CRF/Cs.
  - If yes, what was your need and experience of the specific infrastructure?

4. Access to clinical research infrastructure

- To what extent do you think that it is easy or difficult to access the CRF/C nearby?
  - Probe: Or link in with the CTNs/TMRN/CRCI.

- In your opinion, what is the **capacity** of the current clinical research infrastructures?

- Do many of your colleagues engage in clinical research?
  - Probe: Of those who engage in clinical research, do many of these colleagues engage with the clinical research infrastructure available?
  - Probe: Barriers, supports, etc.
  - Probe: Which CRIs are accessed the most?

- What do you see as key barriers to use of the clinical research infrastructures?
  - Probe: Which ones in particular (CRFs versus CTNs, etc.). Is there a difference between accessing the CRIs?

- What are the supports you see as available if you link in?

- Where/what organisation funds your clinical research?
  - Is there a shortfall?
  - Where is the most critical shortfall?
    - Probe: Physical infrastructure, core funding for staff, duration of funding contracts.

- In your opinion, is there sufficient funding available for academic investigator-led clinical research activity?

- If there was one thing that would facilitate you to conduct clinical research what would it be?

- Have you ever worked internationally?
  - If yes, in what way is accessing clinical research infrastructure different in Ireland?
  - Is there a key element of any international model that could be applied?

5. Going forward (7 minutes)

- Can you think of any ways to ensure sustainability in CRIs into the future?

- Are there other sources of funding that you think should be used to fund clinical research infrastructure?
  - Probe: Industry, universities, Hospital Groups?
    - Should they be playing a bigger role?

- Thinking of clinical research, what CRIs are needed going forward in Ireland?
  - Going forward, more healthcare will be provided in the community or at primary care; do you think we are currently set up to do research in that context?
    - Probe: What (else) would be needed?

In summary, in your opinion, what/where do you think the HRB should invest to maximise the impact of clinical research infrastructure in Ireland?

Appendix F International Advisory Committee membership

DR LOUISE WOOD

Director of Science, Research and Evidence at the Department of Health and Social Care

Dr Wood is accountable to the Department's chief scientific adviser (Professor Chris Whitty) for policy and the National Institute for Health Research's budget to ensure it delivers ground breaking research to improve patient care and population health, and cements the UK's reputation as a leading international centre for healthcare research and science. As the Department of Health's Director of Science, Research and Evidence, she also has responsibility for science policy and research to support evidence-based policymaking.

She previously held a variety of posts in the Department's R&D Directorate and at the Medicines and Healthcare Products Regulatory Agency, where she served on the agency's board as founding director for the General Practice Research Database, forerunner to the Clinical Practice Research Datalink. She recently spent a year on secondment as Director of Policy and Public Affairs at the Association of Medical Research Charities.

Dr Wood has an honours degree in physiology from the University of Edinburgh and a PhD in biomedical science from the University of London.

DR CHRISTINE KUBIAK

Operations Director at the European Clinical Research Infrastructure Network

Dr Kubiak directs project development and the implementation of ECRIN-supported trials.

She has more than 20 years' experience in the planning, setup, and management of multinational clinical trials in various therapeutic areas and in the coordination of clinical programmes in the pharmaceutical industry.

At ECRIN since 2006, she played a key role in ECRIN's FP6- and FP7-funded projects. She currently oversees project development and the implementation of ECRIN-supported trials, and contributes to strategy and business development.

Prior to joining ECRIN, she was a project and quality manager for academic research, and an international clinical trial project manager in the pharmaceutical industry.

Dr Kubiak holds a PhD from the University of Paris XI in pharmaceutical sciences.

DR DUNCAN STEWART
Executive Vice-President of Research at The Ottawa Hospital
CEO and Scientific Director at the Ottawa Hospital Research Institute
Professor, Department of Medicine, Faculty of Medicine at the University of Ottawa
Evelyne and Rowell Laishley Chair at the Ottawa Hospital Research Institute
Senior Scientist, Regenerative Medicine Program at the Ottawa Hospital Research Institute

Dr Stewart is a pioneering Canadian cardiovascular researcher, recognised for his many important discoveries in blood vessel biology, as well as his dedication to translating these discoveries into benefits for patients and society. After beginning his career in academic cardiology at McGill University in Montreal, he moved to Toronto as Head of Cardiology at St Michael's Hospital and later became Director of the Division of Cardiology, and Executive Director of the McLaughlin Centre for Molecular Medicine at the University of Toronto. He was recruited to lead the Ottawa Hospital Research Institute (OHRI) in 2007.

Dr Stewart has published more than 200 peer-reviewed manuscripts and has received a number of distinctions and prizes, including the Dexter Man Chair of Cardiology and Research Achievement Award of the University of Toronto, and the Research Achievement Award of the Canadian Cardiovascular Society. Throughout his career, Dr Stewart has demonstrated leadership in bringing diverse groups of clinicians and scientists together to put Canada on the world stage for translational cardiovascular and regenerative medicine research.

As well as serving as CEO and Scientific Director of the OHRI, Dr Stewart is a senior scientist in OHRI's Regenerative Medicine Program and holds the Evelyne and Rowell Laishley Chair. He is Vice-President of Research at the Ottawa Hospital and a professor in the Department of Medicine at the University of Ottawa.

Bibliographical notes

[1]. For further information, visit: https://health.gov.ie/wp-content/uploads/2018/08/Sl%C3%A1intecare-Implementation-Strategy-FINAL.pdf

[2]. For further information, visit: https://www.hrb.ie/funding/evaluation/how-we-monitor-and-evaluate/

[3]. For further information, visit:

https://health.gov.ie/blog/publications/action-plan-for-health-research-2009-13/

[4] Braun, V. and Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*, 3, 77–101.

[5] *HRB Strategy 2016–2020*: Section 4, page 12: "We will consolidate and build on the progress we have made in constructing a coherent and integrated clinical research infrastructure nationally (including facilities, equipment, coordination, research support, and networks)."

[6] The 11 HRB-funded hospital sites are: St. James's Hospital; St. Vincent's University Hospital; Beaumont Hospital; Mater Misericordiae University Hospital; St Luke's Radiation Oncology Hospital; Tallaght University Hospital, incorporating the National Children's Hospital; Our Lady's Children's Hospital, Crumlin; Cork University Hospital; University Hospital Limerick; University Hospital Galway; and University Hospital Waterford.

[7] Clinical research is defined in HRB funding scheme guidance notes, see *Research Leader Awards (RL) 2020*, page 7: https://www.hrb.ie/fileadmin/2._Plugin_related_files/Funding_schemes/Research_Leader_Awards_2020_Guidance_Notes.pdf

[8] A regulated clinical trial is a clinical trial that falls under the remit of the competent authority – in Ireland, the Health Products Regulatory Authority (HPRA) – that is, they need HPRA approval. These trials typically involve an investigational medicinal product (IMP) or medical device that falls under the IMP regulatory framework (S.I. No. 190/2004), which makes compliance with a specific set of good clinical practice guidelines (ICH GCP) and the European Union (EU) clinical trial regulation (Regulation (EU) No 536/2014) or the EU medical device regulation (Regulation (EU) No 2017/745) a legal requirement for study conduct.

[9] A non-regulated clinical trial is a clinical trial that does not fall within a specific legislative framework.

[10] Additional information can be found at https://www.hrb.ie/funding/funding-schemes/all-funding-schemes/grant/definitive-interventions-and-feasibility-awards-difa-2018/

[11] In 2018, the annual HRB non-capital budget was €33 million and the overall healthcare budget in Ireland was €15.3 billion.

[12] It is important to note that the acronyms CRCI and CRDI were used interchangeably by respondents and may not always accurately reflect the body being referred to.

[13] *Research infrastructure in Ireland – building for tomorrow 2007*. Dublin: Higher Education Authority. https://ec.europa.eu/research/infrastructures/pdf/roadmaps/ireland_national_roadmap.pdf#view=fit&pagemode=none

[14] For further information, visit: https://www.hrb.ie/funding/funding-schemes/health-research-career-paths/

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