Centralisation of specialised health care services (CENT): Integration of specialised services for eating disorders and functional symptoms in children and young people, a mixed methods study

RESEARCH TEAM

Stephen Morris
Naomi J. Fulop
Saheli Gandhi
Josefine Magnusson
Efthalia Massou
Angus I. G. Ramsay

DOCUMENT HISTORY

Previous version: 18 November 2020, version 1.2
This version: 8 August 2022, version 2.0

STUDY SUMMARY

Full Title:	Centralisation of specialised health care services (CENT): Integration of specialised services for eating disorders and functional symptoms in children and young people, a mixed methods study
Health condition(s) or problem(s) studied	Centralisation of specialist health care services
Study type	Mixed methods study comprising a scoping review of studies examining the centralisation of specialised health services, and an evaluation of the integration of specialised services for eating disorders and functional symptoms in children and young people, comprising a systematic review, economic analysis, examination of preferences for centralisation using qualitative research and discrete choice experiments, and qualitative research to investigate the factors influencing implementation of new models of care.
Research team	Stephen Morris, Naomi J. Fulop, Saheli Gandhi, Josefine Magnusson, Efthalia Massou, Angus I. G. Ramsay
Start Date	April 2022
End of Study definition and anticipated date	Completion of final report March 2023
Key Study milestones	Project set-up October 2022 Scoping review September 2022 Systematic review August 2022 Economic analysis October 2022 Qualitative research to analyse preferences and understand factors that will influence implementation February 2023 Discrete choice experiments March 2023 Final report March 2023

KEY WORDS

Centralisation
Specialised health care services
Quality improvement
Service models
Mixed methods
Scoping review
Taxonomy
Integration
Physical and mental health services
Children and young people
Eating disorders
Functional symptoms
Systematic review
Survey
Discrete choice experiment
Stakeholder preferences

LIST OF ABBREVIATIONS

CCH – Cambridge Children's Hospital
CYP – Children and Young People
DCE – Discrete Choice Experiment
DSM-5 – Diagnostic and Statistics Manual of Mental Disorders 5th edition
ED – Eating Disorders
FTP – File Transfer Protocol
HS&DR – Health Services and Delivery Research
IP – Intellectual Property
IT – Information Technology
MDT – Multidisciplinary Team
MHRA – Medicines & Healthcare products Regulatory Agency
NHS – National Health Service
NIHR - National Institute for Health Research
PPI – Patient and Public Involvement
PPIAG – Patient and Public Involvement Advisory Group
PIS – Participant Information Sheet
RAP - Research Advisory Panel
SDHS – Secure Data Hosting Service
UCL – University College London
WS – Workstream

Contents

STUDY SUMMARY 2
KEY WORDS 3
LIST OF ABBREVIATIONS 3
1. INTRODUCTION 6
1.1 Brief Overview 6
2. BACKGROUND 9
2.1. Centralising specialised health care services 9
2.2. Collaboration Between Specialist Health Care Services For Children And Young People 9
2.3. Argument For Integrating Physical And Mental Health Services For The Management Of Functional Symptoms 11
2.4. Argument For Integrating Physical And Mental Health Services For The Management Of Eating Disorders (ED) 12
3. AIMS AND OBJECTIVES 12
4. STUDY DESIGN AND METHODS 13
4.1. Workstream 0. Scoping Review and Taxonomy 13
4.2. Empirical Case Studies 15
4.3. Workstream 1. Systematic Review, Documentary Analysis Of Pathways And Logic Model 16
4.4. Workstream 2. Economic Evaluation 17
4.5. Workstream 3. Qualitative Study Of Staff Experience And Preferences 18
4.6. Workstream 4. Qualitative Study Of Parent/Carer Experience 19
4.7. Workstream 5. Discrete Choice Experiment (DCE) 20
5. PATIENT AND PUBLIC INVOLVEMENT (PPI) 22
6. ETHICAL ISSUES 22
6.1. Assessment And Management Of Risk 22
6.2. Ethical Approval 23
7. GOVERNANCE 23
8. FUNDING 24
9. INDEMNITY ARRANGEMENTS 24
10. INTELLECTUAL PROPERTY 24
11. ARCHIVING 25
12. OUTPUTS AND DISSEMINATION 25
12.1 Predicted outputs 25
12.2. Funder requirements 26

13. DATA MANAGEMENT....26
13.1. Qualitative Data (Interviews)....26
13.2. Quantitative Data (DCE)....26
14. TIMELINE....27
REFERENCES....29

1. INTRODUCTION

1.1 Brief Overview

There have been significant changes in the provision of specialised clinical care in the NHS in recent years, with plans to centralise specialist services into fewer centres. Specialised services are not available in every hospital because specialist teams of health care professionals with the required knowledge, skills and experience usually deliver them. There have been longstanding recommendations for centralisation of specialised services. [1,2]

There are two parts to this study, each with a separate aim. The first part will be to undertake a review of the literature to investigate how the centralisation of specialised health care services in the UK can be characterised. The second part will be an empirical study to be undertaken with the planners of the new Cambridge Children's Hospital (CCH) to investigate the centralisation and integration of physical and mental health services for children. CCH is under development, planning to open fully in 2026. One of the main focuses of the hospital is to generate improved clinical outcomes for children and young people through new models of care that integrate physical and mental health care. Two clinical settings in which this might be manifested are the integration of physical and mental health care for eating disorders and for functional symptoms (sometimes referred to as physical persistent symptoms) in children.

The overall aims of the study are to:

(1) Investigate how the centralisation of specialised health care services in the UK can be characterised.

(2) Use qualitative and quantitative methods to support and inform the planned integration of physical and mental health services for eating disorders and for functional symptoms at CCH.

(3) Make recommendations that will guide the implementation of these services at CCH.

(4) Identify lessons that will guide the reconfiguration of specialist services into integrated models of care elsewhere in the NHS.

The objectives are to:

a. To undertake a novel scoping review to identify what "centralisation" as a service innovation means in the context of specialised health care services, and what the dimensions of centralisation are.

b. To use the scoping review to develop a taxonomy to map the different models of centralisation.

c. Undertake a rapid systematic review of the literature on centralisation and integration of physical and mental health services for eating disorders and for functional symptoms that supplements other ongoing work.

d. Undertake a documentary analysis to delineate the current and planned pathways of care and identify key stakeholders related to the planned changes at CCH.

e. Develop a logic model describing the anticipated impacts of the planned changes.

f. Undertake an economic analysis using economic modelling to evaluate the impact of the planned pathways of care identified in objective b in terms of effectiveness and cost-effectiveness, including

exploring the uncertainty in these findings. This would explore potential savings (e.g., in terms of time, resources, distress, costs of travel, etc.) by centralising services from different viewpoints (e.g., NHS, families) balanced against the costs of centralising care.

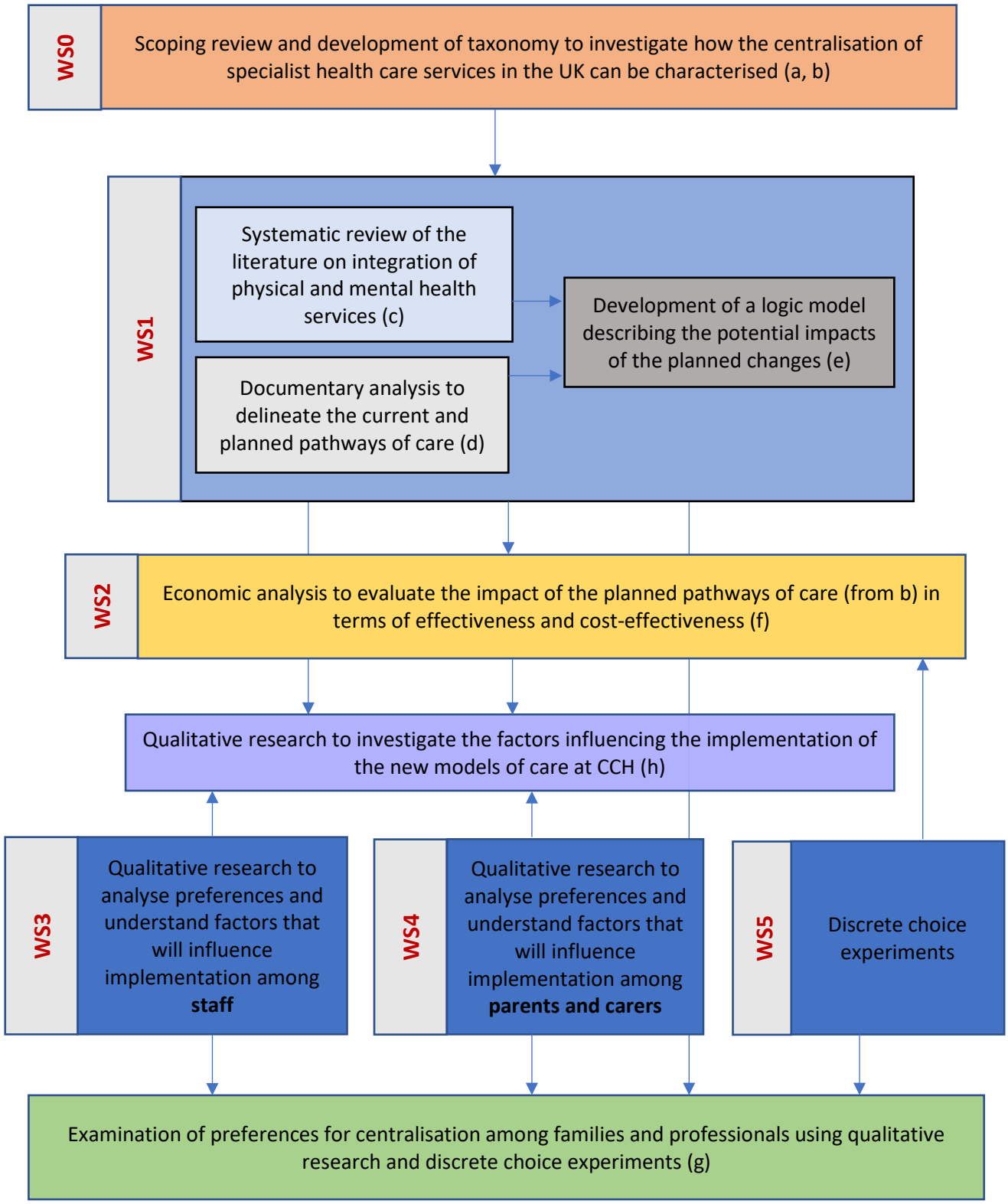
g. Examine preferences for centralisation among families and professionals using qualitative research and discrete choice experiments.

h. Undertake qualitative research to investigate the factors that may influence implementation of the new models of care at CCH.

i. Identify lessons learned that might be applied to future service changes of this kind.

The study will have six workstreams (WS). WS0 will comprise a scoping review and development of a taxonomy to address aim (1) and meet objectives a and b. WS1-WS5 will address aim 2. WS1 will comprise a systematic review, documentary analysis of pathways, logic model, to meet objectives c, d and e. WS2 will comprise an economic analysis, to meet objective f. WS3 will comprise qualitative research to analyse preferences and understand factors that will influence implementation among staff. WS4 will comprise qualitative research to analyse preferences among parents and carers. WS5 will comprise a discrete choice experiment. Combined, WS3, WS4 and WS5 will meet objective g, and WS3 and WS4 will also meet objective h. We will draw the findings and learning from all workstreams to meet objective i. See Fig. 1 below for a flowchart summarising the key elements of the study.

Figure 1. CENT study flowchart



The letters in brackets related to the study objectives described in the text above. The arrows indicate how the different elements of the research inform each other.

2. BACKGROUND

2.1. Centralising specialised health care services

Studies from several countries have suggested that centralising specialised health care services into fewer consolidated units can improve provision of evidence-based care processes by increasing access to specialists, reaping better outcomes associated with higher volumes, and reducing hospital stay. [3-27] The rationale is that centralisation leads to increased volumes of cases at specialist centres, meaning that more patients have access to specialist staff expertise, resource availability and specific processes of care correlated with volume. [28,29] In addition, treating more cases can lead to greater experience and expertise in dealing with patients. Under centralised systems specialist services may also be able to enhance access to innovative techniques and technologies, including less invasive procedures. [30,31]

On the downside, for many patients and families centralisation affects distance to hospital and travel time. Some studies have indicated that patients may be, to some extent, willing to travel further and longer to receive specialist care in return for clinical benefits, however, research evidence indicates that distance and travel time are largely seen as limiting factors in patients' decisions to access treatment, especially for patients living in socio-economically deprived areas. [32-41] Increased opportunity costs and direct out-of-pocket payments associated with travel are also more likely to affect less well-off families, which may also be in the greatest need.[42] Moreover, increased journey distances increase travelling times that may lead to increased risks in patients with life-threatening medical emergencies.[43] Some research has suggested that, with centralisation, patients who do not reach a specialised centre experience significantly worse care in the other services.[44] While, as discussed above, there are several studies examining the impact of centralisation of health services on patients' outcomes, there has been little research to understand the main characteristics of centralisation, including no previous reviews. In addition, there are many different ways in which services may be centralised, and different approaches/models to centralisation might work better in different settings (such as rural versus urban settings). A comprehensive taxonomy that maps the underlying dimensions of centralisation, and describes the circumstances under which different models would work best, is currently lacking. The development of such a taxonomy would help in pinpointing the focus of future investigations and would also allow exploring centralisation in other healthcare contexts and specialities. Additionally, there are only a few studies that look at stakeholders' preferences for centralising health care, and such studies tend to focus on particular services or aspects of services while there is a clear need for the understanding of how centralisation works in different settings. Priorities and preferences of different stakeholder may be quite different depending on the care context and therefore there is a need to understand such priorities and preferences especially when it comes to different settings. [45]

2.2. Collaboration Between Specialist Health Care Services For Children And Young People

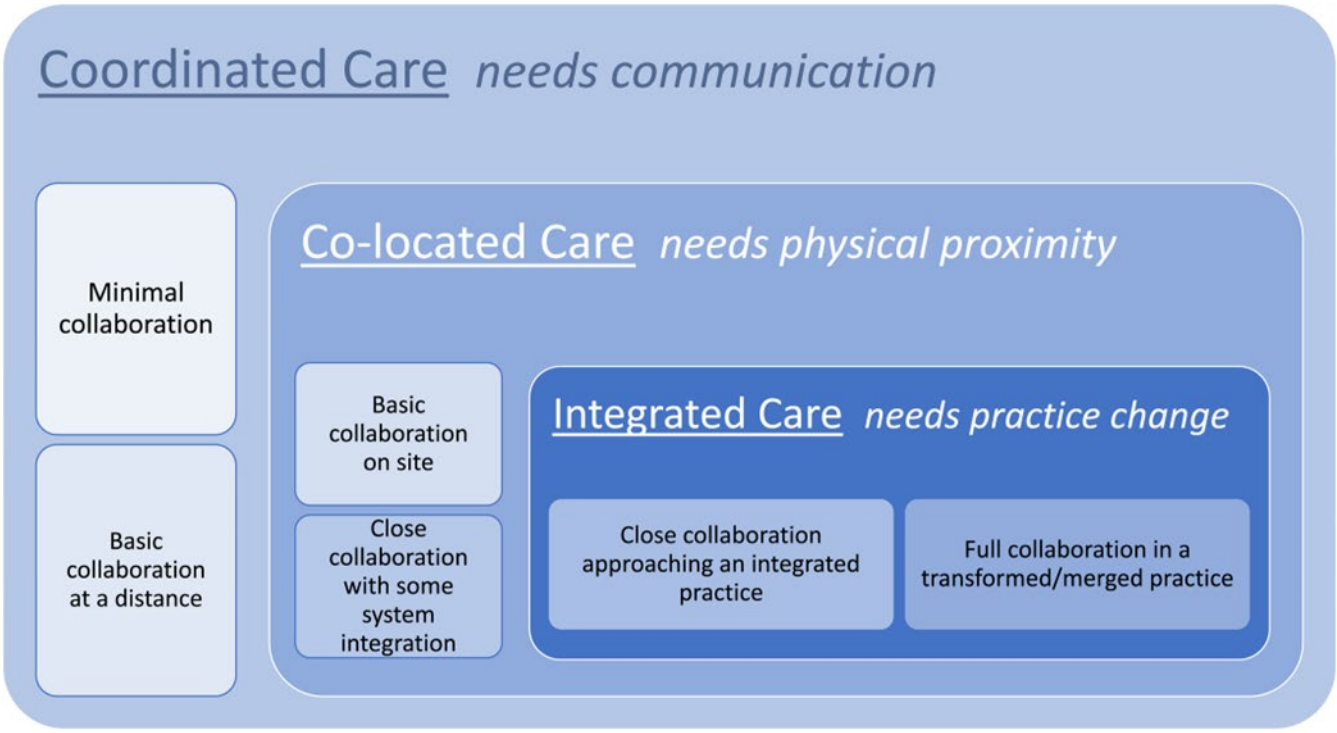
Traditionally, children and young people requiring specialist health care were cared for by a single specialist, who could address the majority of their immediate health care needs. Throughout the 20th century, as mental health services for children developed from roots in social work and "child guidance" and from paediatric departments in acute hospitals, mental and physical health were increasingly provided by separate services, often provided by different organisations . More recent trends in care involve greater collaboration between specialists, with more team-based care for children and adolescents, commonly involving expert multidisciplinary teams (MDTs) to manage complex chronic health conditions and disabilities among children and young people.[46] This trend

is coupled with an increasing recognition of the importance of holistic care for the patient, that addresses both physical and mental health care needs. For example, there is growing awareness of the extent of mental health difficulties such as anxiety and depression in young people in general, but in particular among those with complex chronic health conditions and disabilities. Conversely, there is increasing evidence that children and young people with mental health problems are at risk of physical health care problems, such as infectious diseases, respiratory problems, and weight-related problems.[47]

In a recent review, Fazel et al [46] discuss the value of greater integration of mental and physical health care services for children and young people, and describe several clinical conditions where a more integrated model of care is likely to be particularly beneficial for patients. For example, they note the need for mental health support among children with life-limiting illnesses such as cancer, the high prevalence of psychiatric morbidities among children with disorders of the brain, and observe that children with psychiatric emergencies such as deliberate self-harm frequently present to medical rather than psychiatric settings but require care from both mental and physical health care services. Conditions where the authors note that appropriate management should involve both psychiatric and medical expertise are eating disorders, somatic symptom disorders, and chronic pain syndromes.

Fazel et al [46] describe three levels of collaboration between services, summarised in Figure 2. The first level of coordination, with minimal collaboration, involves efforts to promote communication between individual medical and psychiatric health care providers. The second level involves the co-location of services. The third level is integrated care, when physical and mental health services more seamlessly promote coordinated care, including through shared access to medical records and multidisciplinary care. Examples include specialist paediatric eating disorder services where access to multidisciplinary care is increasingly the norm, or having psychologists based within epilepsy clinics as services become increasingly focused on outpatients.[48,49]

Figure 2. Levels of collaboration in models of integrated care



Source: Fazel et al.[46] Darker blue signals a higher level of collaboration.

2.3. Argument For Integrating Physical And Mental Health Services For The Management Of Functional Symptoms

Functional symptom disorders, previously called Medically Unexplained Symptoms, is the name given to physical symptoms for which there are no clear pathological explanation.[50,51] The term has been debated and criticised; alternative labels, including 'somatisation', 'bodily distress syndrome', and 'persistent physical symptoms', are sometimes used interchangeably.[52,53] Diagnostic and Statistics Manual of Mental Disorders 5th edition (DSM-5) has helpfully clarified naming and classification by subsuming all these names in the category 'somatic symptom disorders', and emphasising that individuals with functional symptoms can also have organic disease.[54] Syndromes frequently found under these labels include Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis, irritable bowel syndrome, functional neurological disorders such as non-epileptic seizures, fibromyalgia, and chronic pain.

Research indicates that the investigation of functional symptoms in children and young people (CYP) consumes considerable healthcare resources owing to the frequent utilisation of services, specialist consultations and numerous investigations and treatments.[50,55] Young people with functional symptoms tend to present to services for management of physical symptoms in the first instance and may be reluctant to be referred to psychological services for fear of not being taken seriously, or of their symptoms being dismissed as 'not real'.[56] Conversely, health care professionals may not always feel equipped to manage CYP presenting in this way, and report feeling a lack of confidence in capacity to support young people with functional symptoms and their families due to limited time and expertise.[57] However, compared to the evidence on the views of CYP and parents, there is relatively little evidence of the experiences of clinicians in this area.[56]

There is some evidence that implementing a multi-disciplinary approach grounded in a biopsychosocial perspective for CYP with functional symptoms can result in cost savings, better recognition of underlying mental ill health, improved short-term functional outcomes, and increased school attendance among affected children.[58]

2.4. Argument For Integrating Physical And Mental Health Services For The Management Of Eating Disorders (ED)

"Eating disorder" is an umbrella term that encompasses a range of disorders related to eating and feeding. DSM-5 lists pica, rumination disorder, avoidant/ restrictive food intake disorder, anorexia nervosa, bulimia nervosa, binge-eating disorder, and eating disorder not otherwise specified under 'Eating Disorders'. The NHS uses a similar classification.

Although ED are often considered mental disorders (as can be seen from their listing in the DSM-5) that are treated primarily through psychological/ psychiatric intervention, they can have extensive impact on physical functions and has the highest mortality of any psychiatric disorder. For example, the effects of anorexia can affect the endocrine system, growth and body height, menarche and menstruation, bone density and brain volume.[59] In severe cases, hospitalisation may be necessary to avoid starvation. Furthermore, physical health problems can persist even after the ED has been successfully treated, and there is significant co-morbidity in ED with other psychological disorders, including anxiety, depression and obsessive compulsive disorder.[59] Consequently, patients with eating disorders are likely to be treated in both physical and psychological health settings, for different aspects of their condition. An integrated approach to ED management would help reduce this separation, and Mairs & Nicholls [60] suggest that an effective integrated team approach is more important for successful outcomes than the specific skills of individual practitioners.

A large portion of the ED evidence base is currently centred on anorexia nervosa, with other forms of ED receiving less attention. The literature is also heavily focused on female populations, and while ED appear to present more frequently among females, this could potentially impact the provision of accessible and appropriate services for boys and young men.

3. AIMS AND OBJECTIVES

Given the background described above, and the planned developments at CCH, the aims of the study are to:

(1) Investigate how the centralisation of specialist health care services in the UK can be characterised.

(2) Use qualitative and quantitative methods to support and inform the planned integration of physical and mental health services for eating disorders and for functional symptoms at CCH.

(3) Make recommendations that will guide the implementation of these services at CCH.

(4) To identify lessons that will guide the reconfiguration of specialist services into integrated models of care elsewhere in the NHS.

The objectives are to:

a. To undertake a novel scoping review to identify what "centralisation" as a service innovation means in the context of specialist health care services, and what the dimensions of centralisation are.

b. To use the scoping review to develop a taxonomy to map the different models of centralisation.

c. Undertake a rapid systematic review of the literature on centralisation and integration of physical and mental health services for eating disorders and for functional symptoms that supplements other ongoing work.

d. Undertake a documentary analysis to delineate the current and planned pathways of care and identify key stakeholders related to the planned changes at CCH.

e. Develop a logic model describing the anticipated impacts of the planned changes.

f. Undertake an economic analysis using economic modelling to evaluate the impact of the planned pathways of care identified in objective b in terms of effectiveness and cost-effectiveness, including exploring the uncertainty in these findings. This would explore potential savings (e.g., in terms of time, resources, distress, costs of travel, etc.) by centralising services from different viewpoints (e.g., NHS, families) balanced against the costs of centralising care.

g. Examine preferences for centralisation among families and professionals using qualitative research and discrete choice experiments.

h. Undertake qualitative research to investigate the factors that may influence implementation of the new models of care at CCH.

i. Identify lessons learned that might be applied to future service changes of this kind.

4. STUDY DESIGN AND METHODS

4.1. Workstream 0. Scoping Review and Taxonomy

Objectives

The objectives are to identify what characterises “centralisation of specialist health care services” as a service innovation. This will include producing a formal definition of what centralisation means in this context, what the components of centralising specialist care are, and the advantages and disadvantages of different models of centralisation in different settings.

Unlike systematic reviews and meta-analyses, scoping studies “aim to map rapidly the key concepts underpinning a research area and the main sources and types of evidence available, and can be undertaken as standalone projects in their own right, especially where an area is complex or has not been reviewed comprehensively before.”[61] In this study we will examine the extent, range and nature of research on centralising specialist health care services and will follow the five stages of the methodological framework for conducting scoping studies. [61-63] This will build on the team’s experience of conducting rapid scoping reviews. [64,65] We will use the Preferred Reporting Items for Systematic Reviews and Meta-Analysis extension for scoping reviews statement to guide the reporting of the methods and findings.[66]

Stage 1: Identifying the research question

The scoping review will aim to provide a rapid mapping of the literature on centralisation of specialist health services (i.e. reorganisation of specialised healthcare services that is characterised by fewer specialised units serving a higher volume of patients), including the main domains/dimensions of centralisation, the settings where it is applied, and the advantages and disadvantages of different models of centralisation in different settings. Specific questions that the scoping review will address are the following: what does "centralising specialist health care services" mean? What are the elements of centralising specialist services? How do the different models of centralisation work in different settings?

Stage 2: Identifying relevant studies

We will conduct a review of the existing evidence on different aspects of centralising specialist care in general (considering all service settings and not limited by disease, condition or type of treatment or investigation provided). This will aim to identify the main factors involved in centralisation of the specialist care.

We will adopt a phased search strategy approach, where we start from broad terms and narrow it down to ones that are more specific. Articles published in peer-reviewed journals, as well as grey literature such as commentaries and think-tank reports will be included and used to develop a theoretical understanding of the main characteristics of decentralisation. We will not be limiting the review by research design including previous literature reviews, quantitative and qualitative studies as well as the grey literature. The searching for evidence will comprise a range of different sources, as follows:

- Electronic databases (e.g., MEDLINE, Scopus, CINAHL Plus, Web of Science, ProQuest Social Science, and ProQuest Nursing and Allied Health);
- Grey literature sources such as Health Management Information Centre, Open Grey and TRIP medical databases, including proposals for centralisations;
- Other researchers working in this area; and,
- Reference lists of retrieved studies.

We will not limit the search to a certain period of time, to capture relevant major policy changes. Unless stakeholders are aware of important papers in languages other than English, foreign language material will be excluded because of the cost and time involved in translating material.

Stage 3: Literature selection

Selection criteria for identifying relevant literature will be developed iteratively, based on increasing familiarity with the literature, including a clear description of the characteristics of the centralised model being implemented. An experienced researcher will screen the articles in the title phase, while a second reviewer will cross-check a random sample of exclusions. Disagreements will be discussed until consensus is reached. We will acknowledge the potential limitations of this approach in the review paper.

Stage 4: Charting the data

We will extract data obtained from the selected research reviews, quantitative and qualitative studies as well as the grey literature included in our scoping review. For each study we will record and then code the following in order to contextualise the domains covered by each of the selected studies:

- What type of service was being centralised (e.g., emergency or elective, type of treatment or investigation).
- The rationale for centralisation.
- How services changed with the centralisation/the centralisation model (e.g., number of centres before and after centralisation, how the services interacted with one another).
- The health condition(s) relevant to the centralisation.
- The setting of the centralisation (e.g., rural or urban, population size/geographical affected).
- How the centralisation was implemented (e.g., consultation process, decision-making processes).
- Over what time period the centralisation was implemented.
- The evidence that was used to inform the centralisation.

A data extraction form will be used for data extraction, in the form of a spreadsheet. It will then be piloted independently by two researchers using a random sample of five articles. Disagreements will be discussed until consensus is reached. The data extraction form will be finalised based on the findings from the pilot.

Our extracted data will include the rationale for centralisation. We do not know if the data will be enough to build the taxonomy, but if this is not possible the data will be used to answer the other research questions outlined for the scoping review.

Our aim of developing mid-range theories will be based on our attempt to explore the different models of centralisation and identify their main characteristics.

Stage 5: Collating, summarising and reporting the results

We will present an overview of all materials reviewed. This will include tables mapping the characteristics of the included studies, and thematic analysis of their results.

Taxonomy

The mapping process from stage 5 of the scoping review will also be used to develop a taxonomy of the different models of centralisation, including how these different models might work better in different settings. A taxonomy is a system for classifying multifaceted, complex phenomena according to common conceptual domains and dimensions. The aim is to distil complex interventions into their essential components, thereby allowing the comparison of alternative service models. To derive the taxonomy, we will utilise the finalised code structure described above for charting the data, with the structure of the taxonomy mirroring closely the conceptual codes and their sub-codes, defining key domains that characterise the centralisation of specialist health services

.

The main outputs from this research will be a series of mid-range theories [67] (theories that are sufficiently abstract to be generalised, while still sufficiently grounded in evidence to be tested in practice) of what “centralising specialist health care services” means.

4.2. Empirical Case Studies

Functional symptom disorders

There is a persistent physical symptoms service at Addenbrookes Hospital that is a specialised service providing psychological support to children and young people who are experiencing persistent physical symptoms that are not explained by illness (e.g., vomiting, limb weakness, paralysis, movement disorders including tremors, seizures, visual, speech or swallowing symptoms, and sensory disturbance such as pain, numbness or tingling). The service includes members of the psychological medicine services team for CYP. When patients present with physical symptoms they are usually seen by the paediatric medical team to diagnose and manage the health problem. When physical symptoms persist the patient tends to then be seen by different physical health specialists and undergo multiple investigations before being seen by the persistent physical symptoms service as a last resort. An alternative model is where the persistent physical symptoms service is involved in the care pathway earlier, to help diagnose and manage the symptoms and underlying health and psychological problems as speedily as possible. Moreover, the ambition for CCH is that this expertise is harnessed for the region, delivering teaching, training and consultations to primary and secondary care, to enable earlier detection and remediation of persistent physical symptoms before they interfere significantly with children's lives and reducing unnecessary costs and psychological impact of investigations and treatments.

Eating disorders

Eating disorders are mental health conditions with significant physical health effects, morbidity and long term mortality; the successful care of children and young people with eating disorders requires input from mental and physical health services. The number of young people in England with restrictive eating disorders requiring hospital admission is increasing;[68] the last resort often being lengthy, expensive, and potentially harmful specialist CAMHS eating disorder inpatient (tier 4) unit admissions. An alternative approach that has been recommended, that may be able to avoid specialist unit admissions is to focus on enhanced outpatient treatment with home support and day care) structured, with supported feeding admissions to paediatric wards for high risk cases.[69] This approach requires input from both paediatric medical services and a dedicated eating disorder team that can provide support for outpatient therapy and rapid access to psychiatry services when required.

4.3. Workstream 1. Systematic Review, Documentary Analysis Of Pathways And Logic Model

The aim of this workstream is to undertake a rapid systematic review of the literature on centralisation of physical and mental health services that supplements other ongoing work, to undertake a documentary analysis to delineate the current and planned pathways of care, and to develop a logic model describing the potential impacts of the planned changes.

The systematic review will review the literature on integration of mental and physical health services for children for the management of eating disorders and functional symptoms. This review will draw on a wider review of integrated healthcare for children and young people in secondary/tertiary care.[70] We will use the search strategy from the wider review but add additional search terms to focus on:

i. Evidence about the processes of change, the outcomes and value for money, and the barriers and facilitators of implementing integrated care focusing specifically on the integration of physical and mental health services
ii. Evidence about integrated care focusing specifically on services for eating disorders and functional symptom disorders.

Of particular interest are studies at the intersection of i and ii. We will write a separate protocol for this literature review and will register it on PROSPERO.

Documentary analysis (e.g. of project plans, and meeting minutes, and business cases) will be conducted to collect documentation that will be used to understand and delineate the pathways used in the current service as well as the planned changes to integrate mental and physical health services for children with functional symptoms and eating disorders, as described above. We anticipate analysing all relevant documentation related to the development and planning of CCH, and identifying key stakeholders in changes of this kind.

We will also use these documents to understand the programme theory guiding the changes in the service. A logic model will be constructed to describe the potential impacts of the planned changes to the pathways of care. This is likely to include the context and objectives of the proposed changes, the inputs and resources used to produce the changes, the activities describing how the changes to the pathways will be delivered, and the outcomes that the changes to the pathways may bring about. As shown in Figure 1 this work will inform the other workstreams, guiding the data to be collected for the economic analysis in WS2, the recruitment and interview topic guides for the qualitative work in WS3 and WS4, and the selection of attributes for the DCE in WS5.

4.4. Workstream 2. Economic Evaluation

The aim of this workstream is to investigate the potential costs and benefits of integrating physical and mental health care services for eating disorders and for functional symptom disorders in children at CCH from the perspective of the NHS and patients and families, compared with usual care.

Basic approach

We will undertake a hypothetical cost-consequences analysis (CCA). A CCA is a form of economic evaluation comparing interventions in which the components of incremental costs (direct or indirect) and consequences (e.g., knowledge, behaviours, processes) are computed and listed, without aggregating these results into a cost-effectiveness ratio.[71,72] This type of economic evaluation enables one to look into outcomes, process measures and qualitative findings in a quantitative manner and compare them to the costs of interventions, allowing for some insight as to how potential benefits compare to the cost of interventions.

Measuring costs

Three categories of costs will be included: i) set-up costs incurred to introduce the care pathways (these are one-off costs), ii) costs of caring for children and young people with the current and new care pathways, and iii) cost savings if the condition is managed successfully (e.g. reduction in the average cost to society of a child with eating disorders).

The specific costs to be included will be informed by the qualitative work in WS3 And WS4. The set-up costs will also be identified from the business case for CCH. The costs of caring for children with each condition will be calculated using the care pathways delineated in WS1, populated with unit cost data from published sources. From these pathways, we will also calculate the costs incurred by families, for example, in terms of travel costs and times by asking families about the distances travelled and travel times, and modes of transport, and costing these journeys using market prices.

Lifetime costs of caring for children with eating disorders and functional symptoms will be obtained from systematic reviews of the health economic literature.

Measuring consequences

Important potential outcomes from the co-location of services will be ascertained from the interviews with staff and families in WS3 and WS4. We will use a range of different outcomes from healthcare and patients' family perspectives. From the health care perspective consequences may include: i) frequency and number of visits needed, ii) length of stay in the hospital and ii) health outcomes related to the degree of success in the management of child's problem. From patient and family perspective consequences are likely to include: i) travel cost and time, ii) time off work, iii) waiting times to visit the specialist, and iv) education-related outcomes, e.g., impact on outcomes and days lost to education. The consequences will be measured from previous studies applied to the CCH setting.

There will be considerable uncertainty in the costs and consequences, owing to the fact that we are evaluating a hypothetical service at the present time. This will be captured using ranges of costs and consequences, which will be reported in the CCA.

4.5. Workstream 3. Qualitative Study Of Staff Experience And Preferences

The aim of this workstream is to a) understand the staff perceptions of current services delivered to children and young people with eating disorders and functional symptoms; and b) analyse staff perceptions of the plans to integrate mental and physical health services for children and young people with eating disorders and functional symptoms. This workstream will link with WS4 and WS5 to examine preferences for centralisation among families and professionals and will inform the development of the DCE in WS5. It will also investigate the factors influencing the implementation of the new models of care at CCH.

Data collection

Interviews with staff

We will undertake semi-structured interviews with a purposive sample of staff involved in the delivery of care or planning of services for children and young people with eating disorders and functional symptoms. We will carry out interviews by telephone or using an online platform such as Zoom or MS Teams to help build rapport with participants. The interviews will focus on capturing their perceptions and experiences with the current service model as well as their views on the planned changes to the service. We will ask staff to reflect on potential factors acting as barriers and enablers in the future implementation of the new service.

Interviews with national leaders and local stakeholders

National leaders working on the reconfiguration of services for children and young people with these conditions will be asked if they would like to take part in an interview. We will also aim to recruit participants from the local area such as representatives from the local authority and patient advocacy groups. The interviews will focus on capturing their perceptions and experiences with the current service model as well as their views on the planned changes to the service. We will ask them to reflect on potential factors acting as barriers and enablers in the future implementation of the new service. We aim to carry out 5-7 interviews at these levels.

Interview sampling

The interviews will be carried out with a purposive sample of study participants that will be designed in relation to the sampling framework outlined in Table 1 and will grow throughout the study due to snowball sampling. We will aim to carry out interviews with staff leading the service, managers and staff delivering services on the ground from a wide range of professional groups. We anticipate recruiting a sample of 18 staff members.

Table 1. Sampling framework for interviews with staff members

Participant category	**Number of interviews**
Service lead/s	2
Area managers	2
Staff delivering services to CYP with eating disorders	7
Staff delivering services to CYP with unexplained medical symptoms	7
Total	**18 interviews**

Recruitment and consent processes for staff interviews

In the case of staff interviews, the researchers will contact potential participants via email and will send them a participant information sheet. Participants will then be given 48 hours to review the information and ask questions about the study. If the participant agrees to take part in the study, they will be asked to sign the consent form. The researcher will then arrange a time to carry out the interview over the phone or an online platform (Zoom or MS Teams). Staff will be also be offered the alternative to take part in a group interview (where feasible) if completing an individual interview is not possible. An informed consent process using participant information sheets and written consent (scanned forms or typewritten/electronic signature) will be used for recruitment to ensure informed and voluntary participation.

Data analysis

Data collection and analysis will be carried out in parallel and facilitated through the use of rapid assessment procedure (RAP) sheets as explained in Vindrola-Padros and Johnson.[73] RAP sheets will be developed per site to facilitate cross-case comparisons and per population (to make comparisons between sub-groups). The categories used in the RAP sheets will be based on the questions included in the interview topic guide, maintaining flexibility to add categories as the study is ongoing.

4.6. Workstream 4. Qualitative Study Of Parent/Carer Experience

The aim of this workstream is to understand the parents' perceptions of current services delivered to children and young people with eating disorders and functional symptoms. This workstream will link with WS3 and WS5 to examine preferences for centralisation among families and professionals and will inform the development of the DCE in WS5. It will also investigate the factors influencing the implementation of the new models of care at CCH.

Data collection

We will undertake semi-structured interviews with a purposive sample of parents and carers whose children have received services for eating disorders or functional symptoms at Cambridge University

Hospitals NHS Foundation Trust and Cambridgeshire and Peterborough NHS Foundation Trust. The interviews with parents will focus on documenting their perceptions and experiences with the service, including aspects of the service that worked well and areas that should be improved. The interviews will be carried out over the telephone or via Zoom or MS Teams. The interviewer will take notes during the interview but the conversation will also be audio recorded.

Interview sampling

The semi-structured interviews with parents will follow a purposive sampling approach. Parents will be sampled in relation to their child's age, gender, ethnicity and health condition. We will aim to recruit up to 20 parents (10 per condition).

Recruitment and consent processes for patient and carer interviews

Clinical staff and/or research nursers working with the clinical teams will first contact parents to see if they are happy to be approached by a researcher. If they agree, the researcher will then contact the parent via telephone or email to discuss the study. Parents will also be given the option to contact the research team if they prefer not to have their details shared. If the parent is contacted via phone, they will be asked if a participant information sheet and consent form can be sent via email. If they prefer post, both of these documents will be sent via post with a pre-paid addressed envelope so they can return the signed consent form to the team. The researcher will then contact them to arrange a time to carry out the interview. Interviews will be carried out via telephone or an online platform (e.g. Zoom or MS Teams) as preferred by the patient.

If the parent is contacted via email, the participant information sheet and consent form will be sent in a subsequent email and the parent will be given the option to schedule a call with the researcher to discuss the study. The participant information sheet will contain information on the study, potential risks and a description of how the data will be used to ensure informed and voluntary participation. If the parent agrees to take part in the study, they will be instructed to email back the signed consent form (scanned forms or type written/electronic signature). Interviews will be carried out via telephone or an online platform (e.g. Zoom or MS Teams) as preferred by the patient.

Data analysis for the interviews

Data collection and analysis will be carried out in parallel and will follow the same procedure as for WS3. RAP sheets will be developed per parent population (based on the child's health condition) to facilitate comparisons.

4.7. Workstream 5. Discrete Choice Experiment (DCE)

The aim of workstream 5 is to analyse the preferences of key stakeholders with regards to the new integrated pathways for the eating disorders and medical unexplained symptoms for children and young people at CCH. This will provide data on what these stakeholders think about the new pathways, which issues matter to them the most when considering this, and how strongly they feel about these issues. This workstream will consist of two DCEs, one for eating disorders and one for medical unexplained symptoms. As shown in Figure 1, this workstream will be informed by WS1, WS3 and WS4; these workstreams will inform the construction of the DCE questionnaires (e.g., the selection of attributes) and the approach to sampling.

Questionnaire development

The process for designing the DCE questionnaires will be as follows:

1. For each of the DCEs we will ask staff and parents/carers during the interviews in WS3 and WS4 to identify the important attributes associated with co-location of services. An initial list of factors that might be affected by re-location of each of the new pathway will then be compiled based on the above interview findings plus the research evidence from the literature review in WS1.

2. A long list of attributes will then be developed by the research team. This will describe the characteristics and potential outcomes of new pathways and could potentially include: health outcomes; processes of care; travel distances or costs; out-of-pocket expenses incurred by families; NHS costs; types of interactions between physical and mental health services; and, health care professionals' workload. Based on previous studies we have run, each of the DCEs will include a maximum of seven attributes, as having more attributes than this can make the DCE difficult for participants to understand and complete. Attributes will be selected so that there is minimal overlap between them; any residual overlap will be accounted for in the multivariate regression analyses (see below).

3. A preferred list of up to seven shortlisted attributes to be included in each of the DCEs will be informed by discussions with the PPIAG and Study Steering committee and asking them to rank the long list, thereby producing a short list of selected attributes. This preferred list of attributes will also be reviewed by the research team.

4. We will assign levels to these attributes based on feasible ranges derived from the literature review and documentary analysis in WS1 and the interviews in WS3 and WS4.

5. We will design each of the condition-specific DCEs questionnaire using a pairwise choice framework and will compile a set of pairwise scenarios that describe the feasible combinations of levels and attributes of different models of co-location. Respondents will complete 8-12 choice questions. Using a pairwise choice framework, in each choice question respondents will be asked to choose one of two models of care presented to them which are differentiated by their attributes. Based on previous evidence and our own experience about the maximum number of choice questions respondents are able to answer, we will keep the total number of feasible pairwise choice questions to a maximum of 12.

6. As part of the questionnaire we will also ask respondents to providing a simple ranking of the attributes according to importance for each of the DCEs.

The questionnaire will then be piloted with 4-6 respondents (2-3 think-aloud interviews, 2-3 providing written feedback) and amended according to the feedback received.

Sampling

For eating disorders and functional symptoms the three main participant groups will be: (i) parents/ carers (ii), members of the general population, and (iii) health care staff, including managers and commissioners. We have a minimum target of 200 responses for each of the DCEs over all groups, with at least 50 respondents in each group.[74,75]

Data analysis

We will quantitively evaluate preferences for the new pathways using either conditional logit or mixed logit regression analysis, as recommended in international guidelines,[76] separately for the two settings. The results will indicate which attributes significantly affect preferences, conditional on the other attributes included in the analysis. Data will be analysed for all respondents jointly and separately for the participant sub-groups. We will deal with sample heterogeneity using covariate adjustment in regression analyses. We will examine marginal rates of substitution between the attributes, calculate the probability that different combinations of the levels of the attributes will be preferred, and calculate the relative importance of the attributes.

The ranking exercise included at the end of each of the DCEs will also be used to show the relative importance of the different attributes; this is an imperfect measure as it does not account for the attribute levels. We will ask respondents to rank the attributes included in each of the DCEs in order of importance to them. We will present the results graphically as 100% stacked bar charts showing the proportion of respondents who ranked each attribute first, second, third, fourth, etc.

5. PATIENT AND PUBLIC INVOLVEMENT (PPI)

Patients and the public will be actively involved in the study in the following ways:

- Design of the project
- Management of the project (e.g. advisory group)
- Developing participant information resources
- Interpretation of study findings.
- Contributing to the reporting of the project.
- Dissemination of findings.

Patient representatives from a local Research Advisory Panel (RAP), comprising 6-8 parents and carers of children and young people affected by eating disorders and functional symptoms, will form the study PPI Advisory Group (PPIAG) and will provide ongoing feedback on the protocol and will provide ongoing review and feedback throughout the study (including dissemination). The PPIAG will meet 3 times during the lifetime of the project, for half a day each time. All meetings will be designed to optimise accessibility and engagement, e.g. ensuring hard copies of papers are available, and shared well in advance of the meeting. In addition, the PPIAG will be asked to comment and feedback on study documents. Recommendations on effective involvement and payment of patients and members of the public will be followed.[25-26] A member of the team will be identified as primary contact with whom patient representative may raise any issues or concerns.

Patient and public involvement will continue to benefit the study in the following ways: ensuring the study focuses on the importance of clinical outcomes by integrating physical and mental health services; ensuring that this focus is reflected in our aims, objectives and research questions; ensuring that these are operationalised suitably in our approach to data collection and analysis; and ensuring that our findings are disseminated effectively and in a manner that is meaningful to patients, carers and the public.

6. ETHICAL ISSUES

6.1. Assessment And Management Of Risk

The interviews in WS4, and the DCEs in WS5, may raise issues for our anticipated participant groups (parents/carers, professionals, general public). For parents/carers, participation in these activities may potentially cause distress, as participants revisit previous experiences of care. For staff, it is possible that the situations presented might cause distress in terms of raising personal concerns in relation to potential changes to their own services, or in terms of their own concerns in relation to quality of care for managing rare diseases. For the general public, there is a potential for distress to be caused by participation in the DCE when describing the circumstances of children and young people with eating disorders and functional symptoms. To address these concerns, the research team and the PPIAG will review the survey tools and interview, focus group and workshop topic guides to ensure that the questions and topics to be discussed are presented in a sensitive fashion. In addition, the Participant Information Sheets will make clear the (minimised) risk of distress, and make clear that participation is voluntary, and that participants may withdraw at any stage. Support will be offered to any patient or carer who seems distressed through appropriate channels, e.g., referral to a relevant support group.

In addition, patients and carers and professionals may feel reluctant to raise criticisms of services provided in any of the above activities, as the research team may not be seen as suitably independent. The Participant Information Sheets will make clear the independence of the researchers involved in these activities, the importance of identifying challenges as well as successes, and that any information will be anonymised as much as possible.

Participants (patients, carers, health professional, general publics) will be informed in the Participant Information Sheet (PIS) about the limits of confidentiality when participating in the study. While the researchers may use quotes from participants in written reports, academic publications or conferences, participant's real names will not be used, and every effort will be made to protect the identity of participants. Participants will be given the opportunity to opt in or out of being quoted on a consent form.

6.2. Ethical Approval

NHS Research Ethics Committee approval will be obtained for the activities in WS4 and WS5.

7. GOVERNANCE

This study will be led by Prof. Stephen Morris (University of Cambridge) and RSET team members will comprise Prof. Naomi Fulop (UCL), Dr. Angus Ramsay (UCL), Saheli Gandhi (UCL), Josefine Magnusson (UCL) and Efthalia Massou (University of Cambridge). The team will meet at least fortnightly throughout the duration of the project to discuss the status of the project, support progress with data collection and analysis, and to ensure effective dissemination of findings and stakeholder engagement. These meetings will be chaired by SM; administration will be provided by the project manager; teleconference and videoconference facilities will be used to optimise participation from research team members based outside of UCL. The research team will report on progress at monthly RSET meetings, and project oversight will also be provided by the rest of the RSET and the RSET Stakeholder Advisory Board.

SM will ensure there are adequate quality and number of monitoring activities conducted by the study team. This will include adherence to the protocol, procedures for consenting and ensure adequate data quality. They will inform the sponsor should he/she have concerns which have arisen from monitoring activities, and/or if there are problems with oversight/monitoring procedures.

Sub-groups of the research team will be formed to lead on particular aspects of data collection and analysis. The subgroups will report on progress to the whole project team at the research team meetings. At these meetings findings from each sub-group will be discussed and interdependencies and mutual learning between each element of the project will be explored.

In addition, the research team will meet monthly with the clinicians and managers involved in planning CCH.

In addition, the study will have an independent Stakeholder Advisory Group comprising:

- PPI members (Parents/Carers)
- Clinical experts in in eating disorders and functional symptoms
- Experts in health care centralisation / integration.

These will be a mix of local stakeholders related to CCH, and independent stakeholders.

8. FUNDING

RSET is funded by the NIHR Health Services and Delivery Research (HS&DR) programme (HSDR 16/138/17).

9. INDEMNITY ARRANGEMENTS

University College London holds insurance against claims from participants for harm caused by their participation in this study. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, if this study is being carried out in a hospital, the hospital continues to have a duty of care to the participant of the study. UCL does not accept liability for any breach in the hospital's duty of care, or any negligence on the part of hospital employees. This applies whether the hospital is a NHS Trust or otherwise.

10. INTELLECTUAL PROPERTY

While the researchers possess substantial know-how relating to this research study, they do not hold intellectual property (IP) in this area.

This research may generate new IP. Any such product will be dealt with appropriately with guidance from UCL Business (see below), and in partnership with the other parties involved in the study.

During the project we anticipate producing the following IP:

- The taxonomy of different models describing how centralisation of the specials care may be coordinated (WS0).
- Survey tools for evaluating the preferences of stakeholders (WS5).
- Dissemination materials produced throughout the study.

These will be protected by copyright law, according to the Copyright, Designs and Patent Act 1988. Copyright law protects any work which is written and is original. We will use “(c) University College London” (followed by the year of creation) to make clear that UCL asserts its right to copyright protection in these works.

IP generated through this research will be managed by UCL Business, who will work closely with the project team to ensure that any valuable IP is protected by patent filing or copyright as outlined above. Our dissemination plan allows for free and open access publication of the intervention manuals and peer-reviewed journal articles.

The aim of the project is to generate knowledge for wider benefit. Nothing we will produce will necessarily generate income and it is likely that all our tools and outputs will be maximally accessible and free at the point of delivery.

As the IP from this research will relate to methodological approaches and lessons relating to how care services should be organised, we do not anticipate regulatory hurdles associated with medical technologies (e.g. MHRA approval). Barriers to adoption will mainly take the form of stakeholders' lack of awareness of and engagement in the lessons derived from our research. To address this, we will disseminate the findings as widely as possible (as described below).

11. ARCHIVING

UCL and each participating site recognise that there is an obligation to archive study-related documents at the end of the study (as such end is defined within this protocol). SM confirms that he will archive the study master file at University College London for 20 years from study end.

12. OUTPUTS AND DISSEMINATION

12.1 Predicted outputs

We will share feedback on a regular basis with the CCH planners. Formative feedback can include: (1) sharing our evolving understanding of the logic model, programme theory and suggested refinements; (2) the likely economic impact of the proposed changes; and (3) analysing staff and parent views and experiences and preferences with processes of change and improvement.

We will produce a final report to the NIHR HS&DR programme, and an accompanying summary of the project in a format to be agreed with the project stakeholders (e.g., slide set in PowerPoint). Findings will also be shared through articles published in peer-reviewed journals and papers presented at academic and professional conferences. In addition, we propose to produce a number of more accessible outputs summarising our findings targeted at a range of audiences, including trusts, regulators, policy makers, and patient groups. The team will maintain the independence of the research.

We anticipate that we will be able to generate the following outputs based on the research findings:

- Findings from the systematic literature review.
- Findings from the economic analyses;
- Results from the DCE and qualitative research describing the preferences of different stakeholders to centralising specialist services.
- Findings from the qualitative research to understand factors that will influence implementation

12.2. Funder requirements

We will follow the guidance stipulated by the NIHR when communicating our research:

- Notification of outputs and copies of any paper/article should be sent to the funder 28 days before is due to be published.
- The NIHR's contribution should be acknowledged in full by including a funding statement.

13. DATA MANAGEMENT

13.1. Qualitative Data (Interviews)

In the study, interview data will be collected from participants in accordance with the participant information sheets and the section on recruitment in this protocol. Interviews will be recorded on an encrypted, password-protected digital audio recorder to which only the researcher knows the password. These data will be anonymised and stored securely on a shared drive within a password-protected IT network, which can only be accessed by named members of the qualitative team. The data will be cleared from the digital audio recording device when it has been transferred. These data will be kept completely separate from other study data. Anonymised interview data will be organised by participant codes. Participant identifier codes will be stored in a password-protected file on a secure drive to which only named team members have access via password-protected computers at the UCL Department of Applied Health Research. Participant identifier codes will be stored separately from the anonymised interview transcripts.

The digital audio recordings of interviews will be appropriately sent to Essential Secretary via secure FTP system (http://www.essentialsecretary.co.uk/) for transcription. Digital audio recordings of interviews, the anonymised interview transcripts, data for the documentary analysis, and quantitative data will be stored for analysis on a secure drive to which only named team members have access via password-protected computers at the UCL Department of Applied Health Research.

13.2. Quantitative Data (DCE)

Electronic data provided as part of the DCE online survey will be transferred securely from the survey company to the University of Cambridge's Clinical School Computing Service Secure Data Hosting Service (SDHS) for analysis. All electronic data will be stored, handled and analysed within the SDHS (- see https://cscs.medschl.cam.ac.uk/server-services/secure-data-hosting-service/). This is a secure electronic environment that has been certified to the ISO27001 information security standard and conforms to the NHS Information Governance Toolkit. It has a mechanism that enables information to be transferred simply and securely.

Professor Stephen Morris (Primary Care Unit, Department of Public Health and Primary Care, University of Cambridge), will act as the data controller of quantitative data for the study. He will process, store and dispose of all quantitative data in accordance with all applicable legal and regulatory requirements, including the Data Protection Act 1998 and any amendments thereto. Data will not be transferred to any party not identified in this protocol and are not to be processed and/or transferred other than in accordance with the participants' consented.

14. TIMELINE

See Fig. 3 for a Gantt chart describing the timelines of the project.

Figure 3. Gantt chart

Year	2022										2023					
Calendar month	**March**	**April**	**May**	**June**	**July**	**August**	**September**	**October**	**November**	**December**	**January**	**February**	**March**	**April**	**May**	**June**
Project start																
Project set-up																
Write full protocol																
Write up service evaluation protocol																
Set up steering committee																
Set up PPI group																
Review of protocols by external researchers and funder																
Ethical and R&D approvals for full protocol																
Ethical approvals for service evaluation protocol																
Scoping review on centralisation of specialised health services																
Review of selected papers																
Write paper																
Systematic reviews, documentary analysis of pathways, logic model																
Systematic review																
Documentary analysis to delineate current and planned pathways of care																
Logic model																
Economic analysis																
Develop model structure																
Collect model inputs																
Data analysis																
Write paper																
Qualitative research to analyse preferences and understand factros that will influence implementation																
Data collection (staff)																
Data collection (patients and families)																
Data analysis																
Write paper on factors infulencing implementation																
Discrete choice analyses of preferences																
Literature review to inform DCE questionnaire development																
Qualitative work to inform DCE questionnaire development																
Pilot DCE questionnaire																
DCE questionnaire distribtion and collection																
DCE data analysis																
Write paper on preferences (qualitative research and DCE)																
Meetings																
Cambridge team																
Steering committee																
PPI																
Final report to funder																

REFERENCES

1. NHS England, Public Health England, Health Education England, Monitor, Care Quality Commission, NHS Trust Development Authority. Five-year forward view. London: NHS England 2014.
2. NHS England. The NHS long term plan. London: NHS England 2019.
3. Morris S., Ramsay A.I.G., Boaden R., Hunter R.M., McKevitt C., Paley L., Perry C., Rudd A.G., Turner S.J., Tyrrell P.J., Wolfe C.D.A., Fulop N.J. Impact and sustainability of centralising acute stroke services in English metropolitan areas: retrospective analysis of hospital episode statistics and stroke national audit data. BMJ 2019; 364:1.
4. Fitzsimons KJ, Mukarram S, Copley LP, et al. Centralisation of services for children with cleft lip or palate in England: a study of hospital episode statistics. BMC Health Serv Res 2012; 12:148.
5. Woo YL, Kyrgiou M, Bryant A, et al. Centralisation of services for gynaecological cancer. Cochrane Database Syst Rev 2012;3: CD007945.
6. Ravi P, Bianchi M, Hansen J, et al. Benefit in regionalisation of care for patients treated with radical cystectomy: a nationwide inpatient sample analysis. BJU Int 2014; 113:733–40.
7. Fosbol EL, Granger CB, Jollis JG, et al. The impact of a statewide pre-hospital STEMI strategy to bypass hospitals without percutaneous coronary intervention capability on treatment times. Circulation 2013; 127:604–12.
8. Gabbe BJ, Simpson PM, Sutherland AM, et al. Improved functional outcomes for major trauma patients in a regionalized, inclusive trauma system. Ann Surg 2012; 255:1009–15.
9. Metcalfe D, Bouamra O, Parsons NR, et al. Effect of regional trauma centralization on volume, injury severity and outcomes of injured patients admitted to trauma centres. Br J Surg 2014; 101:959–64.
10. Morris S, Hunter RM, Ramsay AIG, et al. Impact of centralising acute stroke services in English metropolitan areas on mortality and length of hospital stay: difference-in-differences analysis. BMJ 2014; 349:g4757.
11. Simpson AN, Wardrope J, Burke D. The Sheffield experiment: the effects of centralising accident and emergency services in a large urban setting. Emerg Med J 2001; 18:193–7
12. Prabhakaran S, O'Neill K, Stein-Spencer L, Walter J, Alberts MJ. Prehospital triage to primary stroke centers and rate of stroke thrombolysis. JAMA Neurol 2013; 70:1126-32.
13. Smith EE, Dreyer P, Prvu-Bettger J, Abdullah AR, Palmeri G, Goyette L, et al. Stroke center designation can be achieved by small hospitals: the Massachusetts experience. Crit Pathw Cardiol 2008; 7:173-7.
14. Weir N, Buchan A. A study of the workload and effectiveness of a comprehensive acute stroke service. J Neurol Neurosurg Psychiatry 2005; 76:863-5.
15. Lahr MM, Luijckx G-J, Vroomen PC, van der Zee D-J, Buskens E. Proportion of patients treated with thrombolysis in a centralized versus a decentralized acute stroke care setting. Stroke 2012; 43:1336-40.
16. Bruins Slot K, Murray V, Boysen G, Berge E. Thrombolytic treatment for stroke in the Scandinavian countries. Acta Neurol Scand 2009; 120:270-6.
17. Cadilhac DA, Purvis T, Kilkenny MF, Longworth M, Mohr K, Pollack M, et al. Evaluation of rural stroke services does implementation of coordinators and pathways improve care in rural hospitals? Stroke 2013; 44:2848-53.
18. Hunter RM, Davie C, Rudd A, Thompson A, Walker H, Thomson N, et al. Impact on clinical and cost outcomes of a centralized approach to acute stroke care in London: a comparative effectiveness before and after model. PloS One 2013; 8:e70420.
19. Morris S, Hunter RM, Ramsay AIG, Boaden R, McKevitt C, Perry C, et al. Impact of centralising acute stroke services in English metropolitan areas on mortality and length of hospital stay: difference-in-differences analysis. BMJ. 2014; 349:g4757.

20. Ramsay AIG, Morris S, Hoffman A, Hunter RM, Boaden R, McKevitt C, et al. Effects of centralizing acute stroke services on stroke care provision in two large metropolitan areas in England. Stroke. 2015; 46:2244–51. doi:10.1161/ STROKEAHA.115.009723.
21. Sampalis JS, Denis R, Lavoie A, Frechette P, Boukas S, Nikolis A, et al. Trauma care regionalization: a process-outcome evaluation. J Trauma Acute Care Surg. 1999; 46:565–81.
22. MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, et al. A national evaluation of the effect of trauma-center care on mortality. N Engl J Med. 2006; 354:366–78.
23. Coupland VH, Lagergren J, Lüchtenborg M, Jack RH, Allum W, Holmberg L, Hanna GB, Pearce N, Møller H. Hospital volume, proportion resected and mortality from oesophageal and gastric cancer: a population-based study in England, 2004-2008. Gut. 2013; 62:961–6.
24. Nuttall M, van der Meulen J, Phillips N, Sharpin C, Gillatt D, McIntosh G, et al. A systematic review and critique of the literature relating hospital or surgeon volume to health outcomes for 3 urological cancer procedures. J Urol. 2004; 172:2145–52.
25. Hanchanale VS, Javale P: Impact of hospital provider volume on outcome for radical urological cancer surgery in England. Urol Int 2010, 85(1):11–5.
26. Moles DR, Cunningham SJ: A national review of mandibular orthognathic surgery activity in the National Health Service in England over a nine-year period: Part 1 - Service factors. Br J Oral Maxillofac Surg 2009, 47(4):268–73.
27. Judge A, Chard J, Learmonth I, Dieppe P: The effects of surgical volumes and training centre status on outcomes following total joint replacement: analysis of the Hospital Episode Statistics for England. J Public Health 2006, 28(2):116–24.
28. Halm EA, Lee C, Chassin MR. Is volume related to outcome in health care? A systematic review and methodologic critique of the literature. Ann Intern Med 2002; 137:511–20.
29. Mesman R, Westert GP, Berden BJ, et al. Why do high-volume hospitals achieve better outcomes? A systematic review about intermediate factors in volume-outcome relationships. Health Policy 2015; 119:1055–67.
30. NHS Commissioning Support for London. Cancer services case for change. London: Commissioning Support for London; 2010.
31. London Cancer. London cancer specialist services reconfiguration: a case for change in specialist cancer services. London: London Cancer; 2013.
32. Exworthy M, Peckham S. Access, choice and travel: implications for health policy. Soc Policy Adm. 2006; 40:267–87.
33. Groux P, Anchisi S, Szucs T. Are cancer patients willing to travel more or further away for a slightly more efficient therapy? Cancer Clin Oncol. 2014; 3:36.
34. L. Vallejo-Torres, M. Melnychuk, C. Vindrola-Padros, M. Aitchison, C. S. Clarke, N. J. Fulop, J. Hines, C. Levermore, S. B. Maddineni, C. Perry, K. Pritchard-Jones, A. I. G. Ramsay, D. C. Shackley and S. Morris. Discrete-choice experiment to analyse preferences for centralizing specialist cancer surgery services. Br J Surg 2018; 105: 587–596.
35. Jones AP, Haynes R, Sauerzapf V, Crawford SM, Zhao H, Forman D. Travel time to hospital and treatment for breast, colon, rectum, lung, ovary and prostate cancer. Eur J Cancer. 2008; 44: 992–9.
36. Exworthy M, Peckham S. Access, choice and travel: implications for health policy. Soc Policy Adm. 2006; 40:267–87.
37. Sauerzapf VA, Jones AP, Haynes R, Crawford SM, Forman D. Travel time to radiotherapy and uptake of breast-conserving surgery for early stage cancer in northern England. Health Place. 2008; 14:424–33.
38. Posnett J. The hospital of the future: is bigger better? Concentration in the provision of secondary care. BMJ 1999; 319:1063–5.
39. Mungall IJ. Trend towards centralisation of hospital services, and its effect on access to care for rural and remote communities in the UK. Rural Remote Health 2005; 5:390.
40. Lee JE, Sung JH, Ward WB, et al. Utilization of the emergency room: impact of geographic distance. Geospat Health 2007; 1:243–53.

41. Turnbull J, Martin D, Lattimer V, et al. Does distance matter? Geographical variation in GP out-of-hours service use: an observational study. Br J Gen Pract 2008; 58:471–7.
42. Stitzenberg KB, Sigurdson ER, Egleston BL, et al. Centralization of cancer surgery: implications for patient access to optimal care. J Clin Oncol 2009; 27:4671–8.
43. Nicholl J, West J, Goodacre S, et al. The relationship between distance to hospital and patient mortality in emergencies: an observational study. Emerg Med J 2007; 24:665–8.
44. Friebel R, Hauck K, Aylin P. Centralisation of acute stroke services in London: Impact evaluation using two treatment groups. Health Econ 2018; 27:722-32. doi:10.1002/hec.3630.
45. Bhattarai, N., McMeekin, P., Price, C., & Vale, L. (2016). Economic evaluations on centralisation of specialised healthcare services: a systematic review of methods. BMJ open, 6(5), e011214.
46. Fazel, M., Townsend, A., Stewart, H., Pao, M., Paz, I., Walker, J., Sawyer, S. M., & Sharpe, M. (2021). Integrated care to address child and adolescent health in the 21st century: A clinical review. JCPP Advances, 1(4), e12045. https://doi.org/10.1002/jcv2.12045
47. Aarons GA, Monn AR, Leslie LK, Garland AF, Lugo L, Hough RL, Brown SA. Association between mental and physical health problems in high-risk adolescents: a longitudinal study. J Adolesc Health. 2008 Sep;43(3):260-7. doi: 10.1016/j.jadohealth.2008.01.013. Epub 2008 May 2. PMID: 18710681; PMCID: PMC2768339.
48. Hughes, E. K., Le Grange, D., Court, A., Yeo, M., Campbell, S., Whitelaw, M., Atkins, L., & Sawyer, S. M. (2014). Implementation of family-based treatment for adolescents with anorexia nervosa. Journal of Pediatric Health Care, 28, 322–330.
49. Plevin, D., & Smith, N. (2019). Assessment and management of depression and anxiety in children and adolescents with epilepsy. Behavioural Neurology, 2019, 2571368.
50. Rosendal M., Olesen F. & Fink P. (2004) Management of medically unexplained symptoms. British Medical Journal 330, 4–5.
51. Berezowski L, Ludwig L, Martin A, Löwe B, Shedden-Mora MC. Early Psychological Interventions for Somatic Symptom Disorder and Functional Somatic Syndromes: A Systematic Review and Meta-Analysis. Psychosom Med. 2022 Apr 1;84(3):325-338. doi: 10.1097/PSY.0000000000001011. PMID: 34524264; PMCID: PMC8983947.
52. Creed F, Guthrie E, Fink P, et al. Is there a better term than 'Medically unexplained symptoms'? J Psychosom Res 2010; 68: 5–8.
53. Marks EM, Hunter MS. Medically Unexplained Symptoms: an acceptable term? Br J Pain. 2015 May;9(2):109-14. doi: 10.1177/2049463714535372.
54. American Psychiatric Association . Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC: American Psychiatric Pub; 2013.
55. Ibeziako P. & Bujoreanu S. (2011) Approach to psychosomatic illness in adolescents. Current Opinion in Pediatrics 23, 384–389.
56. Hinton & Kirk (2016) Families' and healthcare professionals' perceptions of healthcare services for children and young people with functional symptoms: a narrative review of the literature. Health and Social Care in the Community 24(1), 12–26.
57. Furness P., Glazebrook C., Tay J., Abbas K. & Slaveska-Hollis K. (2009) Medically unexplained physical symptoms in children: exploring hospital staff perceptions. Clinical Child Psychology and Psychiatry 14, 575–587.
58. Pales et al. (2019) A biopsychosocial model of care for children and young people (CYP) with persistent, unexplained, physical symptoms (PUPS) BMJ Paediatrics Open 3(Suppl 1):A4.1-A4.
59. Herpertz-Dahlmann & Dahmen, Children in Need—Diagnostics, Epidemiology, Treatment and Outcome of Early Onset Anorexia Nervosa. Nutrients 2019, 11(8).
60. Mairs & Nicholls (2016) Assessment and treatment of eating disorders in children and adolescents. Archives of Disease in Childhood 101 (12).
61. Arksey, H. and O'Malley, L. (2005) Scoping studies: towards a methodological framework, International Journal of Social Research Methodology, 8, 1, 19-32.

62. Levac D, Colquhoun H, O'Brien KK. 2010. Scoping studies: advancing the methodology. Implement Sci, 5:69.
63. Daudt HM, van Mossel C, Scott SJ. 2013. Enhancing the scoping study methodology: a large, inter professional team's experience with Arksey and O'Malley's framework. BMC medical research methodology, 13:48.
64. Ranieri V, Barratt H, Fulop NJ, Rees G. Factors that influence career progression among postdoctoral clinical academics: a scoping review of the literature. BMJ Open 2016;6:e013523. doi:10.1136/bmjopen-2016-013523.
65. French C, Ferlie E, Fulop NJ. The International Spread of Academic Health Science Centres: a Scoping Review and the Case of Policy Transfer to England Health Policy. Health Policy; 2014, 117(3): 382-391.
66. Moher, David, Larissa Shamseer, Mike Clarke, Davina Ghersi, Alessandro Liberati, Mark Petticrew, Paul Shekelle, and Lesley A. Stewart. "Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement." Systematic reviews 4, no. 1 (2015): 1.
67. Jagosh, J., Salsberg, J., Pluye, P., Macaulay, A.C. & Bush, P.L. (2011). Realist Review: An Introduction. Canadian Public Health Association presentation.
68. Health and Social Care Information Centre (HSCIC) www.hscic.gov.uk/article/3880. January 30th, 2014. (30 Jan 2014).
69. Street K, et al. Structured, supported feeding admissions for restrictive eating disorders on paediatric wards. Arch Dis Child 2016;101:836–838. doi:10.1136/archdischild-2016-310506.
70. Joanna Anderson, Tamsin Ford, Ian Goodyer, Naomi Pygott, Lillian Green, Sohini Pawar. Integrated healthcare for children and young people – a systematic literature review of effectiveness and cost-effectiveness.. PROSPERO 2020 CRD42020185235 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020185235
71. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. Oxford, UK: Oxford University Press; 2015.
72. Greenhalgh T. How to read a paper. Papers that tell you what things cost (economic analyses). BMJ, 1997; 315(7108):596.
73. C Vindrola-Padros, GA Johnson. Rapid techniques in qualitative research: a critical review of the literature. Qualitative Health Research 30 (10), 1596-1604.
74. Johnson FR, Lancsar E, Marshall D, et al. Constructing experimental designs for discrete-choice experiments: report of the ISPOR conjoint analysis experimental design good research practices task force. Value Health 2013;16:3–13.
75. Soekhai, V., de Bekker-Grob, E.W., Ellis, A.R. et al. Discrete Choice Experiments in Health Economics: Past, Present and Future. PharmacoEconomics 37, 201–226 (2019). https://doi.org/10.1007/s40273-018-0734-2.
76. Hauber BA, González JM, Groothuis-Oudshoorn CGM, Prior T, Marshall DA, Cunningham C, IJzerman MJ, Bridges JFP. Statistical Methods for the Analysis of Discrete Choice Experiments: A Report of the ISPOR Conjoint Analysis Good Research Practices Task Force. Value in Health 2016; 19: 300-15. https://www.ispor.org/Conjoint-Analysis-Statistical-Methods-Guidelines.pdf.
77. NIHR. Briefing notes for researchers - public involvement in NHS, health and social care researchhttps://www.nihr.ac.uk/documents/briefing-notes-for-researchers-public-involvement-in-nhs-health-and-social-care-research/27371 [last accessed 28 July 2022].
78. NIHR. Payment guidance for researchers and professionals. https://www.nihr.ac.uk/documents/payment-guidance-for-researchers-and-professionals/27392 [last accessed 28 July 2022].