

A Review of the United Kingdom Experience with Primary Care Research Networks

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Table of Acronyms

Keywords	Acronyms
CAG	Confidentiality Advisory Group
CCGs	Clinical Commissioning Groups
CCRN	Comprehensive Clinical Research Network
CI s	Chief Investigators
CLRN s	Comprehensive Local Research Networks
CPMS	Central Portfolio Management System
CPRD	Clinical Practice Research Datalink
CRN	NIHR Clinical Research Network
DHSC	Department of Health and Social Care
EOI	
ETC	Excess Treatment Costs
GDPR	General Data Protection Regulation
GP, GPs	General Practitioner, General Practitioners
HRA	Health Research Authority
IRAs	
LCRN s	Local Clinical Research Networks
LPMS	Local Portfolio Management Systems
LSG	Local Specialty Group
MHRA	Medicines and Healthcare products Regulatory
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NSG	National Speciality Group
NSL	National Speciality Lead
PC	Primary Care
PCNs	Primary Care Networks
PCRN	Primary Care Research Network
PECR	Privacy and Electronic Communications Regulations
PI s	Principal Investigators
PPI	
RCGP	Royal College of General Practitioners
REC	Research Ethics Committee
R&D	Research and Development
UK	United Kingdom
UKCRC	UK Clinical Research Collaboration
UKCRN	UK Clinical Research Network

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Background

Although Practice Based Research Networks (PBRNs) are now widespread in Canada, they lead a tenuous existence. Without exception, they lack the infrastructure and stable funding that would allow them to reach their potential. Their lack of resources stifles their capacity to grow and to engage their members in identifying research priorities, undertaking research that addresses both local and pan-Canadian health care challenges, and improving policy and practice at the local, regional, provincial and national levels. Given this reality, the Research Department of the College of Family Physicians of Canada at the request of the College's Section of Researchers Action Group for Advocacy in Research commissioned a review of the United Kingdom (UK) experience with primary care research networks. The objective of the review was to identify lessons from the UK experience that could inform the further development of PBRNs in Canada.

Methodology

The purpose of this literature review is to examine the United Kingdom (UK) experience with primary care research networks. The review focuses on England where primary care research networks have been and continue to be most active. The review explores the origins, organizational structure, funding, infrastructure, scope, research output/impact, and challenges.

To identify literature on the primary care research networks in England, numerous exploratory keyword searches were done in bibliographic databases including MEDLINE, EMBASE, and SCOPUS. To identify relevant literature, keyword searches included 'primary care research networks' OR 'practice-based research networks' OR 'clinical research networks' AND 'England' OR 'United Kingdom'. There was no time limit specified in the search. The grey literature was also examined using the same keyword searches in Google Scholar. The literature review was supplemented by conducting key informant interviews with leaders that had experience or knowledge of primary care research networks. In total, seven key informant interviews were conducted. Refer to Appendix for Interview Guide.

Literature Review

Origins and Evolution of Primary Care Research Networks in the United Kingdom

Bottom-up Approach

In the UK, the concept of 'networks' in primary care (PC) was pioneered by three general practitioners (GPs) (James MacKenzie, William Pickles, John Fry) who used data from their immediate practice to conduct research for the purpose of improving care to their patients and local communities.^{1,2}

The movement to establish research networks started in the late 1960s and early 1970s.³ In 1967, a group of practitioners started collecting morbidity data to examine changes that might be related to influenza – a surveillance initiative of the Birmingham Research Unit of the Royal

College of General Practitioners (RCGP).⁴ In 1969, the UK General Practice Research Club was established to support and foster cooperation among practitioners.^{3,4} In 1973, the Medical Research Council fostered the development of a group of practices for the purpose of studying mild hypertension.³ This initiative fostered the development of the General Practice Research Framework by the Medical Research Council which was set up to deliver clinical trials.

The first structured networks (i.e., Midlands Research Networks) were developed in the 1980s through predominately local movements to support the development of PC research.³ This was done by providing expert support, resources, and training for local PC staff.³ The networks were supported by local research organizations such as academic departments of general practice, research support units and PC teaching networks.^{3,4}

In 1993, the Northern Primary Care Research Network (PCRN) and the Wessex Research Network were formed and eventually funded by National Health Service (NHS) research and development funds.³ These networks aimed to increase the capacity for research in PC through the provision of research training and links with academic institutions. They also aimed to increase the quantity of research by fostering research ideas, undertaking pilot studies, enabling researchers to access research funds, and providing channels for developing cooperative and multicentre research.⁴ In 1995, ten research practices in the South and West regions were funded by the NHS.^{3,4}

In the 1990s, a number of significant reports and developments were released that focused on the importance of PC.⁵ In 1994, the Culyer taskforce recommended that Department of Health funding of health related research should be allocated to support research and development activity in NHS trusts and be clearly identifiable and distinct from funding for clinical services.^{5,6} The national NHS Research and Development (R&D) programme recognized the importance of community-based research and included a large funded program on the primary–secondary care interface.^{5,7,8}

In 1996, the release of the White Paper (Mant report) entitled “*Primary Care: Delivering the Future*” stimulated the growth of more networks by changing research funding when Culyer money (funds allocated to NHS research) was extended to PC.³ The paper recognized the importance of expanding the knowledge base of PC and committed 25 million in research & development (R&D) funds for PC research.⁹ The goal was to facilitate coordination of activities, investment in research support services and skills development and a forum for developing research that was based in the practice.^{3,9} This was considered the “bottom-up” approach – an approach that was meant to foster local relationships and build primary care research networks from the ground upwards so that staff working in PC drove research development and implementation. The research activities of the networks included collection of morbidity data, clinical research, practice-based research, large multi-centre trials, and research training.⁴

In 1997, a study of 23 primary care research networks found there was considerable variation in organizational structure, staffing and funding between networks.³ The primary care research networks were mainly funded by regional health authorities and primarily hosted within an academic PC unit (five were hosted in a general practice).³ There were three national networks included the RCGP research club.³ In 1998, in response to policy and funding changes, a national

federation of primary care research networks was established which consisted of 30 members by 2001.⁴ Building on this experience, the NHS Executive funded primary care research networks in England and Wales to increase the capacity for research in PC.⁴

In the early 2000s, the traditional approaches to clinical research in the UK were considered to be failing in academic and commercial sectors.¹⁰ There were fewer gifted practitioners entering academic medicine, fewer studies were funded due to increased regulation and more rigorous methodology, and recruitment was declining due to service pressures on clinicians.¹⁰ Recognizing this crisis, the Government asked Sir John Pattison, Director of Research and Development at the Department of Health to propose solutions. A report from the Research for Patient Benefit Working Party led to the creation of the UK Clinical Research Collaboration (UKCRC) in April 2004.¹⁰ This collaboration brought together government and first-time funders of clinical research including research charities, the private sector, academic institutions, regulatory bodies, patients and the public.¹⁰ Strengthening the research infrastructure for clinical research was one of the key workstreams of the UKCRC with the goal of building on the UK's unique advantage of the NHS to produce a world-class infrastructure for clinical research.¹⁰ It aimed to increase UK clinical research activity by an expansion of the NHS clinical infrastructure for research. Ministers supported the initiative and announced the largest ever sustained increase in NHS R&D funding (£100 million over 4 years), including the establishment of topic-specific, managed research networks in the NHS.¹⁰

Top-Down Approach

In 2006, the “Best Research for Best Health” strategy called for the development of the NHS as a world leader in delivering high-quality and timely clinical research.^{11,12} To achieve this mission, the strategic goals were to: 1) establish the NHS as an internationally recognized centre of research excellence; 2) attract, develop and retain the finest research professionals to conduct people based research; 3) commission research focused on improving health and care; 4) strengthen and streamline systems for research management and governance; and 5) act as custodians of public money for public good.^{11,12}

In March 2006, Sir David Cooksey undertook an independent Review to advise on the best design and institutional arrangements for the public funding of health research in the UK. The Review found there was/were¹³:

- No overarching health research strategy to ensure UK health priorities were considered through all types of research;
- Gaps in translating ideas from basic and clinical research into the development of new products and approaches to treatment of disease and illness and implementing those new products and approaches into clinical practice;
- Lack of coordination with respect to funding arrangements for supporting translation of ideas from conception to practice;
- Cultural, institutional and financial barriers to translating research into practice in the publicly funded research arena; and
- Challenges in translating research into health and economic benefit in the pharmaceutical industry.

The Review recommended that the Government focus on achieving better coordination of health research and more coherent funding arrangements to support the translation of research into practice.¹³ There was also the desire to make the UK “more friendly to commercial trials”.¹³ This Review ignited the movement toward the current state which involved shifting from a “bottom-up” to a “top-down” approach. The national government streamlined health research funding and disbanded small research networks and developed a national structure that would support large-scale clinical trials to enhance the research priorities of the NHS and Department of Health, with practices acting mainly as research hosts.³ The initiative was championed by the national government for the primary purpose of setting up a system that would promote the “health of the nation” but in the context of wanting to attract commercial income that was being lost to Eastern Europe.

In 2006, the National Institute for Health Research (NIHR) was established by the Department of Health. The purpose of the NIHR was to ‘create a health research system in which the NHS supported outstanding individuals, working in world-class facilities, conducting leading-edge research, which focused on the needs of patients and the public’.¹⁴ The NIHR is a virtual organization whose work is hosted by NHS Trusts, universities and life science organisations.¹⁴ The NIHR Clinical Research Network (CRN) was established to deliver high quality ethically-approved research studies on its portfolio, across all clinical specialties within the NHS.^{10,12} The NIHR CRN Portfolio refers to the database of clinical research studies that are eligible for support from the NIHR CRN in England.¹³

The CRN was comprised of six topic-specific CRNs during the first phase of network development. This included: cancer; dementia and neurodegenerative diseases; diabetes; medicines for children; mental health; and stroke.¹⁶ Since this development, CRNs have been established in Scotland, Northern Ireland and Wales funded by the UK Health Departments. Together these national networks form the UK Clinical Research Network (UKCRN), strategic oversight for which is provided by the UKCRC.¹⁷ The structure of the networks varies between each country, but all share the common goal of providing the infrastructure to support high quality clinical research studies for the benefit of patients.¹⁷

The National School for Primary Care Research was established in 2006, which is currently a partnership between nine leading academic centres for PC research in England.¹⁸ Currently, the School brings together academics and practitioners from across the country to collaborate on PC studies that have an impact both at policy level and in general practices around the country.¹⁹ The centres affiliated with the School are Bristol, Cambridge, Keele, Manchester, Nottingham, Oxford, Southampton, and University College London.¹⁹ The School is a significant generator of studies in England and has contributed 29% of the PC portfolio during 2016 and 2017.¹⁹ LCRNs with an affiliated School for Primary Care centre consistently recruit higher numbers of patients into PC studies than those that do not have a centre locally.¹⁹

In 2007, the NIHR subsequently created one Primary Care Research Network (PCRN) as part of the wider NIHR CRN.^{18,20} This was part of a larger initiative, which included the six topic specific networks and a comprehensive clinical research infrastructure through which service support, research governance, and academic staff were funded. The PCRN consisted of central coordination of eight distinct local networks. The central objective of the PCRN was to ‘inform

the prevention, diagnosis, treatment and management of illness and disease in primary care'.²⁰ The network would build a portfolio of studies that would be eligible for PCRN support (technical and research nurse support; NHS service support costs), and these studies would be offered to one or more of the regional networks, who in turn would offer the study to network members.²⁰ These networks linked interested practice teams and local academic units of general practice to participate in a wide range of national projects led from the NHS, universities, and industry. The network was intended to offer a managed approach to hosting high quality research with significant focus on the recruitment and retention of study participants. The networks were also much larger and are more removed from contact with practices with a bureaucratic structure modelled on a national template.³ The initiative had clearly shifted from building capacity and research activity at the local level to supporting engagement and participation in studies.³

Following the success of the original topic specific research networks, a Comprehensive Clinical Research Network (CCRN) was created in 2008 to cover the remaining 24 medical specialties.²¹ The aims of the CCRN were to²¹:

- Ensure patients and healthcare professionals across the country could participate in and benefit from clinical research;
- Integrate health research and patient care;
- Improve the quality, rate and coordination of clinical research;
- Increase recruitment to studies in the NIHR portfolio (with the aim to double recruitment in the first 5-year period); and
- Increase collaboration with industry partners and ensure that the NHS can meet the health research needs of industry.

The CCRN consisted of 25 Comprehensive Local Research Networks (CLRNs), each representing a population of approximately 2 million.²¹ CLRNs provided service support costs (as opposed to the direct costs of doing the research) of NIHR approved clinical research studies in the NIHR CRN portfolio.²¹ These included research nurses and other research staff support (including consultant time) required for patient identification, recruitment, data entry and follow-up, as well as funding for extra NHS costs linked to a given study (e.g., extra time taken for a procedure) and involvement of other local NHS services.²¹ CLRNs did not provide direct research costs (e.g., equipment, drug costs or extra procedures). These costs were covered by research grant funding from the NIHR or an eligible NIHR partner organizations. The CLRN had a designated local lead and formed a Local Specialty Group (LSG) in the specialty area.²¹ The role of the LSG was to coordinate research activities across local Trusts so that research infrastructure was used efficiently.²¹ CLRN local leads met with CRN Coordinating Centre representatives, as a National Specialty Group (NSG) several times per year.²¹ NSGs took a national view on study feasibility issues, recruitment targets and resolved potential blocks to study recruitment.²¹ The NSGs also played a crucial role on advising the CRN about adoption of commercially funded and sponsored studies to the NIHR CRN portfolio.²¹

Clinical Commissioning Groups (CCGs) were established by the Health and Social Care Act 2012 to replace Primary Care Trusts.²² CCGs are local, clinically led NHS organizations.²² In April of 2013, two hundred and eleven CCGs replaced 152 trusts and became formally responsible for urgent and emergency care, elective hospital care, community services, mental

health services and maternity services. Specialised services were commissioned by NHS England and health improvement services were commissioned by local authorities.²² CCGs are made up of GP practices, but to ensure that a broad range of healthcare perspectives are taken into account, CCGs seek advice from a range of other healthcare professionals. NHS England funds and oversees the operation of CCGs.²²

The establishment of the CLRN structure resulted in 102 NIHR CRN local research networks across 70 NHS organizations across all specialities.²³ There was significant overlap and duplication in terms of the studies that were being funded (i.e., diabetes) and lack of coordination and organization. In 2014, the national government announced the shift to a “locally centralized” model in which the NIHR CRN would be configured to become 15 Local Clinical Research Networks (LCRNs) that would cover all the regions of England (Refer to Figure 1).²⁴ The geographical boundaries of these networks would correlate with the Academic Health Science Networks.²⁵

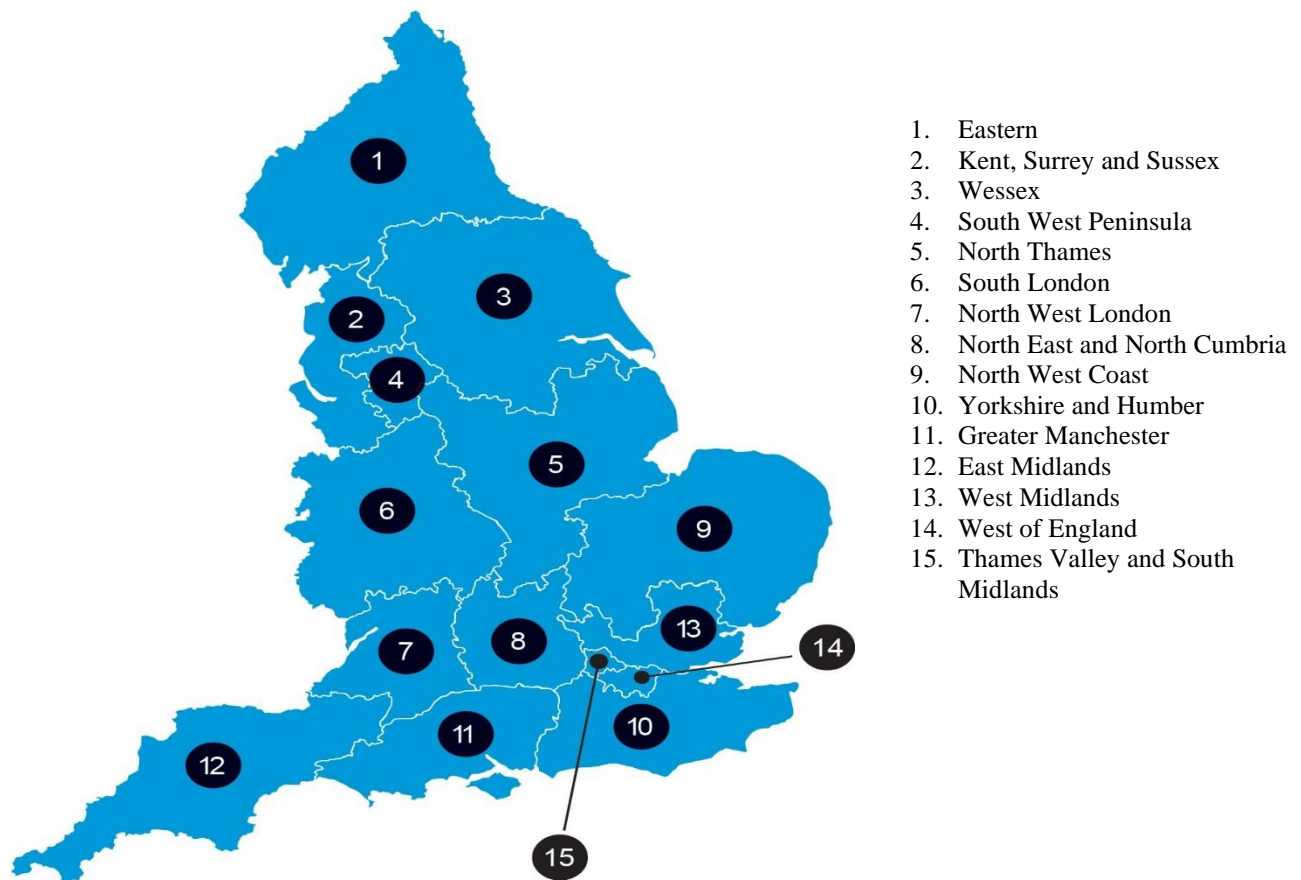


Figure 1: Local Clinical Research Networks (LCRNs)

Reprinted from Evans, P. The NIHR CRN in England and Primary Care Research. June 14, 2019: Montreal, Quebec.²⁵

The 15 local CRNs are currently overseen by the NIHR Coordinating Centre which has offices in Leeds, London, Liverpool, Newcastle and Preston.²⁴ Each LCRN delivers research across 30 clinical specialties (Refer to Figure 2).²⁵ PC is one of 30 clinical specialties within the CRN.²⁵

In 2017 the Life Sciences Industry Strategy was released, which provided recommendations from industry, academia, charity, and research organisations to the Government on the long-term success of the life sciences sector.¹⁵ The recommendations emphasized the importance of reinforcing the UK science offering, including a further improvement of the UK’s clinical trials capabilities.¹⁵ The Strategy established the strategic goal ‘to support a 50% increase in the number of clinical trials over the next five years’.¹⁵ It was recommended that the UK focus on designing novel trials and ensuring it remained ‘at the cutting edge of translational research’. In response to the Strategy, the first Life Sciences Sector Deal was released at the end of 2017 which committed to strengthening the UK clinical research environment by: investing £950 million through the NIHR, in research infrastructure for five years; and to review the Health Research Authority (HRA) research systems to improve integration and optimization of approval processes for clinical trials.¹⁵

In January of 2018, the NIHR CRN extended support into health and social care research taking place in non-NHS settings and the Department of Health was renamed as ‘Department of Health and Social Care’ (DHSC).²⁶ This meant that the CRN would support research conducted outside of NHS settings such as: 1) public health research studies; 2) social care research studies; and 3) studies taking place outside of NHS settings (e.g. hospices).

In December 2018, the Second Sector Deal was released and included the following commitments¹⁵:

- investment of more than £950 million of NIHR investment in NHS research infrastructure;
- development of a national model to manage excess treatment costs related to non-commercial research;
- implementation of processes for NHS research through a standard costing methodology and contract to increase transparency and decrease variation;
- removal of the 70-day benchmark for clinical trials to permit the publication of accurate performance data using a standardized national framework;
- increasing adoption of the Clinical Practice Research Datalink in GP practices by approximately 30% since the end of 2017; and
- improving the HRA and Medicines and Healthcare products Regulatory Agency (MHRA) approvals process by offering a combined approach.

Clinical Specialties

Ageing
 Anaesthesia, perioperative medicine and pain management
 Cancer
 Cardiovascular disease
 Children
 Critical care
 Dementias and neurodegeneration
 Dermatology
 Diabetes
 Ear, nose and throat
 Gastroenterology
 Genetics
 Haematology
 Health services and delivery research
 Hepatology
 Infectious diseases and microbiology
 Injuries and emergencies
 Mental health
 Metabolic and endocrine disorders
 Musculoskeletal disorders
 Neurological disorders
 Ophthalmology
 Oral and dental health
Primary care
 Public health
 Renal disorders
 Reproductive health and childbirth
 Respiratory disorders
 Stroke
 Surgery

Figure 2: Clinical Specialties

The national government also committed to improving the clinical research environment by increasing the speed and efficiency of clinical trials, by¹⁵:

- establishing five centres for late phase commercial research in 2019 and 2020, with the intention to increase the NHS's capacity to deliver research and to enable patients' early access to innovation;
- exploring opportunities to recognise and incentivize NHS Trusts and GP practices acting as participant identification centres;
- improving research set-up timelines by converging HRA approval to the one specified in the EU Clinical Trials Regulation; and
- addressing challenges in NHS workforce resourcing required to deliver commercial clinical trials.

In 2019, another structural change was made in England. As part of the five-year framework for GP contract reform, Primary Care Networks (PCNs) were established. PCNs are groups of GP practices working closely together with other primary and community care staff and health and care organizations to provide integrated services to their local populations.²⁷ CCGs play an important role in ensuring PCNs provide safe and effective services. They approve PCNs, they support PCNs and they hold them to their contracts. Approximately 1250 PCNs cover all of England.²⁸ In the new 2020/21 Primary Care Network Contract for GPs, a critical decision was made to foster the development and implementation of research. - the requirement that the PCN's Clinical Director facilitate "*participation by practices that are members of the PCN in research studies* and act as a link between the PCN and local primary care research networks and research institutions."²⁹

Funding

The UK is one of the top countries in the world with respect to expenditure on "health R&D". UK spending was more than double that of other countries (Germany, Japan, Canada, Spain, France, Italy, Netherlands, Sweden, Belgium and Ireland) between 2013-2015 and only second to the United States.¹⁵ NIHR receives £1 billion per year for overseeing the delivery of research.³⁰ The NIHR is primarily a funding body that supports the NHS to undertake research by funding a range of infrastructure facilities, including the NIHR CRN. Figure 3 depicts the current funding streams of the NIHR.²⁵

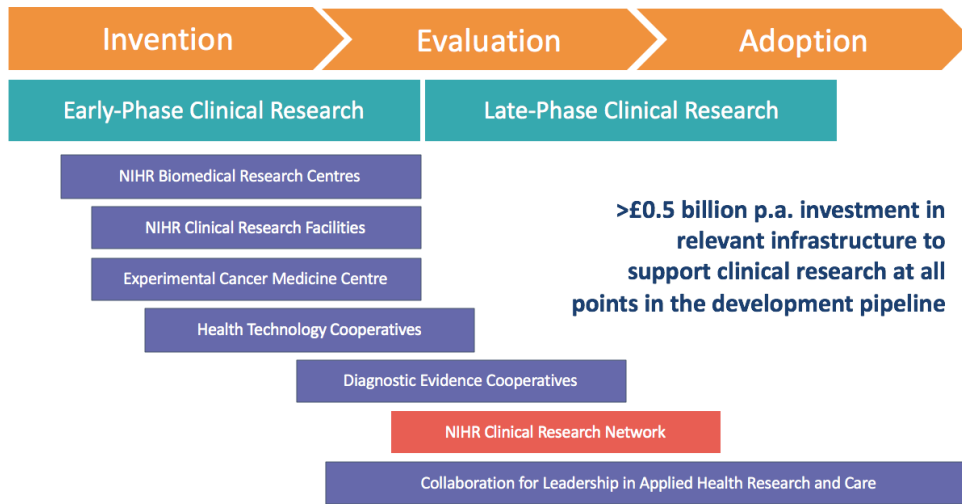


Figure 3: NIHR Funding Stream

Reprinted from Evans, P. The NIHR CRN in England and Primary Care Research. June 14, 2019: Montreal, Quebec.²⁵

The CRN receives funding (approximately £350 million) from the DHSC. The Coordinating Centre for the CRN allocates the funding to the LCRNs (See Table 1 for allocation of budgets to each LCRN in 2019/2020) for all specialities including PC.³¹

LCRN	Fixed funding element1 £	Variable Element2 £	Total pre-top sliced £	Top-sliced £	ETC Service Funding £	Final allocation £
East Midlands	16,739,800	4,143,826	20,883,626	20,040	75,000	20,978,666
Eastern	14,774,132	3,489,905	18,264,037	1,243,040	84,000	19,591,077
Greater Manchester	14,372,205	4,324,981	18,697,186	77,500	78,000	18,852,686
Kent, Surrey and Sussex	11,297,656	2,779,394	14,077,050	0	58,000	14,135,050
North East and North Cumbria	14,328,680	3,796,411	18,125,091	48,701	78,000	18,251,792
North Thames	23,778,436	5,399,367	29,177,803	52,040	128,000	29,357,843
North West Coast	12,861,884	3,023,738	15,885,622	80,263	49,000	16,014,885
North West London	11,053,785	3,458,837	14,512,622	42,742	87,000	14,642,364
South London	19,303,139	4,892,007	24,195,146	59,491	138,000	24,392,637
South West Peninsula	8,501,859	2,479,550	10,981,408	65,701	41,000	11,088,109
Thames Valley and South Midlands	12,134,992	3,234,887	15,369,879	36,040	85,000	15,490,919
Wessex	14,158,880	3,576,999	17,735,879	29,500	73,000	17,838,379
West Midlands	21,820,648	4,435,868	26,256,516	20,040	87,000	26,363,556
West of England	10,043,354	2,470,607	12,513,961	13,500	66,000	12,593,461
Yorkshire and Humber	20,854,428	4,999,593	25,854,021	281,555	89,000	26,224,576
Total	£226,023,878	£56,505,968	£282,529,846	£2,070,154	£1,216,000	£285,816,000

Table 1: LCRNs Funding Allocations

Reprinted from NIHR website.³¹

Primary care research is also funded through NIHR's School for Primary Care Research, NIHR funding streams (NETS-CC), Research Council funding, funding bodies (e.g. Diabetes UK), CRN Service Support Costs, and NHS Excess Treatment Costs.²⁵

The CRN funding model has two components: 'core' and 'top-sliced' (NIHR, funding allocation).³¹ The core component is a two-part model consisting of a fixed and a variable element. The fixed element makes up 80% of core funding (using the previous year allocations as the baseline) and the variable element makes up 20% of core funding which is used to incentivise and reward LCRNs in pursuance of DHSC strategic initiatives and objectives.³¹ This incentive is determined by the number of participants recruited into studies and the number of studies that achieved recruitment to *time and target* (recruitment on time) aim of 80%.³¹ The 'top-sliced' component includes national NHS service support functions and CRN National Specialty Leads (described in section on Organizational Structure).³¹ In addition, DHSC will provide separate funding to LCRNs for the provision of services related to Excess Treatment Costs (ETC) and the costs of the existing standard treatment (described in section on Infrastructure).³¹

The LCRNs have significant autonomy to decide how the funding is allocated across specialities (including PC). The LCRN leadership makes this determination by examining the level of research activity and patient recruitment. The overall budget for PC research is "less visible" and transparent due to the overlap in the delivery of PC research with other speciality groups. It is estimated that between 5 and 10% of the total LCRN budget is allocated to primary care. However, there is a perception that the budget allocated to PC as the lead for research studies is less than their speciality counterparts.

For commercial clinical research on the CRN Portfolio, the NHS Trusts and other care providers receive income for delivery. This income compensates the provider for the costs associated with delivering the research, as well as an allowance which is intended to enable investment in research capacity and capability longer term.¹⁵ In addition, all commercial trials involving new pharmaceutical products, sponsor companies provide the pharmaceutical products used in the trials free of charge to NHS Trusts.¹⁵

Organizational Structure

The work of the NIHR is directed by the Chief Scientific Adviser at the DHSC and by the Senior Management Team of DHSC's Science Research and Evidence Directorate.³² LCRNs are contracted to DHSC but managed through the CRN Coordinating Centre (Refer to Figure 4).³²

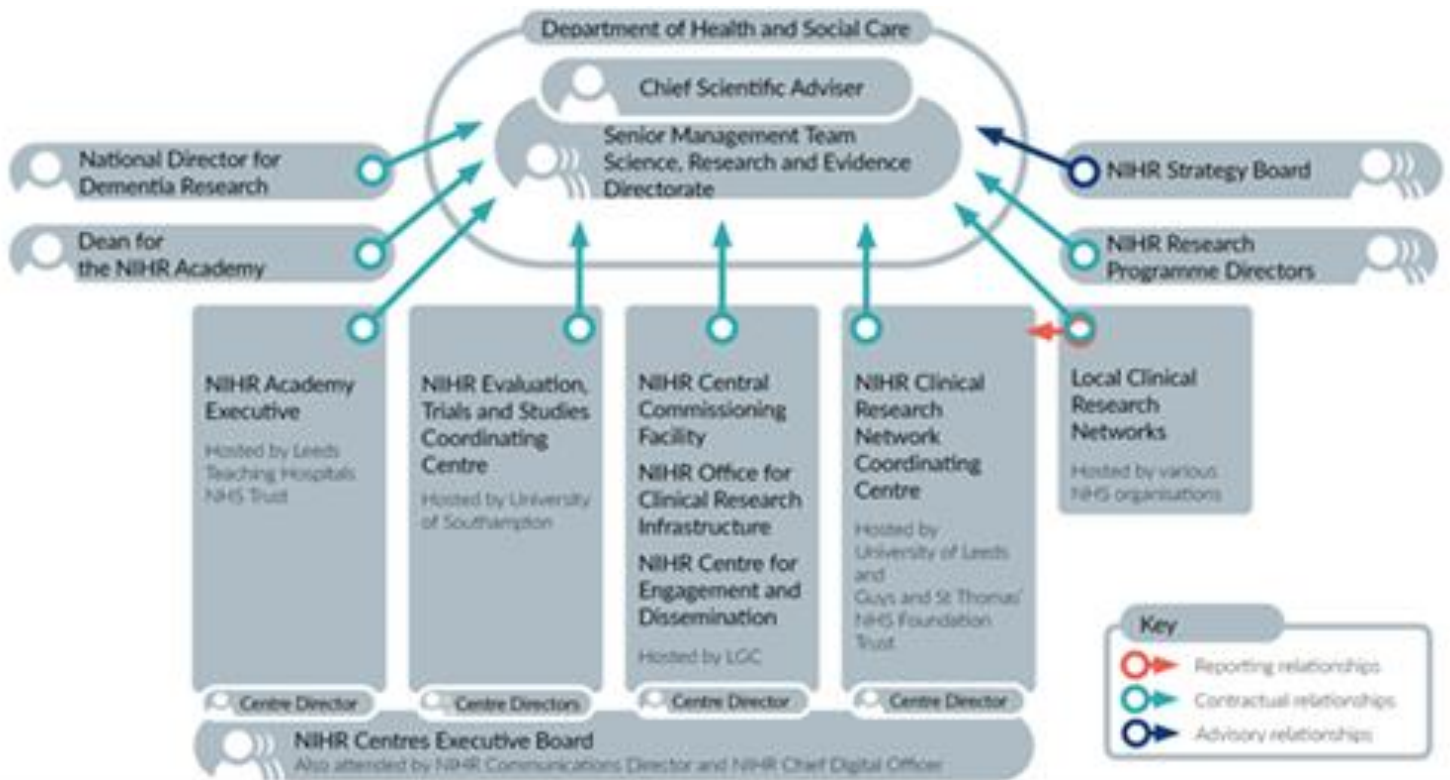


Figure 4: NIHR Organizational Structure

Reprinted from NIHR website.³²

The NIHR CRN funds and coordinates 14,000 research support staff in every single NHS Trust in England, in thousands of GP practices, and in numerous other research sites including care homes, hospices, local authorities, dental surgeries, schools, and prisons.³² The NIHR CRN aims to support research delivery by³³:

- Introducing effective systems to reduce the length of time it takes for a study to be set up and start.
- Putting a broad-based infrastructure in place, so that researchers have access to the facilities and research support personnel they need to carry out the study activities.
- Being able to direct researchers towards local patient populations and research capacity, so that participant targets can be achieved.

The CRN also has a wider role in reducing the barriers to both non-commercial and commercial clinical research including¹⁵:

- Increasing patient and public involvement and engagement in clinical research
- Working with partners, for example charities and industry organizations, to streamline administrative procedures related to clinical research
- Engaging with NHS in research and promoting a research culture in the NHS
- Providing consistent commercial costing templates and a model contract for use between NHS Trusts and practices

- Promoting England and the UK as a place to undertake research

The NIHR CRN Coordinating Centre manages the CRN by providing executive and operational leadership, management, and governance of the network. It is responsible for the funding and coordination of 30 clinical specialities across the 15 LCRNs. The CRN Coordinating Centre is hosted by the University of Leeds and Guy's and St Thomas' NHS Foundation Trust in partnership.²⁴

The CRN National Speciality Cluster Hub is part of the CRN Coordinating Centre and is led by the Medical Director.³⁴ The CRN Speciality Cluster Hub provides oversight on building capacity for clinical research and working with those involved with portfolio development to create a portfolio that benefits patients and the NHS. The CRN Speciality Cluster is responsible for³⁴:

- Providing leadership and support to Specialty National Leads, their National Speciality Groups and other national research communities to improve research portfolio volume, balance and performance
- Understanding how best to deliver health and care research is incorporated into CRN processes and practices at all levels and providing information and advice to the CRN Research Delivery Directorate
- Staying up to date on the broader research environment and incorporating changes into CRN strategy to enable the UK to remain at the top of research at international level
- Promoting the NIHR CRN to customers and stakeholders by building effective relationships with public sector decision-makers, charity, commercial funding organisations, Biomedical Research Centres and parts of the NIHR
- Engaging with health and care professionals in different settings to maximize the reach, impact and delivery of the CRN and its initiative through the NIHR CRN National Specialty Leads and the Local CRN staff

There are six National Speciality Cluster Hubs hosted by Higher Education Institution members of the Clinical Research Alliance.³⁴ The NIHR CRN Specialty Cluster Leads report to the Medical Director. Each speciality area has a National Speciality Lead (NSL) that reports to the respective CRN Cluster Lead.³⁴

The role of LCRNs is to increase opportunities for participants to take part in clinical research, support recruitment of participants into eligible studies and ensure that all studies are conducted to the highest standard. The LCRNs promotes research within their region and aim to increase involvement of various health care organizations (hospitals, general practices). Each LCRN has a host NHS trust/hospital that has a contract with the DHSC to deliver the CRN Portfolio across the corresponding geographical area. The LCRN has the authority to decide which studies are implemented after acceptance to the CRN Portfolio.

The organizational structure of the LCRN is depicted in Figure 5.²³

LCRN core roles and groups

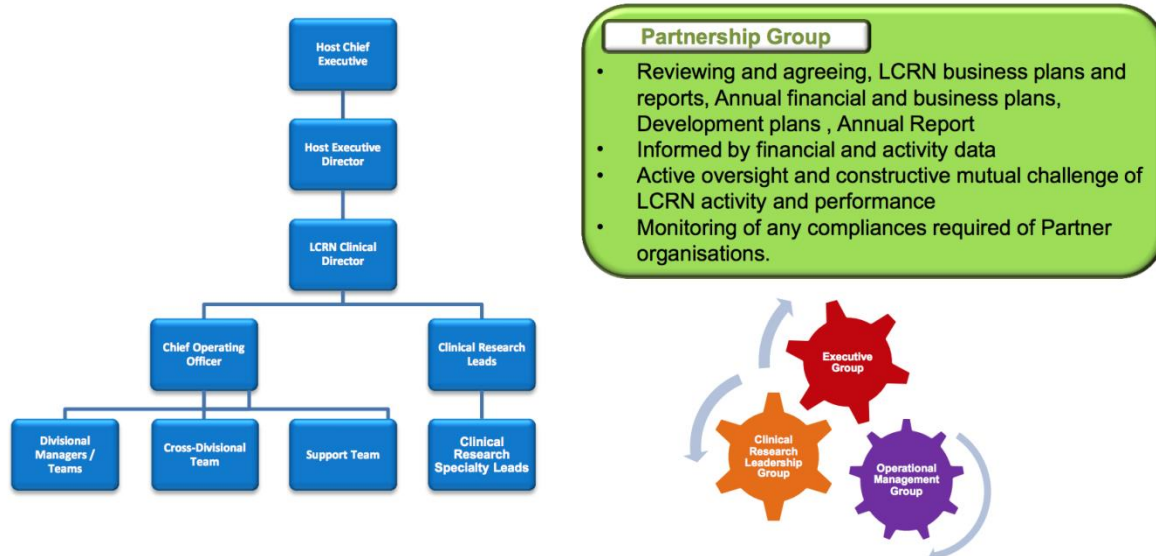


Figure 5: LCRN Organizational Structure

Reprinted from NIHR. *Update on the Transition of the NIHR Clinical Research Network.*²³

The LCRN Board is accountable to the national CRN for the development, management and performance of the organization. The LCRN must report on national performance metrics to the CRN Coordinating Centre. Each LCRN has an executive team (Host Chief Executive, Host Executive Director, LCRN Clinical Director), organizational management team (Chief Operating Officer and team), and clinical research leadership group (Clinical Research Leads, Clinical Research Specialty Leads).²³ There is a Division for each speciality or cluster of specialities. Some specialities are part of one Division. PC is grouped with ageing, Health Services and Delivery Research, Oral/Dental Health, Public Health, Musculoskeletal Disorders, Dermatology) while others have their own Division (cancer). A Division typically consists of a Delivery Manager and Clinical Research Lead. In each of the 15 LCRNs, there is at least one nominated local Clinical Specialty Research Lead for PC. The role of the GP Lead is to encourage and facilitate local PC research, as well as to contribute to the national agenda.

The Clinical Speciality Leads in the 15 LCRNs are accountable to the National Speciality Lead who reports to the Cluster Lead.²³ These local members form a national network called the National Speciality Group (NSG). Local leads, together with additional members representing the devolved entities and important PC stakeholders have meetings during the year to discuss national research and the support they can provide to portfolio studies. For example, they identify the portfolio studies that are struggling to recruit participants, and which need to be made available to additional sites. The NSG also provides detailed subspecialty clinical advice to researchers investigating a specific condition/area.

The COO is responsible for the support team, cross-divisional team and divisional managers. Each LCRN has a team (nurses, managers, facilitators) that assist practices with the recruitment of patients for research studies.²³

Infrastructure

The NIHR CRN provides the clinical research infrastructure for the support and delivery of research studies. This infrastructure includes¹⁵:

- NHS resources to fund the people and facilities needed to carry out research.
- Dedicated systems to assist researchers in gaining approvals to open their studies within the NHS.
- Trained staff that advise and support study design and delivery including feasibility, site set-up, patient recruitment and study management.
- Practical assistance with identifying and recruiting patients onto Portfolio studies, so that researchers can complete the study on time, and on target.
- Access to a local network of dedicated research support staff (research nurses and other allied health professionals), who help identify eligible patients, arrange consent to participate and monitor patients throughout the study.
- Supports to ensure that a study can be successfully undertaken and the possibility of securing protected time for NHS staff to conduct research.
- Training support, so that researchers have access to experienced front-line staff, who can carry out the practical activities for the study (obtaining patient consent for participation, carrying out extra tests, and collecting clinical data).
- Funding to meet the costs of using facilities such as scanners and x-rays for the study.
- Improved quality, speed and co-ordination of clinical research by removing the barriers to research.
- Streamlining and performance managing NHS Support for eligible studies to ensure that the NHS Service Support Cost of these studies are met in a timely and efficient manner.
- Monitoring monthly performance of portfolio studies.

Training Support

In the UK, every GP or staff member that actively takes part in research needs to have *Good Clinical Practice (GCP) training* which is provided by the NIHR free on-line. GCP includes basic courses tailored to the different types of clinical research. These courses include corresponding refresher courses for retraining and advanced learning.³⁵ There is also the *Improving Healthcare through Clinical Research Program* which is a free four-week online course designed for anyone who wants to know more about modern healthcare and the role of clinical research within it. It covers how treatments and cures are discovered; the impact of clinical research; and how clinical research is undertaken and why clinical research is done.³⁵

Research Ready® is a quality assurance programme for all research-active and potentially research-active UK GP practices.³⁶ To facilitate readiness for the undertaking of research, GPs can obtain accreditation with the RCGP Research Ready© scheme. The programme was developed by RCGP and NIHR CRN in England, the Northern Ireland CRN, NHS Research Scotland, and Health and Care Research Wales.³⁶

Research Ready® is designed in alignment with the UK Research Governance Framework's legal, ethical, professional, and patient safety requirements. The programme provides information, support and guidance to accredited practices to assist with meeting the requirements, and with considering and conducting research.³⁶ The program can be used by practice staff (clinical and non-clinical).³⁷

The programme has two levels of accreditation: Research Ready® Universal and Research Ready® Advanced. Research Ready® Universal provides access to training and support for the whole practice team to engage with research. Research Ready® Advanced permits practices to demonstrate their capability and experience in performing complex research. It can be used by general practices who have excelled at, and have demonstrable experience of, successfully undertaking at least two Clinical Trials of Investigational Medicinal Products in the last 2 years.³⁶

The RCGP and the Research Ready® stakeholders are currently conducting a consultation across the UK involving GPs, members of the practice team, research organisations and patient/carer representatives to develop a revised Research Ready® programme.³⁶

A relatively small proportion of general practices are research active. In October 2019, the RCGP lists 604 practices as 'Research Ready', some 8% of all practices in England, and 34 (<1%) as 'Research Ready Advanced' (Peckham, S. personal communication, March 29, 2020).

Research Study Support for Researchers

Study Support Service

Researchers have access to the NIHR CRN Study Support Service.³⁸ This Service aims to help researchers and the life sciences industry plan, set up and develop proposals and deliver quality research on time.³⁸ Figure 6 and 7 illustrates and describes the support that is provided at each stage of the research journey.^{38,39}

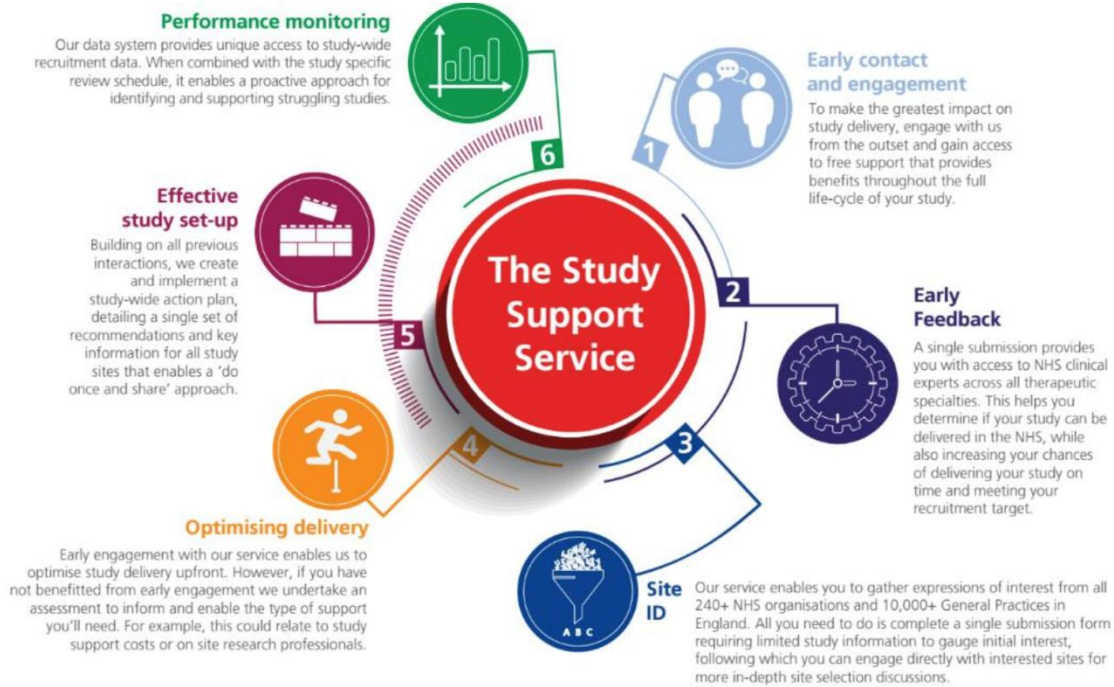


Figure 6: NIHR CRN Study Support Service

Reprinted from Good, P. *NIHR Costing for Trials – Where to Start*³⁹

WELCOME TO THE INDUSTRY ROUTE MAP OF THE NIHR CRN STUDY SUPPORT SERVICE

HOW TO USE THE INTERACTIVE ROUTE MAP | WE ARE LISTENING TO YOUR FEEDBACK

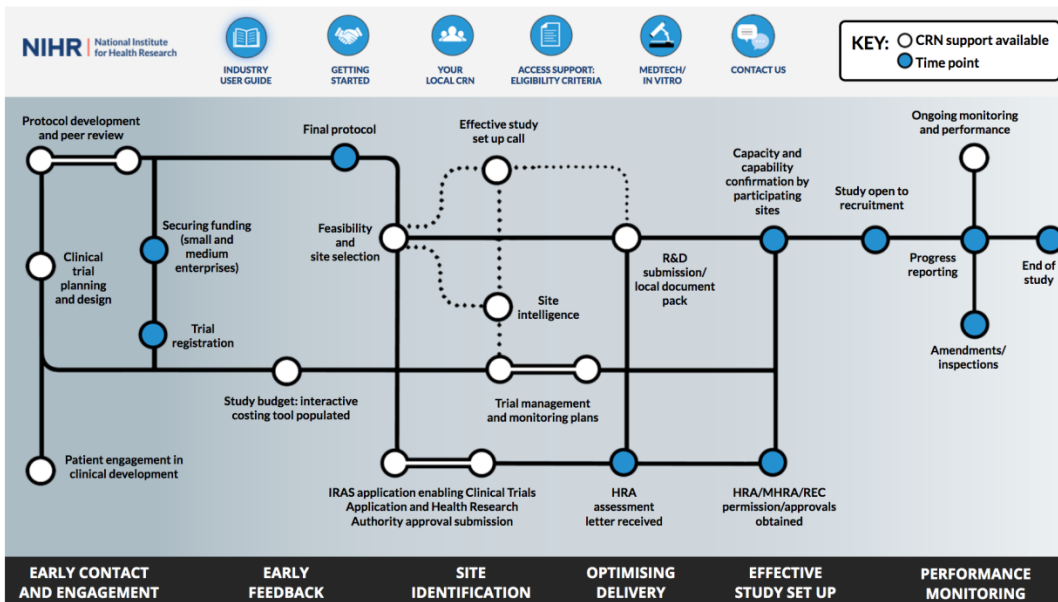


Figure 7: NIHR CRN Study Support Service Process

Reprinted from NIHR website.³⁸

Researchers can call the *Early Contact and Engagement Service* prior to starting a grant application, which permits them to have a conversation with the relevant LCRN.⁴⁰ This permits the researcher to receive tailored *feedback* on their study. All LCRNs provide a central study support team for PC which provides advice and support to PC sites in their regions. The LCRN can also assist with finding *suitable sites* to undertake the study by reaching out to organizations and seeking expressions of interest. Researchers can then engage directly with interested sites for more in-depth discussions.⁴¹

To *optimize delivery*, a team of experts can undertake a Network delivery assessment, and utilization of local expertise to identify any study challenges which may impact delivery to time and target.⁴² This permits for the identification of staff training or specialist equipment to support the study. *Effective study-set up* is communicated through a study-wide action plan (a set of recommendations for all study sites involved in the research).⁴³ The measures to address any challenges identified by the Delivery team are discussed, agreed and implemented. *Performance monitoring* is a key part of service and assists researchers to deliver studies on time and to target. NIHR's Integrated Research Intelligence System (IRIS) is used to collate site level information, which enables proactive performance monitoring and helps sites to stay on top of their study performance.⁴⁴ This service provides a Performance Review Lead who is responsible for monitoring study progress. Regular performance review meetings are scheduled with researchers to discuss performance concerns. Once all the terms are accepted, a Master Non-Commercial Agreement is set up with the research team.⁴⁴

Study Support Costs and Resources

The LCRN is responsible for study support costs for eligible studies. The DHSC Attributing the costs of health and social care Research & Development (AcoRD) outlines the list of research costs activities that are supported for all NIHR portfolio studies by the LCRN (Refer to Table 2).⁴⁵

Activity	Task
Feasibility assessment	<ul style="list-style-type: none"> - Read Protocol - Support and advise funders and research teams to identify suitable sites, approach and assess capacity and capability of these sites - Initial assessment of capacity and capability by the site research team and feedback to funders - In house meetings to assess feasibility and deliverability of study - Work with funders/research/clinical teams to establish recruitment targets
Support regulatory submission for local confirmation of capacity and capability to deliver the research (where applicable)	<ul style="list-style-type: none"> - Support Principal Investigators and their R&D offices, where required, in preparation of the study documentation and submission through IRAS - Support investigators, where required, with preparation of the study documentation and liaison with NHS colleagues - Allocation of local resources based on nationally agreed attribution of Service Support Costs
Performance Management of study delivery	<ul style="list-style-type: none"> - Work with funders and study/clinical teams to monitor progress against recruitment targets - Work with funders and study/clinical teams to identify blocks/barriers to achieving recruitment targets at site level - Work with funders and study/clinical teams to develop and implement action plans to overcome barriers to recruitment at site level

Table 2: Research Cost activities and tasks provided by NIHR Clinical Research Network for ALL NIHR Portfolio studies

Reprinted from Department of Health and Social Care. DHSC Attributing the costs of health and social care Research & Development (AcoRD). Published 2019.⁴⁵

Once a study is funded and assessed as eligible, the LCRN determines the cost of each study by using standardized national costing templates. This can include research nurses and other research staff support (including consultant time) required for patient identification, recruitment, data entry and follow-up, as well as funding for extra NHS costs linked to a given study (e.g., extra time taken for a procedure) and involvement of other local NHS services. There is set-up fee (£100) (not covered by NIHR) prior to the research study for meetings, training etc. Once the study is ready for execution, the LCRN works closely with study teams, to ensure that recruitment targets are met within the planned time frame.

Since the implementation of the 15 LCRNs, different models of local support have emerged. Some LCRNs have utilized a hub and spoke model whereby highly research active practices with research staff act as a hub to co-ordinate and support less-active practices.¹⁹ Other models range from embedding research staff in an NHS Trust to support a geographical PC area to central co-ordination/oversight of activity within the LCRN by research nurses/health professionals who aid with recruitment of subjects and proactive performance-monitoring activities.¹⁹ The decision on who should be recruiting patients is determined by the who is the most appropriate for the task.

Excess treatment costs - patient care costs that would continue if the patient care service in question continued to be provided after the R&D study stopped – are supported by NHS commissioners and operationally managed by the CRN and LCRNs. Payments for these costs are through the CCG contractual payment.⁴⁶

For commercial contract studies, the NIHR Industry Costing Templates are used to calculate consistent and transparent prices associated with commercial contract studies to support the Life Sciences Industry and the NHS.⁴⁷ The template format identifies standard rates for specific bands of NHS staff time representing the direct costs. Any indirect costs (including overheads) are covered.

Financial Incentives for Patient Recruitment

The LCRNs have general practice incentive schemes that financially reward those PCNs/GP practices undertaking CRN research and recruiting patients. The Research Site Initiative (RSI) enables GP practices to support PC research. Annual funding (£1,000 to £6,000) is available to GP practices through PCNs, depending on their level of research activity.²⁵ To obtain the incentive, the Lead GP and all practice partners must sign up, attend the annual PC meeting and CRN meetings and engage in performance measurement.²⁵ The lowest level of activity is when it involves a patient search and mail out to identify volunteers for a study or for displaying posters in the waiting room.²⁵ A higher-level activity would involve a practice acting as a study site, and one of its GPs acting as a Principal Investigator.²⁵ Although the RSI is a national scheme, there are differences in the way these are run across England. For example, the criteria in SW Peninsula is defined as follows (Refer to Table 3)²⁵:

Level	Definition	Criteria	Incentive Amount
1	Low level activity – data base searches/patient identification centre activity	<5 studies	£1800
2	5 or more studies/benchmarked for EOI and recruitment. Some feasibility and complex work	5+ studies	£3800
3	Embedded research, funded nurse/GP/administrator time	7+ studies	~£10K

Table 3: SW Peninsula Research Site Initiative

Patient and Public Involvement

NIHR has been making health research more relevant to patients and to the public by involving members of the public at all stages of research, from setting priorities to communicating and implementing study findings, as well as improving public awareness of research and actively improving public participation in research studies.³⁰ Patient and public involvement (PPI) is an important priority since it improves the quality of research.

The following initiatives have been implemented to facilitate PPI:

- Patient engagement in the clinical development service to inform the design process of company-led clinical trials

- Patient engagement to advise on what NIHR research should be funded
- Patient engagement in the design of studies through the grant application process
- Patient Research Ambassador initiative which includes patients who can promote health research from a patient's perspective^{25, 48}
- LCRN Patient Committees^{25,48}
- Patient Advisory Groups in GP practices that assist with patient recruitment
- NIHR Centre for Engagement and Dissemination (formerly IMPROVE) which engages patients, service users, carers and the public across the NIHR, provides coordination and thought leadership across the health and care system⁴⁹
- NIHR Evidence website provides high quality summaries of findings from health and care research, making research informative, accessible, relevant and ready for use⁵⁰
- CRN annual patient experience survey²⁵

In England, there are no incentives for patients to participate in research. However, the Patient Experience of Research National Survey provides insight on the reasons for participation. Survey results from 2017-2018 (n=4300) found²⁵:

- ⇒ 87% of patients had a good experience participating in research
- ⇒ 83% would be happy to take part in another study

Key survey themes that emerged from the results included:

- Motivation: Patients' reasons for participating in studies included altruism; improving health condition; better medical monitoring; learning about medical conditions; general interest in the research process.
- Research staff: The friendliness, professionalism, knowledge, availability, informativeness, helpfulness, and respectfulness of healthcare staff.
- Information: Responses stressed the importance of patients having the right info at the right time and being told about results.

Information Systems

At the heart of the CRN's activities is the NIHR CRN Portfolio. Both non-commercial (researcher-led) and commercial (industry-led) studies can be registered in the CRN Portfolio. To apply for inclusion on the portfolio, non-commercial studies by researchers must submit an application for Health Research Authority (HRA) approval. For commercial studies, researchers are required to call the Study Support Service before applying for HRA approval. Once HRA approval has been obtained, the information is shared with the CRN so that a decision can be made on NIHR CRN Portfolio eligibility.⁵¹ Studies outside traditional NHS settings do not require HRA Approval. Instead, researchers can contact the LCRN directly who will assist with the submission of a CRN application to permit decisions on eligibility.⁵¹

This application process is supported by the NIHR's Integrated Research Intelligence System (IRIS) - digitally connected systems that provide access to CRN services and record essential information about studies to support research delivery, continuous improvement and performance management.⁵² The IRIS consists of the following key systems:

Integrated Research Application System (IRAS) (NIHR, IRIS)

Applications for NIHR CRN support are made via the Integrated Research Application System (IRAS). This is a single system for applying for the permissions and approvals for health, social and community care research.⁵³ This system allows applicants to submit research applications to the HRA for HRA Approval, applications for Research Ethics Committee (REC) review, and applications for the Confidentiality Advisory Group (CAG).⁵³ Applicants can enter information about their project once instead of duplicating information in separate application forms to ensure that the data collected and collated is appropriate to the type of study and the permissions and approvals required.

The Central Portfolio Management System (CPMS)/ Local Portfolio Management Systems (LPMS)

The Central Portfolio Management System (CPMS) holds the NIHR CRN Portfolio, as well as the network portfolios of Northern Ireland, Scotland and Wales. CPMS is used by the CRN to support study management.⁵¹ It's also used by commercial partners to submit CRN service requests. Each of the 15 LCRNs have their own local portfolio management system (LPMS), which is a database that records the activity for each of the research sites including general practices. These LPMSs submit data to the CPMS, which enables the CRN to monitor recruitment and site activities. A number of different LPMSs have been procured by the LCRNs including: EDGE, ReDA, R-Peak, Studyline/Siteline, Documas.⁵²

Currently, there are Big Data Initiatives taking place that allow GP practices to submit routine clinical data to: Clinical Practice Research Datalink (CPRD); NHS Digital; QResearch; and RCGP Research Surveillance Centre.²⁵ The CPRD collects de-identified patient data from a network of GP practices across the UK. PC data are linked to a range of other health related data to provide a longitudinal, representative UK population health dataset.⁵⁴ The data encompass 50 million patients, including 14 million currently registered patients.⁵⁴

The challenges that have been encountered with the use and implementation of information systems in England include: GPs' uncertainty about and attitudes to information governance, quality of the data entered, governance issues related to the General Data Protection Regulation (GDPR) and the Privacy and Electronic Communications Regulations (PECR), the ability to extract data for PC study follow up, systemizing nomenclature of medicines, and the lack of data being submitted by GP practices.²⁵

Scope (number of networks, geographic spread, longevity, number of participating practices/physicians, number of patients covered)

As of December of 2018, England had 7012 open and active practices with 308 million estimated appointments in the last year in these practices (i.e. > 1 million appointments every working day).²⁵ There were 44,396 GPs and 34,510 full-time equivalent GPs in England.²⁵ In 2018/19, national level data showed that 100% of CCGs recruited participants into NIHR CRN portfolios studies and patients from every single CCG in the country took part in NIHR supported studies in this year - the first time since 2015/16.²⁵ In addition, there were 870,250 participants that took part in

clinical research across England.²⁵ This was equivalent to 2,383 per day - an increase of over 140,000 since 2017/18.²⁵ In England, PC is one of the leaders in patient recruitment compared to other specialties.

Figure 8 provides national and regional level data on PC. National data shows²⁵:

- In 2018/19, 2721 GP practices (38%) were actively engaged in recruitment (target was 45%)(Figure 8 – top left corner); this has declined from 48% in 2016/17³⁷
-
- 176 did commercial work (2.4% of all practices) (Figure 8 – top right corner)

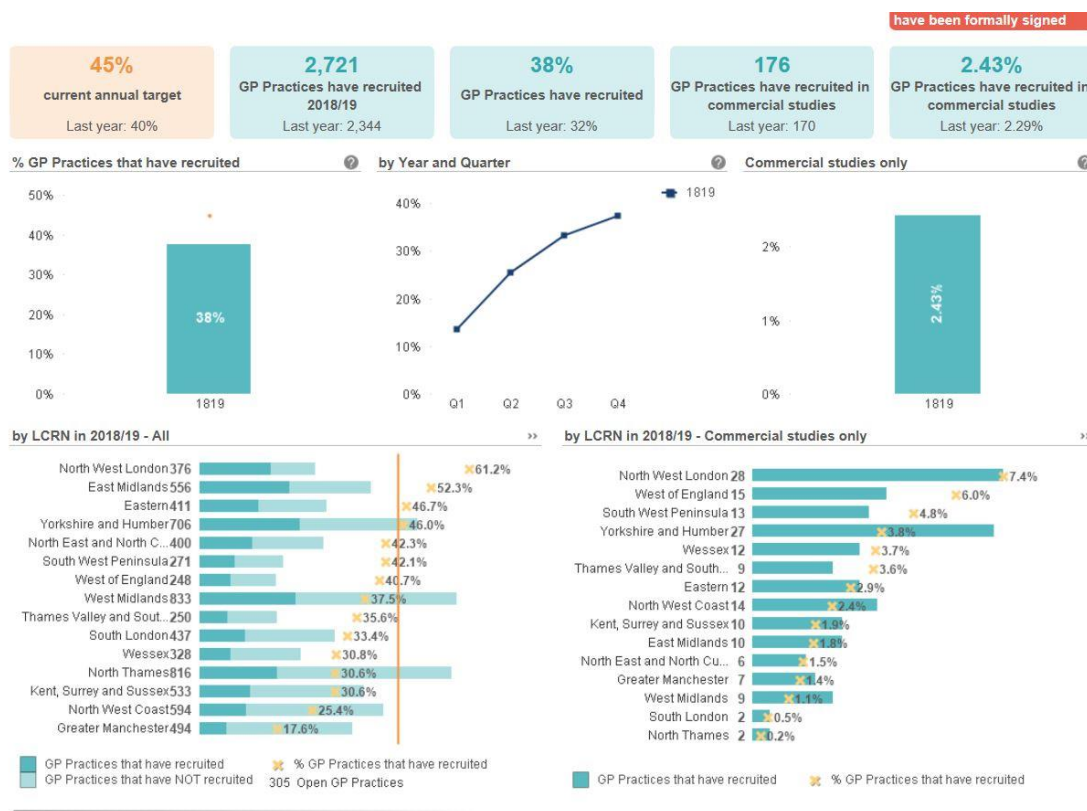


Figure 8: National and Regional Level Data on Primary Care

Reprinted from Evans, P. The NIHR CRN in England and Primary Care Research. June 14, 2019: Montreal, Quebec.²⁵

Table 4 shows that more than 160,000 patients were recruited in PC²⁵ (Refer to Table 4 (PC)). Recruitment in primary care has not increased since 2015/15, while most other specialties have seen increases, some dramatic.



Specialty Recruitment in England - Managing & Supporting				
Specialty	2015/16	2016/17	2017/18	2018/19
Ageing	14,962	13,967	21,518	16,235
Anaesthesia, Perioperative Medici...	2,839	36,489	19,604	42,240
Cancer	72,614	76,317	89,505	122,664
Cardiovascular Disease	53,831	49,871	45,141	35,648
Children	56,504	60,554	81,780	127,960
Critical Care	14,819	57,814	37,649	41,045
Dementias and Neurodegeneration	36,934	29,430	36,487	45,918
Dermatology	14,299	16,385	11,632	12,786
Diabetes	40,087	37,857	44,855	26,629
Ear, Nose and Throat	11,006	10,221	5,513	3,798
Gastroenterology	19,820	20,792	32,948	41,660
Genetics	32,798	33,862	35,995	82,637
Haematology	7,920	8,173	6,580	6,332
Health Services Research	21,071	40,742	62,134	115,450
Hepatology	10,188	6,647	4,796	5,359
Infection	29,002	31,751	44,923	88,163
Injuries and Emergencies	24,879	25,989	71,533	74,677
Mental Health	40,051	40,587	49,058	80,046
Metabolic and Endocrine Disorders	9,153	7,548	6,981	7,618
Musculoskeletal Disorders	39,939	42,400	39,865	45,185
Neurological Disorders	21,879	19,805	16,656	18,225
Ophthalmology	17,317	14,526	16,244	9,429
Oral and Dental Health	2,660	5,468	6,517	22,587
Primary Care	160,855	129,413	154,220	160,146
Public Health	11,593	40,371	82,083	97,571
Renal Disorders	29,164	34,906	26,019	24,432
Reproductive Health and Childbirth	77,682	96,151	76,920	92,513
Respiratory Disorders	21,937	19,238	18,995	24,681
Stroke	22,735	29,366	18,037	20,963
Surgery	15,175	46,640	48,285	57,981

Table 4: Patient Recruitment by Speciality in England

Reprinted from Evans, P. The NIHR CRN in England and Primary Care Research. June 14, 2019: Montreal, Quebec.²⁵

The drop of participation by GP practices was perceived to be because of a smaller GP and nurse workforce, tighter funding, increasing costs and burnout. However, the COVID-19 pandemic has ignited interest in research by GPs. There is a large COVID-19 study (PRINCIPLE) that is being led by the Oxford Royal College of General Practitioners Surveillance Centre.⁵⁵ The study will evaluate the potential treatments for COVID-19.⁵⁵ Through the NIHR CRN infrastructure, the trial has been able to recruit 450 GP sites across the country and is being supported by all the LCRNs. Refer to Figure 9 for the set-up process for the trial.

The Oxford Royal College of General Practitioners Research Surveillance Centre
(RCGP RSC) registered sites PRINCIPLE Trial set-up Process

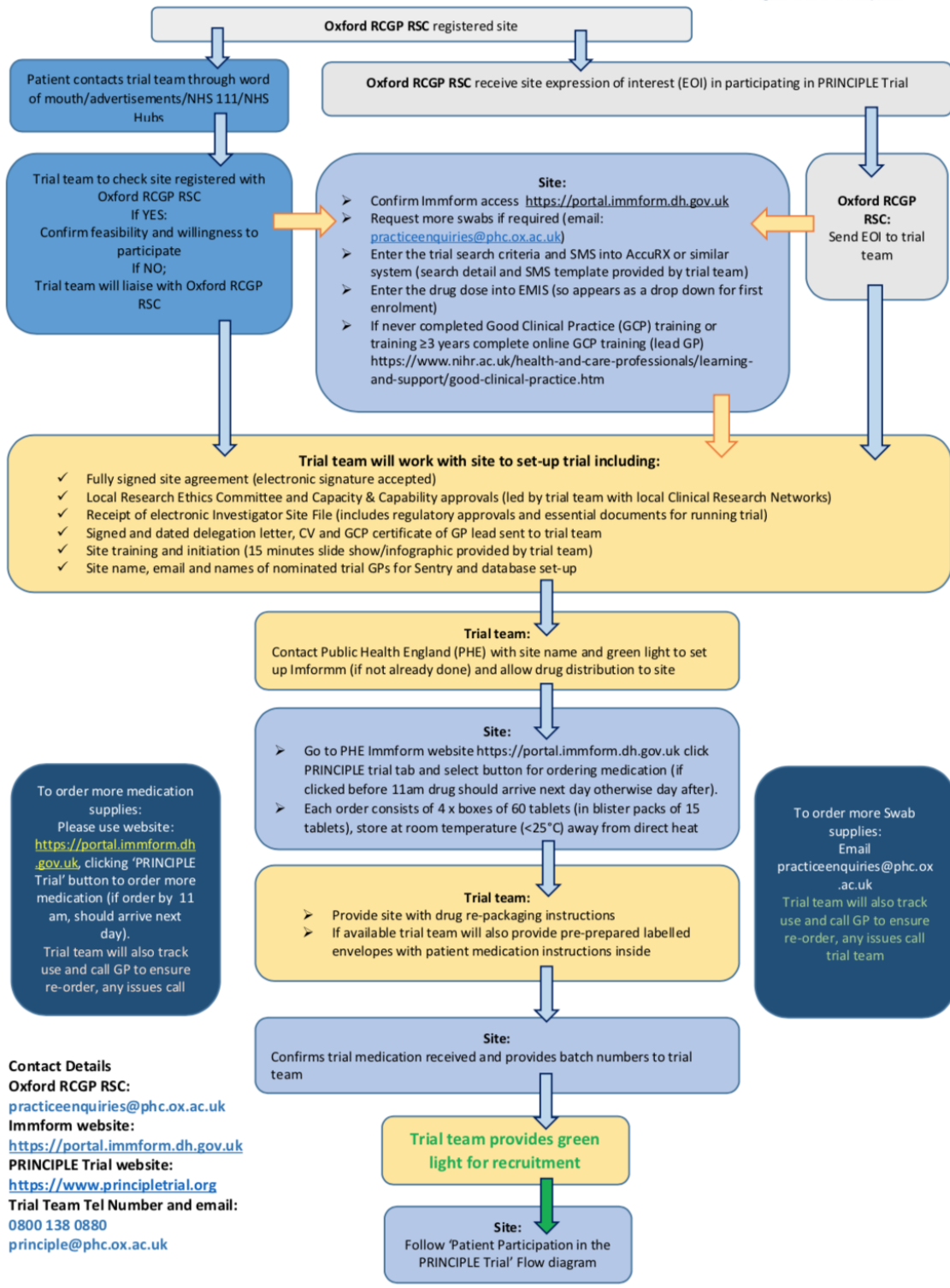


Figure 9: COVID-19 Trial Set-up Process

Received from Dr. Paul Wallace. personal communication, April 30, 2020.

Research Type, Output and Impact

In PC, researchers and PC practitioners (GPs, practice nurses, pharmacists and dentists) are involved in delivery of research studies. The types of research that are supported include⁵⁶:

- Promoting a healthier lifestyle
- Disease diagnosis and prevention
- Management of long-term illnesses such as diabetes or hypertension
- Prevention of future ill-health
- Treating common conditions such as tonsillitis or influenza

In situations where there is overlap with other specialty areas (i.e., diabetes, mental health and cardiovascular disease), the CRN works with colleagues from across the Network to deliver high quality research in a PC setting⁵⁶.

Studies that are supported in PC include²⁵:

- Large numbers of cluster RCTs (often pragmatic)
- Adaptive trial designs e.g. ALICE
- Stepped wedge designs for implementation
- Platform trials
- Complex studies in stratified/personalised medicine e.g. genomics studies in PC
- Real world studies including point of care randomization e.g. DIRECT

Data obtained from the NIHR for 2018/19 indicates²⁵:

- 6,106 studies were supported by the NIHR CRN in which 1,523 were commercial studies
- 2,194 new studies were opened to recruitment (740 were commercial contract studies)
- 82% of non-commercial studies and 69% of commercial studies were delivered on time

In terms of PC studies, there were (Refer to Figure 10)²⁵:

- 501 studies recruiting in 2018/19
- 160,146 patients recruited in 2018/19
- 794 new studies since 2015/16
- 875 studies recruiting since 2015/16

Specialty Research Activity

Key information about research activity in England in your chosen specialty

NIHR | National Institute
for Health Research

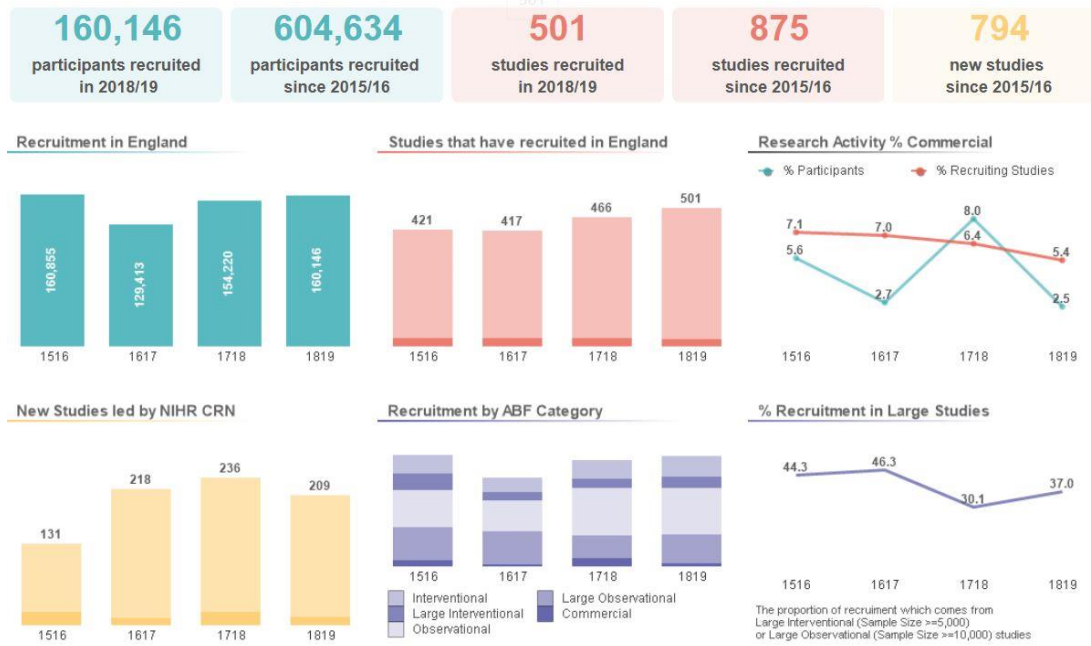


Figure 10: Primary Care Led Research Activity (2018/19)

Reprinted from Evans, P. The NIHR CRN in England and Primary Care Research. June 14, 2019: Montreal, Quebec.²⁵

For NIHR data from 2019 – 2020, Figure 11 provides details on the number and characteristics of research studies for the PC specialty managed studies which are led by PC.²⁵ The results show:

- 479 studies were undertaken
- 442 studies recruited patients
- 154,622 participants were recruited
- 40.5% of the overall portfolio were PC led studies
- 450 studies were non-commercial studies and 29 were commercial studies
- 246 studies were observational, 150 were interventional and 83 were both
- 297 were non-randomized studies, 180 were randomized studies and 2 were both
- 216 studies were funded by NIHR, 127 by charities, 78 by industry and 71 by government
- 464 studies were from England, 12 were from Wales and 3 from Scotland
- 353 studies involved multi-sites, 102 were single site, and 24 were international multi-site

Composition of my specialty's portfolio

Understand the balance of your portfolio by either the number of studies or recruitment activity for all studies on the CRN Portfolio.

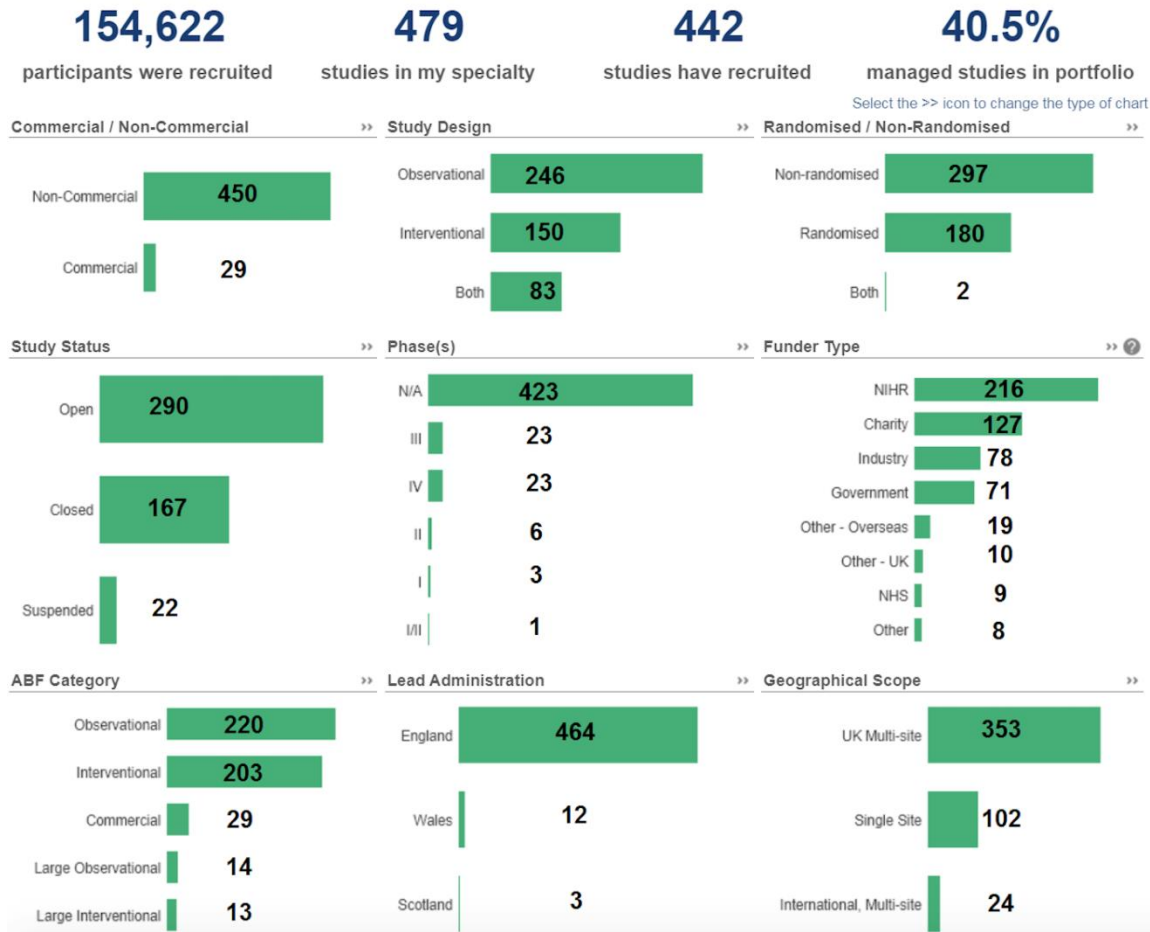


Figure 11: Composition of Primary Care Led Research Activity (2019/20)

Received from Dr. Phillip Evans. personal communication, June 8, 2020.

Figure 12 provides information on PC-led studies with secondary care specialties supporting PC studies. The results below show that the most common collaborations from highest to lowest:

1. Health Services Research
2. Ageing
3. Public Health
4. Musculoskeletal
5. Cardiovascular
6. Mental Health
7. Cancer
8. Diabetes
9. Children

Research activity with cooperating specialties

View research activity by specialty, for studies where you are a collaborating specialty from 19/20

Select the >> icon to change the type of chart

Number of STUDIES THAT HAVE RECRUITED by YEAR where Primary Care is a managing specialty >>



Figure 12: PC-led studies with supporting secondary care specialties

Received from Dr. Phillip Evans, personal communication, June 8, 2020.

Figure 13 shows the number and characteristics of the studies that PC both managed AND supported for other specialties. The results show:

- 194 studies were supported
- 178 studies recruited patients
- 71,451 participants were recruited
- 179 studies were non-commercial studies and 15 were commercial studies
- 94 studies were observational, 57 were interventional and 43 were both
- 115 were non-randomized studies and 179 were randomized studies
- 107 studies were funded by NIHR, 43 by charities, 29 by industry and 24 by government
- 183 studies were from England, 9 were from Wales and 2 from Scotland
- 160 studies involved multi-sites, 21 were single site, and 10 were international multi-site

Composition of my specialty's portfolio

Understand the balance of your portfolio by either the number of studies or recruitment activity for all studies on the CRN Portfolio.

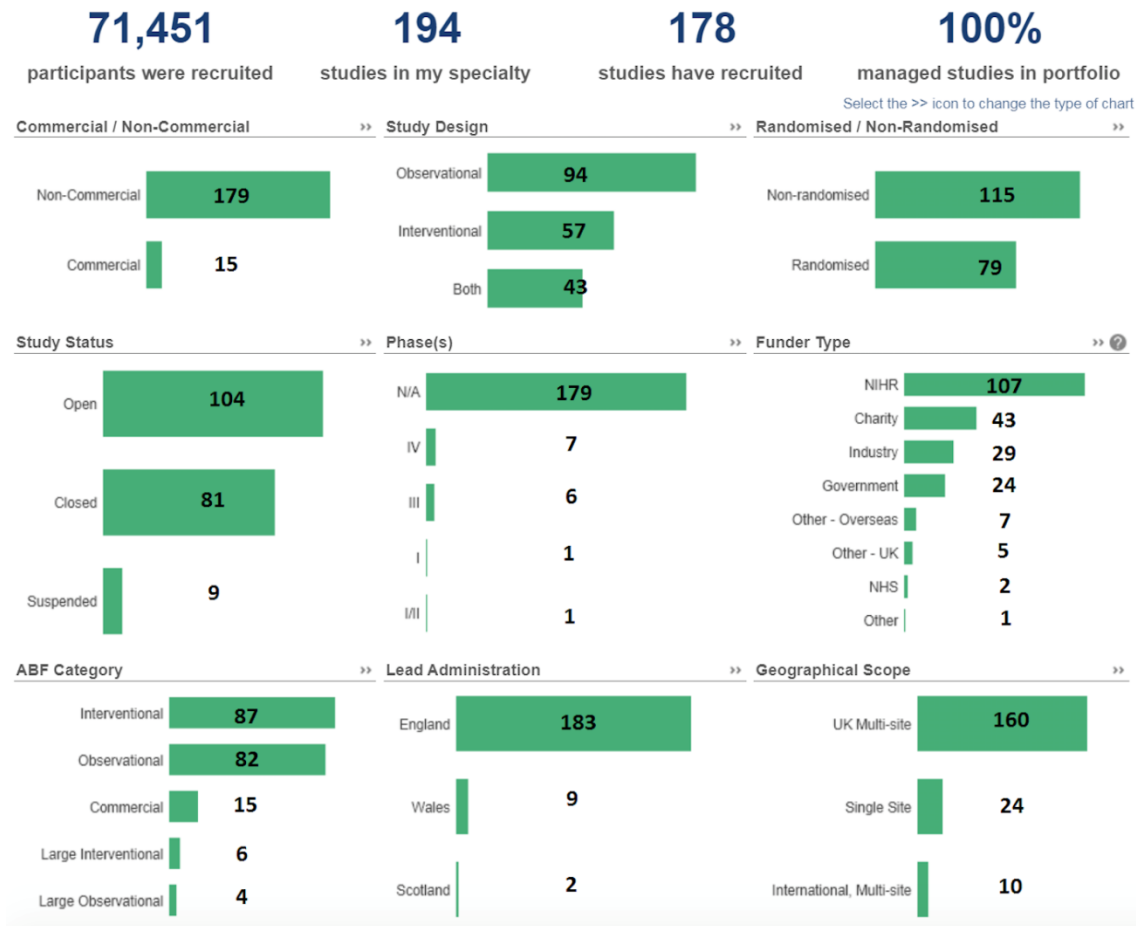


Figure 13: Composition of Primary Care Managed and Supported Research Activity (2018/19)

Received from Dr. Phillip Evans. personal communication, June 8, 2020.

Figure 14 shows the number and characteristics of the studies that PC both managed AND supported studies for other specialities. The results show that the most common collaborations from highest to lowest:

1. Health Services Research
2. Mental Health
3. Diabetes
4. Ageing
5. Public Health
6. Musculoskeletal
7. Cancer
8. Children
9. Cardiovascular Disease

Research activity with cooperating specialties

View research activity by specialty, for studies where you are a collaborating specialty from 19/20

NIHR | National Institute for Health Research

Select the >> icon to change the type of chart

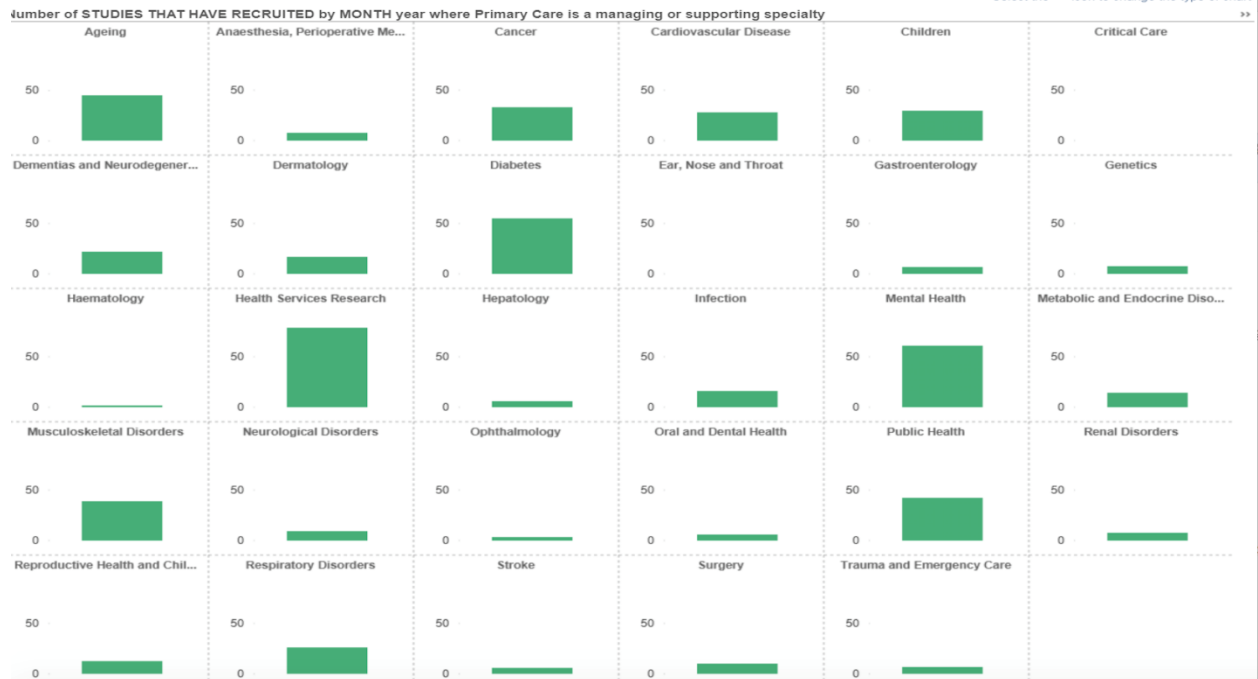


Figure 14: Primary Care Managed AND Supported Studies for Other Specialities

Received from Dr. Phillip Evans, personal communication, June 8, 2020.

The following high-impact studies were identified as the product of CRN support:

1. TxTstop smoking cessation trial - RCGP Research Paper of 2011
 - The txt2stop smoking cessation programme significantly improved smoking cessation rates at 6 months⁵⁷
2. TASMIN-SR Randomized Clinical Trial - RCGP Research Paper of 2015
 - Among patients with hypertension at high risk of cardiovascular disease, self-monitoring with self-titration of antihypertensive medication compared with usual care resulted in lower systolic blood pressure at 12 months⁵⁸
3. The STarT Back Study
 - Developed a stratified approach to managing back pain. The study showed improved patient outcomes and estimated cost savings of £34 per patient. The new approach has been rolled out via; Map of Medicine; QIPP; NICE; DHSC spinal task force; It has also generated international interest⁵⁹
4. A study at the School for Primary Care Research, found that a mobile device that measured patients' blood pressure while they were ambulatory was more accurate and cost effective than either clinical or home monitoring. The National Institute for Health and Care Excellence (NICE) has since updated its hypertension guidelines to recommend ambulatory monitoring, and the research is also cited in South African guidelines for hypertension.³⁰

Evaluation

To date, no evaluation has been done to assess primary care research networks. However, in November 2018, the CRN commissioned KPMG to assess the impact and value of CRN's activity from 2016/17 to 2018/19 fiscal year.¹⁵ The study provides an assessment of the economic impact of the NIHR CRN's activities to support clinical research in England over the period from 2016/17 - 2018/19. The mixed-methods study focused on:

- Assessing the economic contribution made to the UK economy through clinical research activity supported by the Network;
- Analysis to quantify the value of payments made to NHS Trusts for commercial studies; and
- Wider impacts in the clinical research market generated by the CRN's activities and contributions made by the CRN, such as through its provision of study support and its database of study-level data.

The assessment found there was an estimated total of £8 billion in Gross Value Added (GVA)¹ and 47,467 FTE jobs. This includes the direct GVA and employment impacts from the clinical research activity and activities within the CRN, as well as those generated in the UK supply chain (indirect effects) and in the wider economy, through spending by employees (induced effects).

Over the three years covered by the study:

- Both the number of studies and number of recruits onto clinical research studies on the CRN Portfolio increased by approximately 30% from FY 2016/17 to FY 2018/19.
- The economic contribution in terms of GVA increased over the time period from an estimated £2.6 billion in FY 2016/17 to £2.7 billion in FY 2018/19, linked to increased GVA from commercial clinical research activity supported by the CRN.
- Employment contributions increased over the time period, with estimated total direct, indirect and induced employment increasing from 47,102 in FY 2016/17 to 47,467 in FY 2018/19.
- Increases in clinical research activity and economic impact occurred in the context of a reduction in funding from Government of 1.9% in nominal terms over the period, and a reduction in staff costs of 2.9% in nominal terms.
- The total value of payments to NHS Trusts and other care providers relating to the delivery of commercial clinical research supported by the CRN reached approximately £950 million from FY 2016/17 to FY 2018/19. After aggregating savings across all studies on the CRN Portfolio over the study period, it was estimated that the total value to the NHS of

¹ GVA measures the contribution to the economy of an individual producer, industry or sector, net of intermediate consumption (for example goods and services that are used in the production process). It is a measure of the economic value of the activity. In our analysis we report employment in full-time equivalent (FTE) terms. This adjusts part time or temporary staff into an annual full-time equivalent based on the proportion of full-time hours worked over a year.

pharmaceutical products provided free of charge was approximately £77.1 million. Of this, approximately £28.6 million of savings were made in FY 2018/19.

- Financial benefits of participation in NHS research were substantial. NHS Trusts receive an average of £6658 per patient in revenue from sponsor companies, and a pharmaceutical cost saving of £5250 per patient recruited to each clinical study. This equated to the estimated totals of £176 million of commercial income and £16 million of pharmaceutical cost savings across the commercial CRN Portfolio in 2014/15.

Stakeholders interviewers found that the CRN's provision of feasibility services and study set-up support had a positive impact on enabling the study to be set up on time and meeting recruitment targets. The early stage support provided by the CRN increased the reach of clinical research since site identification support allowed more NHS Trusts to be involved in clinical research. This increased patients' access to clinical research, and the improvement of health outcomes. When stakeholders were asked about impacts on efficiency, speed and costs with which organizations delivered trials and support in studies delivery, the majority indicated that without CRN infrastructure there would have been a loss of efficiency in the way clinical research was delivered. Stakeholders said CRN infrastructure increased the speed at which clinical studies were delivered, which benefited patients' health outcomes since it allowed patients to access improved treatment more quickly. The provision of research nurses by the CRN was considered a significant benefit since it increased cost saving to the organization and allowed for the delivery of more research.¹⁵

Key Challenges

The most significant challenge that was identified by key informants with the national approach to facilitating PC research was the *lack of engagement and participation* of non-academic GPs in practice-based PC research. The top-down approach has led to a shift in emphasis from building capacity and research activity (including research training, building a research culture and supporting PC research leaders locally) to supporting engagement and participation in clinical trials led by academics. Consequently, much of the previous emphasis on support and development of research and research skills has been lost despite the development of clinical academic centres and clinical fellowships. As one key informant noted: "the top-down approach" has "left practice-based research out in the cold." The key driver for this shift was seen to be the emphasis on financial incentives which focus on patient recruitment targets. The more patients that are recruited in studies by PCNs/GP practices, the more income they earn.

In 2017, a proposal was developed by the PC Specialty Lead to examine how GP participation in research could be improved – the proposal recognized the need to improve GP participation and to embed research into GP practice. It was also acknowledged that there was a pressing need for new Chief Investigators (CIs) and Principal Investigators (PIs) in PC. Recently, there have also been calls for proposals on how to engage GPs in conducting research.

Key challenges included:

- GP participation in patient recruitment has declined
- Inability to determine the actual budget for PC research due to overlap between PC and other specialties
- Perception of small investments in PC relative to other specialties
- Lack of funding to permit non-academic physicians to engage in practice-based PC research
- Rewarding specialty colleagues for patient recruitment when patient identification or mailing is done by GPs
- Financial incentives have resulted in gaming at the practice and network level
- Research dissemination to practices and patients has not been effective
- The three-year training program does not provide sufficient time to learn about research
- Insufficient opportunities for academic trainees to work in LCRN
- Insufficient engagement of early career physicians in research activities
- Lack of mentorship opportunities for trainees and early career physicians
- Lack of collaboration and linkages between research active practices and non-research active practices
- Small proportion of GPs are clinical academics, considering the large GP workforce
- Data protection issues (privacy, security)
- Lack of GP participation in Big Data initiatives
- Keeping up with changing architecture of PC

Lessons Learned

The key lesson that emerged from this literature review is that the type of organizational structure that is used to implement primary care research networks influences the outcomes that are achieved. The UK's experience with primary care research networks demonstrates that the bottom-up approach facilitated grass roots participation of GPs, contextually relevant research evidence and fostered communities of practice.³ This approach also resulted in duplication of studies and lack of coordination across networks. The top-down approach permitted the institutionalization of structures and processes that facilitated the support needed to deliver large-scale, well-coordinated research studies in rapid manner by senior researchers. However, this approach failed to engage local GP in conducting research that had relevance to their practice and patient population. The theme that emerged from key informant interviews was that neither approach helped the UK achieve its desired goals – the production of high-quality research by all GPs. It was recommended that as Canada embarks on scaling up their own practice based research networks that an organizational structure that combines and integrates the best of both the bottom-up and top-up approach is considered. Key informants emphasized that funding and incentives alone would not be sufficient to drive GP participation in primary care research networks - instead policymakers would need to make a concerted effort to understand and fund the types of research that would '*win the hearts and minds of GPs*' and ignite their desire to participate in research to improve the care they deliver and the quality of their work life.

Advice for Canada from key informants:

- Provide research training for family physicians and practice staff
- Engage practice staff (administration, manager, inter-professional team) in research
- Include targeted funding to support practice-based research by local non-academic family physicians
- Support family physicians by providing incentives for research time
- Invest in PhD opportunities for family physicians
- Build trust between academic and local physicians
- Ensure that family physicians understand the value and impact of research
- Provide opportunities for research active practices to assist and mentor non-research active practices
- Ensure there are opportunities to disseminate knowledge and lessons learned
- Ensure that the portfolio of studies includes high quality studies that mean something to primary care providers
- Include a Clinical Lead that is the champion for the initiative
- Implement a ‘research ready’ practice so that practices are accredited and have regulatory and governance structures
- Target and encourage early career family physicians to participate in research
- Leverage senior academics to champion research initiatives among family physicians
- Obtain buy-in from the leaders of primary care practices for research
- Consider piloting the organizational structure for primary care research networks before scaling it up at the provincial/territorial level
- Use provincial/territorial research driven metrics for performance measurement
- The provision of a “nurturing” environment for exposure to research experience and “seeding” of research concepts in service-driven family medicine residents, preferably in research-active training practices using nationally developed materials

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Appendix

1. Who championed PBRNs (e.g., professional associations, academic departments, health authorities, local, regional or national governments)?
2. How have PBRNs evolved over time?
3. What is the organizational structure of PCRNs? What is the governance model? How are accountabilities implemented? Are PCRNs formally connected to Primary Care Networks? How are local level initiative supported? Would you call it a top-down approach?
4. How are PBRNs (PCRNs) funded?
5. What is the Infrastructure to support research and quality improvement? Is there support for training of non-academic physicians?
6. How are research priorities determined?
7. Who is involved in the PCRNs? How does the initiative encourage physician participation? What are the incentives?
8. Are local physicians participating in PCRNs? How have PCRNS encouraged or discouraged research collaborations with academic institutions and local practices/community?
9. How does the initiative encourage patient participation?
10. What is the scope of PBRNs (number of networks, geographic spread, longevity, number of participating practices/physicians, number of patients covered)?
11. What types of research are being conducted?
12. How is research knowledge disseminated to different audiences?
13. What is the research output and impact? Have the PCRNs been evaluated? If so, what are the findings?
14. What have been the key successes of the initiative?
15. What have been the challenges?
16. What lessons have been learned? What strategies should Canada consider for implementation of PCRNs more widely?
17. Could you provide any documents, reports, papers on this topic?