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Project Title

Reorganising specialist cancer surgery for the 21st century: a mixed methods evaluation (RESPECT-21)

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Contents

ABSTRACT

Centralisations of specialist cancer services in two regions of England provide an opportunity to study the implementation and outcomes of such changes. *London Cancer* (a network of providers across North Central and North East London, and West Essex; population 3.2 million) and *Greater Manchester Cancer* (covering Greater Manchester and East Cheshire; population 3.1 million - formerly called *Manchester Cancer*) planned to centralise specialist surgical pathways for prostate, bladder, kidney, and oesophago-gastric cancers, so that specialist aspects of these services are provided through a smaller number of hospitals.

This study combines measuring the impact of centralisation in terms of clinical processes, clinical outcomes, cost-effectiveness, and patient experience ('what works?') with a qualitative analysis of development, implementation and sustainability of the centralisations ('how and why'). This mixed methods evaluation will use a controlled before and after design, and parallel qualitative study of implementation processes. We will use an adapted version of the framework developed by the research team in a study evaluating centralisation of acute stroke services[1], structured around key interrelated processes of service reconfigurations, covering: 1) stakeholder preferences in relation to changes of this kind; 2) reaching a decision to change; 3) developing and agreeing the new service models; 4) implementing the new models; 5) adherence to the new models throughout the system; 6) impact on provision of care; 7) impact on outcomes (including clinical outcomes, patient experience, and costs). The qualitative analysis will draw on findings from a recent review of large-scale transformation initiatives which identified five 'simple rules' likely to enhance 'successful' implementation [2] relating to: leadership approaches, feedback and learning; history of change; and engagement of professionals, patients and families. Members of the research team have developed these 'rules' further through our study of centralisations of acute stroke services in London and Greater Manchester [3], identifying the importance of combining 'bottom up'-led change with 'top down' central leadership, and of understanding of the social and political context of the changes and their impact on outcomes.

This multi-site study covering specialist surgical pathways for four cancers in two large conurbations in England will address established gaps in the evidence on centralisations of specialist cancer surgery, including processes, impact, and cost-effectiveness of changes, and patient, public and professional preferences.

Our research questions are:

RQ 1. What are patient, public and professional preferences in relation to these centralisations?
RQ 2. What are the key processes in centralising specialist cancer surgery services in London Cancer and Greater Manchester Cancer, and what factors influenced progress of centralisation?
RQ 3. What is the impact on staff and healthcare provider organisations, including ways of working, skill mix and approaches to collaboration?
RQ 4. What is the impact of the London Cancer centralisations on provision of care, in terms of clinical processes and outcomes?
RQ 5. What is the impact of London Cancer centralisations on patient experience, including choice and continuity of care?
RQ 6. What are the cost and cost-effectiveness of the London Cancer changes?

RQ 7. How might lessons from centralising specialist cancer surgery services be applied in future centralisations of specialist cancer services and other specialist settings?

We will conduct a Discrete Choice Experiment to examine patient, public and professional preferences for centralisations of this kind (RQ 1). Qualitative methods will include documentary analysis, stakeholder interviews and non-participant observations of meetings (RQs 2, 3). Quantitative methods will include analysis of local and national data on clinical processes and outcomes (RQ4), National Cancer Patient Experience Survey data (RQ5) as well as joint comparison of costs and effects to allow consideration of the cost-effectiveness of the transformation (RQ 6). Finally, we will hold a workshop for those involved in planning centralisations of specialist cancer services elsewhere, and those involved in centralising other types of 'non cancer' specialist service; it will include providers, commissioners and patients/patient groups. The workshop will focus on how these lessons might apply more widely, and we will incorporate this feedback into our final conclusions (RQ7).

This protocol presents an update on how we are conducting this evaluation in light of implementation progress in London and Greater Manchester. The evaluation was originally funded to study centralisations of specialist surgery in four cancer pathways in London Cancer and Greater Manchester Cancer. However, while in London Cancer the changes were implemented by April 2016, in Greater Manchester Cancer the implementation is still in progress. We will therefore study the impact and cost-effectiveness of the changes in London only; we will study the processes of change in both London and Greater Manchester.

In addition, this updated protocol reflects changes in access to certain data as well as delays in obtaining other data. While we originally expected receipt of oesophago-gastric national audit data, we have learned after conversations with the data stewards that this will no longer be possible and therefore this dataset will not be used. There have also been delays in obtaining National Cancer Registration and Analysis Service data, which has resulted in the need for no-cost extensions totalling 17 months, reflected in our timelines.

The research team is from London, Greater Manchester, and Cambridge, and draws together patients, clinicians, and researchers with the knowledge and expertise necessary to conduct an evaluation of this scale and complexity. Optimising the configurations of specialist services to maximise patient benefit and efficiencies is likely to remain a priority in the English NHS over the coming years. Lessons from this study will be of value to those who commission, organise and manage specialist services, not just by providing evidence on how changes of this kind might benefit patients, but also in terms of giving insights on how service changes of this kind are developed and implemented, and what contextual factors are influential. Further, through a stakeholder workshop we will ensure these lessons will be of use in a wide range of specialist healthcare settings.

1. BACKGROUND

CENTRALISING SERVICES TO IMPROVE QUALITY OF CARE AND PATIENT OUTCOMES

There is an association between high volume and better outcomes in many clinical settings: for example, recent research by members of the research team has indicated that centralising acute stroke services into a smaller number of high-volume units is associated with significantly better provision of evidence-based clinical interventions[4], and significantly better clinical outcomes, including patient mortality[5]. High volume is associated with better

outcomes in specialist surgery for oesophago-gastric (OG) cancers[6] and urological cancers[7]. However, the strength of this relationship varies between specialties[8].

There are longstanding recommendations to centralise specialist services[9-11], citing potential to reduce variations in access, increase patient volumes, and improve patient outcomes by increasing the likelihood of patients receiving care in hospitals that have a full range of experienced specialists and equipment to support provision of care. Recent guidance indicates that centralising specialist services will remain a priority in the English NHS in the future[12,13]. However, little is known about the processes by which services are centralised, the impact of changes on patients and staff, and which factors influence implementation[14]. Recent research indicates that there is limited evidence of the cost impact of centralising cancer services [14,15], and limited evidence on patient, public and professional preferences in relation to centralisations of this kind[16,17]. Research indicates that centralisation of cancer services is likely to place increased travel demands on patients and families, and may limit some people's access to quality care[18]. A review of research evidence indicates patients are more willing to travel for a number of reasons: for specialist care; to a hospital with a good reputation; if a condition is serious or urgent; if of a higher socioeconomic status; in contrast, older patients and frequent users of services are less willing to travel further[19]. A recent study suggests that while cancer patients are willing to make more frequent journeys to services if it means they will receive care that is slightly more effective or associated with fewer side-effects, similar effects are not reported for longer journeys[20].

SPECIALIST SURGICAL SERVICES FOR UROLOGICAL AND OESOPHAGO-GASTRIC CANCERS IN LONDON CANCER AND GREATER MANCHESTER CANCER

Networked cancer systems London Cancer [LC; covering North Central and North East London, and West Essex (population 3.2 million)] and Greater Manchester Cancer [GMC; formerly Manchester Cancer, covering Greater Manchester and East Cheshire (population 3.1 million)] have been working towards centralising specialist surgery services separately for a number of cancers[21,22]. This study will evaluate changes conducted in four surgical cancer pathways that are being centralised in both areas: prostate, renal, bladder, and OG cancers. There are over 60,000 new cases of these cancers in the UK every year[6,23-25]. Prostate cancer is the second highest cause of cancer deaths in men [23], while five year survival rates for bladder and renal cancers range from 50-60%[24,25], 12% for oesophageal cancer and 16% for gastric cancer[6].

PRE-CENTRALISATION PATHWAYS

In Greater Manchester at the time of planning the changes, patients were referred to a local cancer centre and, depending on diagnosis, either remained at that service for staging or palliative care, or were referred to a specialist centre for specialist surgery, chemotherapy and/or radiotherapy (Figure 1). Specialist centres were located across the Greater Manchester region, and took patients referred from nearby hospitals; certain aspects of urological care (e.g. robotic surgery) were provided by the Christie Hospital. While there was broad agreement in process across the pathways, there existed variations in the protocols used for referral to specialist centres. Across specialist centres, patient volumes were substantially lower than recommended, and there were variations in access to technology (e.g. robotic surgery), innovative techniques, and opportunities to participate in research. At the time, all surgeons provided all types of radical surgery within their specialty (e.g. urologists offered all specialist surgery for bladder, prostate and kidney) and there was

limited opportunity for greater 'subspecialisation' (e.g. a urologist becoming expert in radical prostatectomy).

In London Cancer at the time of planning changes, potential cancer patients were referred to their local cancer centre for diagnosis, and either remained there or were referred to a specialist centre (Figure 1). The care received by patients varied across specialist centres. For example, prostate and bladder patients could only receive robotic surgery in certain specialist centres; the majority of renal surgical patients underwent surgery in a local non-specialist centre (performed by a specialist or general urologist), rather than a specialist centre (potentially limiting the surgical options afforded these patients); and OG patients were not guaranteed to see a specialist out of hours or at weekends. Similar to Greater Manchester, there was substantial variation in patient volumes across specialist centres.

CENTRALISATIONS PROPOSED BY LONDON CANCER AND GREATER MANCHESTER CANCER

In both areas, it was proposed that specialist surgical services for these cancers should be centralised in a reduced number of centres (Figure 1). Patient pathways were to be standardised, with the aim of reducing variations in care. It was anticipated that increased patient volume would permit greater specialisation of staff, and greater experience and expertise across teams, and specialist services would offer a full range of surgical technologies (e.g. robotics), and equal access to innovative techniques, such as less invasive procedures. Local units would continue to provide much patient care closer to home, including diagnosis, ongoing radiotherapy and chemotherapy. However, post-centralisation, local units would benefit from closer involvement of specialist centre staff, e.g. joint multi-disciplinary teams (MDTs), and specialists providing training and delivering some outpatient care, thus improving quality of care across the whole system. Both centralisations emphasised the importance of continuity of care.[21,22] Table 1 provides an overview of the proposed changes in terms of the number of cases and specialist centres for each type of cancer.

Figure 1. Simplified models summarising specialist cancer surgery, before and after centralisation

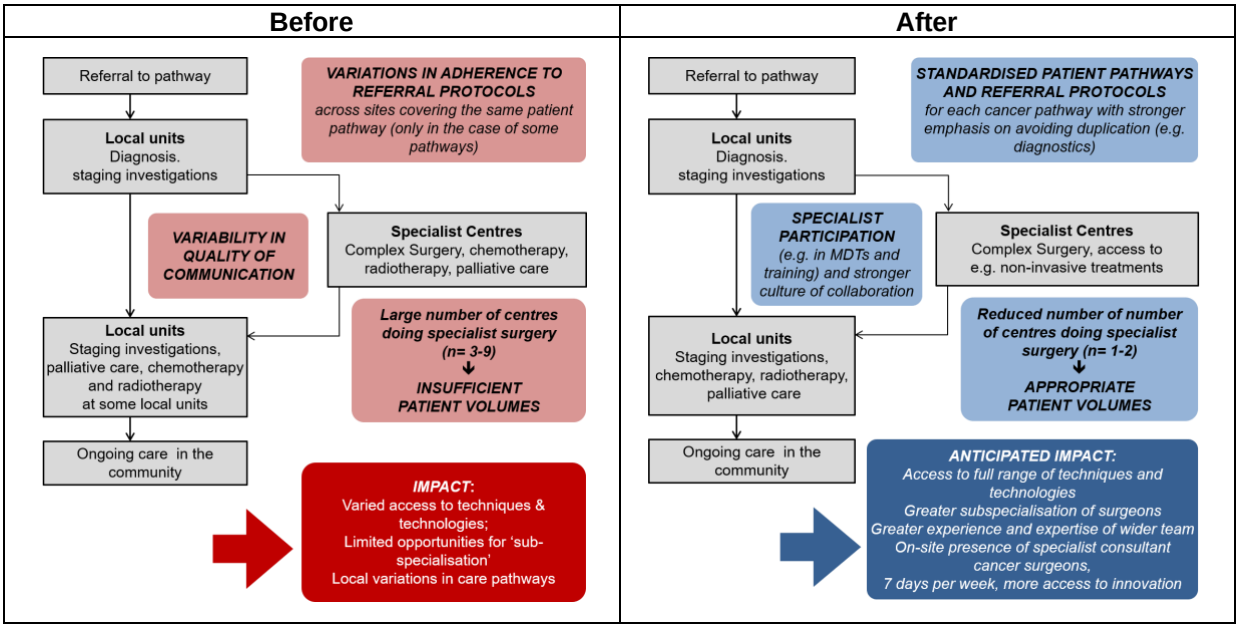


Table 1. Overview of planned changes to specialist surgical services – number of cases and number requiring complex surgery, and anticipated number of specialist services pre and post centralisation (total cases and numbers requiring surgery are annual figures)

Cancer	London Cancer				Greater Manchester Cancer			
	Total cases	Require Surgery	Specialist centres		Total cases	Require surgery	Specialist centres	
			Before	After			Before	After
Prostate & bladder	1900	350	4	1	2500	400	5	2
Renal	250	190	9	1	400	250	8	2
Oesophago-gastric	500	150	3	2	800	150	3	2

London Cancer figures [21,26]; Greater Manchester Cancer figures [22,26]

CURRENT STATUS OF CENTRALISATIONS

When RESPECT-21 was originally funded in January 2015, it was understood that centralisation of specialist surgical pathways for OG, prostate, bladder and kidney cancers would be implemented by December 2015 at the latest. The London Cancer centralisations were implemented between December 2015 and April 2016 (broadly in line with anticipated timelines). However, implementation in Greater Manchester has been delayed for a range of reasons, including the changes in links to NHS England Specialist Commissioning resulting from the process of devolution of health and social care funding to Greater Manchester, and the proposed changes to acute provision resulting from the Healthier Together initiative in GM [27]. OG cancer surgery services were centralised in September 2018, transferring all elective and emergency OG surgery to one specialist centre, and with establishment of GM-wide surgical specialist multidisciplinary team (SMDT) meetings and GM-wide on-call rota. For urological cancers, progress is less certain: a model of care has been agreed but implementation has been delayed, particularly because of concerns about the impact of moving urological cancer surgery services on benign urological services. An implementation board has been established and is now meeting, and it was anticipated that all prostate surgery would be centralised to one site by September 2018. Timelines for the centralisation of bladder and kidney cancer surgery are uncertain, and full centralisation of these services is unlikely to be completed before April 2021. As a result of these delays, we will study the impact and cost-effectiveness of the changes in London only, while we will study the processes of change in both London and Greater Manchester. We provide details of our updated study design in the sections that follow.

2. AIMS AND OBJECTIVES

This study will use qualitative and quantitative methods to evaluate centralisation of specialised cancer surgery services in two regions of England, and identify lessons that will guide centralisation work in other areas of specialist services. The objectives of this study are to:

- examine preferences for centralisation, the most important attributes of services that affect these preferences, and how these preferences vary between patients, the public, and professionals;
- identify factors influencing development, implementation, and sustainability of centralisations of specialist cancer surgery;
- analyse the impact of changes on staff skill mix, patient choice, patient experience, and continuity of care;
- analyse the impact of changes on patient outcomes and processes of care in London Cancer;
- analyse the relationship between processes of care and outcomes in London Cancer;
- analyse incremental cost and cost-effectiveness of the changes in London Cancer;

- present lessons on centralising specialist cancer surgery services that might be applied in future centralisations of specialist cancer services and other specialist settings.

To address these objectives we will conduct a mixed methods evaluation of the processes, impact, and costs of the centralisations of specialist surgical pathways for four cancers in London Cancer, using a controlled before and after design and parallel qualitative study of implementation processes. The study in Greater Manchester will focus only on the qualitative elements. The four surgical pathways (prostate, bladder, renal, and OG) have been selected because they are being centralised in both areas, permitting analysis of how such changes occur in different contexts. There is also potential to analyse different scales of change, as the 4 pathways vary in relation to the extent of centralisation of specialist cancer surgery centres planned, as follows:

- Renal (London Cancer) 9 to 1
- Prostate and bladder (London Cancer) 4 to 1
- OG (Greater Manchester Cancer) 3 to 1
- OG (London Cancer) 3 to 2

Analysing these different extents of centralisation will allow comparison of the work involved in developing and implementing them (e.g. whether different extents of centralisation require different levels of planning; whether the political issues differ; whether there is more resistance to the 'high' centralisation cases).

To examine patient, public and professional preferences for centralisations of this kind, we will conduct a Discrete Choice Experiment (RQ1). To understand how changes were implemented and sustained we will use qualitative methods, including documentary analysis, stakeholder interviews and observations of relevant meetings (RQ2, 3). Quantitative methods will include analysis of local and national data on clinical processes and outcomes (RQ4), National Cancer Patient Experience Survey data (NCPES; RQ5), as well as joint comparison of costs and effects to allow consideration of the cost-effectiveness of the transformation (RQ6). Finally, we will hold a workshop both for people planning centralisations of specialist cancer services elsewhere, and for people centralising or planning to centralise other types of 'non-cancer' specialist services. It will focus on how these lessons might apply more widely, and we will incorporate this feedback into our final conclusions (RQ7).

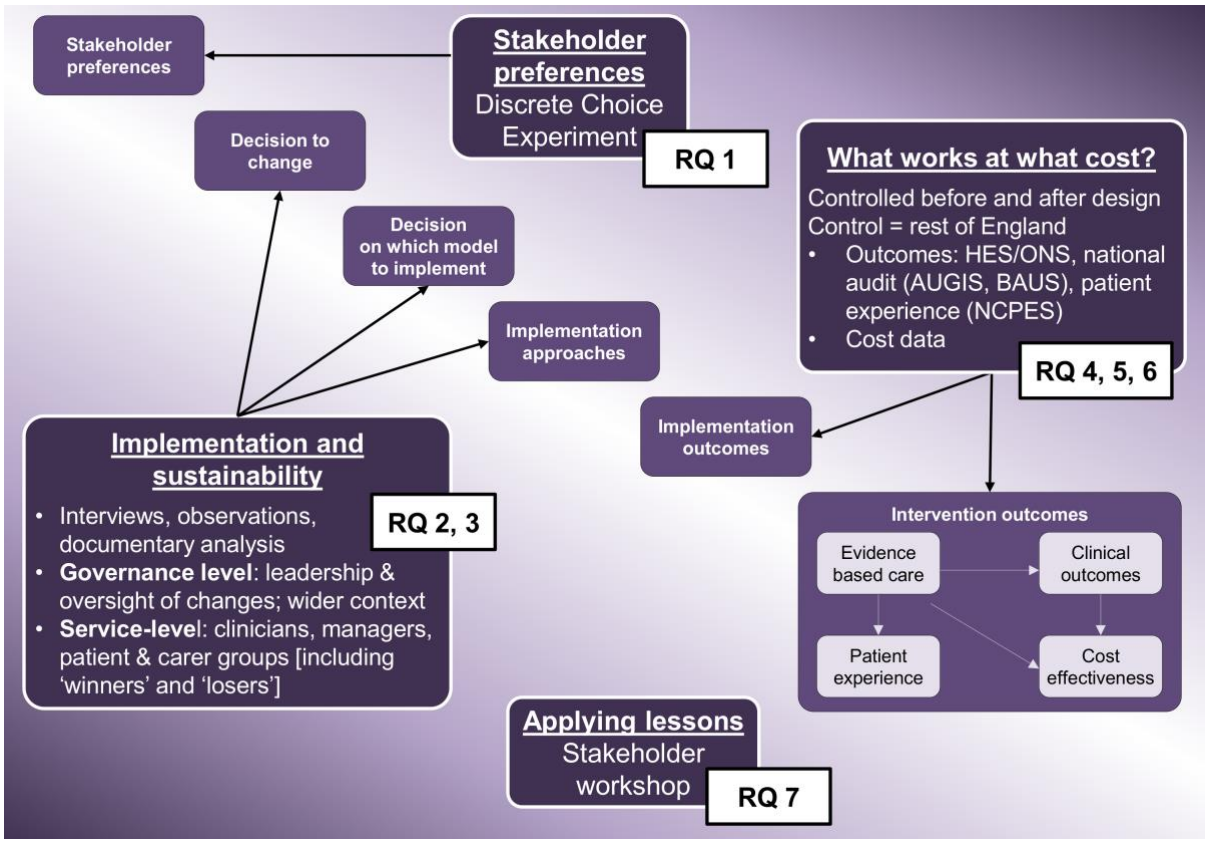
3. DESIGN

This is a multi-site study of centralisation of specialist surgical pathways for four cancers in two large conurbations in England. It will combine measuring impact of centralisation in terms of clinical processes, clinical outcomes, cost-effectiveness and patient experience, using a controlled before and after design ('what works?') with a parallel qualitative analysis of the development, implementation and sustainability of the centralisations ('how and why?').

These approaches will be combined in a framework that has been adapted from the HS&DR funded evaluation of stroke service centralisations[1] (Figure 2). This framework reflects key processes of centralisation, and how they are inter-related. It covers: 1) stakeholder preferences (NB this was an addition to the original framework); 2) reaching a decision to change; 3) developing and agreeing the new service model; 4) implementing the new model; 5) adherence to the new model throughout the system; 6) impact on provision of

care; 7) impact on outcomes (including clinical outcomes, patient experience, and costs) (NB ordering these factors should not be taken to imply a linear relationship between them).

Figure 2. Summary of framework for analysing centralisations



There are important differences between the context in which this framework was developed and the context in which it will be applied in this study. Whereas stroke is a healthcare event that requires immediate response, specialist cancer surgical services operate at a different pace, and thus offer greater opportunities for service providers to engage with the patient and family regarding treatment choices. Therefore, different factors may influence the decision to change, and different types of model may be implemented. Both of these considerations might influence the way in which changes progress.

Our research questions are:

RQ 1. What are patient, public and professional preferences in relation to these centralisations?

RQ 2. What are the key processes in centralising specialist cancer surgery services in London Cancer and Greater Manchester Cancer, and what factors influenced progress of centralisation?

RQ 3. What is the impact on staff and healthcare provider organisations, including ways of working, skill mix and approaches to collaboration?

RQ 4. What is the impact of the London Cancer centralisations on provision of care, in terms of clinical processes and outcomes?

RQ 5. What is the impact of the London Cancer centralisations on patient experience, including choice and continuity of care?

RQ 6. What are the cost and cost-effectiveness of the London Cancer changes?

RQ 7. How might lessons from centralising specialist cancer surgery services be applied in future centralisations of specialist cancer services and other specialist settings?

We will address these questions using qualitative and quantitative methods.

Patient, public, and professional preferences for centralisation (RQ1) (LC, GMC, national)

The proposed centralisations are likely to represent a significant change in how patients experience care, with many having to travel further to receive surgery or specialised investigations, but with a greater choice of treatments, and with potentially better outcomes. To examine the acceptability of such changes to patients, the public, and professionals, we will conduct a discrete choice experiment (DCE)[28-30], which will examine preferences for centralisation; relative importance of attributes of surgical services; and how preferences vary between stakeholders. The DCE will follow international best-practice guidelines[30].

Implementation and sustainability (RQ2, 3) (LC, GMC)

Documentary analysis (e.g. of project plans, meeting minutes, and local press) will be conducted to develop a clear understanding of what processes were carried out, and when, to develop and implement the centralisations of specialist cancer surgery.

We will interview a range of stakeholders related to the centralisation of specialist cancer surgery in Greater Manchester Cancer and London Cancer. Interviews will focus on the drivers for change, and factors influencing the centralisations at key stages (such as agreeing the case for change, selecting the service model, planning and implementation of changes, and their impact on quality of care). To examine issues associated with implementation and sustainability of the changes, we will observe meetings related to the governance and implementation of the centralised services. The focus of our analysis will be extended, in order to capture not just how changes were implemented and sustained in LC, but also to explore factors that led to changes in GMC being delayed.

Impact on clinical processes, clinical outcomes, and patient experience (RQ4, 5) (LC only)

We will study the impact of centralisation in LC on clinical outcomes and delivery of clinical interventions. We will assemble data from the National Cancer Registration and Analysis Service (NCRAS) data linked to Hospital Episodes Statistics (HES) to analyse the impact of selected cancer surgery service centralisations on a range of outcomes (e.g. mortality, readmission, length of stay) and national audit data from the British Association of Urological Surgeons (BAUS) to analyse impact on care process measures (e.g. surgical complications, surgical technique). We will also aim to delineate the association between the outcomes and the care processes. To examine further the impact of the centralisations on aspects of patient experience, we will analyse NCPES data, with a focus on such key issues as patient choice, confidence in staff, communication, and teamwork.

Cost-effectiveness (RQ6) (LC only)

We will also evaluate the costs of the LC centralisations, and their value for money. This will be reported as an incremental cost per quality-adjusted life year gained and incremental cost per outcome gained as informed by the DCE.

Exploring how lessons might be applied in other contexts (RQ7) (LC, GMC, national)

In order to draw out the lessons from our findings for the centralisation of other specialist services, we will share our findings at a workshop both for people involved in planning centralisations of specialist cancer services elsewhere, and for those involved in centralising

or planning to centralise other types of 'non cancer' specialist services. These will include providers, commissioners and patients/patient groups. Based on feedback from this workshop we will provide an analysis of factors influencing the generalisability of our findings to other specialist services, and based on this learning develop lessons that will be of use in these settings.

4. SAMPLING

Much of the data collected will relate to the areas undergoing centralisation. In addition, changes of this kind must be understood in a wider context, and we will thus also collect/obtain national data where appropriate. Therefore, reflecting the changes to study design agreed with the funder, we will be collecting data as outlined in Table 2:

Table 2. Areas covered by study components

Study component	Areas covered
Discrete Choice Experiment (RQ1)	LC, GMC, national
Documentary analysis, stakeholder interviews and non-participant observations (RQ2,3)	LC, GMC
Clinical processes, clinical outcomes, and patient experience (RQ4, 5)	LC only; national
Cost-effectiveness (RQ6)	LC only; national
Sharing lessons through a stakeholder workshop (RQ7)	LC, GMC, national

Discrete Choice Experiment (RQ1) (LC, GMC, national)

The DCE will elicit preferences for the way in which cancer surgery services are organised for three sub-groups: patients; the general public; and professionals (surgeons, specialists, nurses). In particular, the patients' subgroup will include representative samples of cancer patients of four cancer types: prostate, bladder, kidney, and OG cancers, with 25% for each cancer type. The professionals' subgroup will include professionals involved in managing these cancers, and the general public subgroup will include people generally interested in healthcare. We will seek to sample these stakeholder sub-groups in London, Greater Manchester and elsewhere in England.

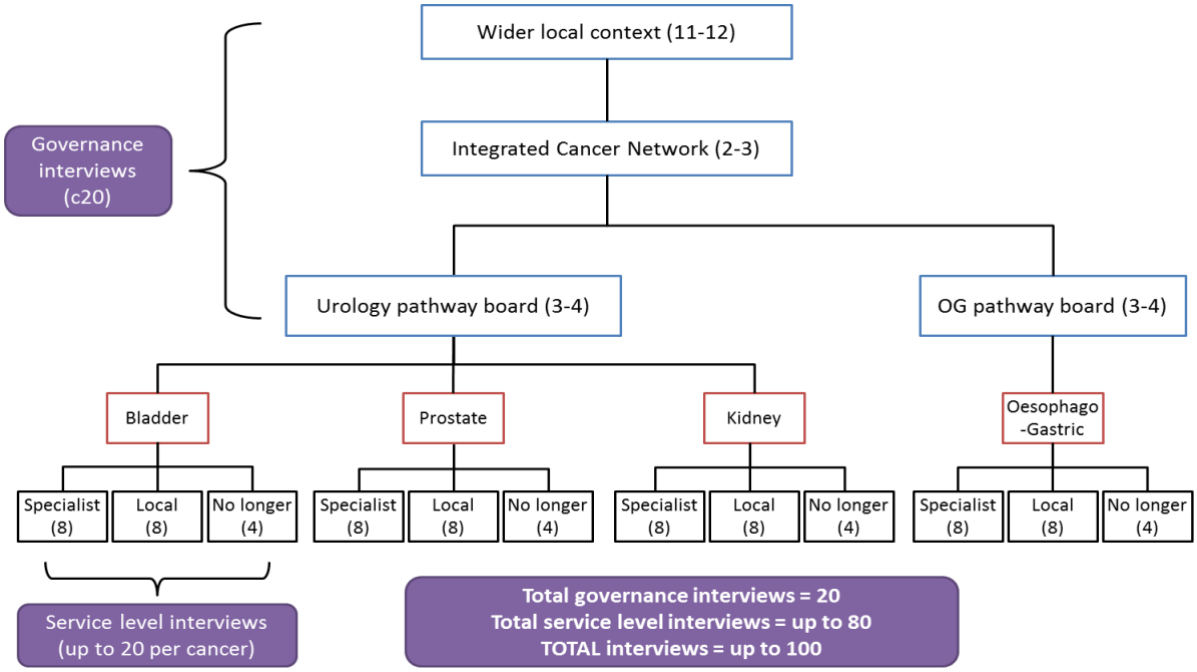
Sample size calculations for DCEs are not straightforward but depend on the question format, the complexity of the choice tasks, the desired precision of the results, the degree of heterogeneity in the target population, the availability of respondents, and the need to conduct subgroup analyses. A sample size of 300 is commonly recommended[31], and this will be exceeded here, with 100 in the professional and public subgroups, and 200 in the patient subgroup (100 London and Greater Manchester, 100 from elsewhere).

Documentary analysis, stakeholder interviews and non-participant observations (RQ2,3) (LC, GMC)

We will collect documentation related to development, planning and implementation of the centralisations in London Cancer and Greater Manchester Cancer. We will also collect data on national contextual factors, such as policy and press coverage. We anticipate analysing relevant local and national documentation covering a time period from 2006, when the Royal College of Surgeons of England launched a consultation on centralisation of surgical services[32], through to the end of the data collection period (month 40 for GMC, month 46 for LC).

Reflecting the proposed centralisations, we will sample up to 210 stakeholder interviewees purposively from a range of settings (an illustration of our sampling is presented in Figure 3). These will include the overarching governance of the centralisations, for example the London Cancer and Greater Manchester Cancer boards, cancer-specific pathway boards, and representatives of the wider community in which the changes take place (including commissioners, health and wellbeing boards, Strategic Clinical Networks, Academic Health Science Networks, and patient and carer representative groups). For each cancer, we will interview clinical staff (including surgeons, doctors, nurses, allied health professionals, radiologists, pathologists, and oncologists) and management (at service and board level) for specialist cancer centres, local cancer centres, and services that no longer provide care (with each representing a case study). These groups were selected after careful consideration of the proposed membership for SMDTs and local MDTs in national documents, academic articles and initial stages of data collection.[33-38] Given the extension of qualitative work in LC, we now anticipate conducting a total of up to 120 interviews (including follow-ups) in this area; given limited implementation of change in GMC, we now anticipate conducting up to 90 interviews (including follow-ups) in this area.

Figure 3. Anticipated interviewee recruitment (illustrative example covers single area)



Note: numbers in brackets reflect upper estimate of anticipated interviewees: where studied services are based in the same organisation, data collection may reduce, in terms of overlapping managerial and clinical staff

Over the data collection period, researchers will observe activities related to the ongoing governance and implementation of the centralised services in the four specialist cancer surgery pathways we are studying. We will observe meetings where reconfiguration of specialist cancer surgery is a topic of discussion (e.g. planning and commissioning committee meetings), meetings focusing on oversight and running of the centralised services (e.g. Pathway Board meetings, SMDT meetings and local MDT meetings), and meetings related to the wider context (e.g. covering oversight and development of cancer services at regional or cross-regional levels). We will identify meetings to be observed in

collaboration with local clinical leaders (including clinical members of the research team), but we will also seek to identify relevant events and meetings through data collection process.

Impact on clinical processes, clinical outcomes, and patient experience (RQ4, 5) (LC only)

Table 3 presents key measures selected for the quantitative analyses in the original Protocol (version 1.0 dated 13th July 2015) submitted to the funder, and a summary of all changes to these measures in subsequent protocol revisions – version 1.2 dated 9th August 2018 and version 1.3 – due to data availability (either because on further exploration the required variables do not exist, they were not available for our entire study period, or it was not possible for the research team to be able to access them).

Clinical members of the research team identified primary and secondary outcome measures, process measures, and mediating factors for each type of cancer. Four outcomes initially identified (one primary and one secondary for prostate cancer, one secondary outcome for bladder cancer, and one secondary outcome for OG cancer) were not available from our data sources. The information for prostate cancer outcomes (proportion of men treated by primary surgery who remain continent at 12 months, and proportion of men treated by surgery with pre-operative erectile function who have erections sufficient for penetration at 12 months) was not available for the 'before' reconfiguration period in London Cancer and the rest of England as it was not collected. We have replaced these with two new primary outcomes for prostate cancer, where information is available for the before and after periods (proportion of men with length of stay longer than 3 days, and proportion of men readmitted as an emergency within 90 days of surgery; see Table 3 below). Another secondary outcome for prostate cancer – diagnostic outcomes defined as proportion of men diagnosed with clinically significant prostate cancer – was split into two: 'over-treatment' and 'under-treatment'. One of our secondary outcomes for bladder cancer (proportion of patients offered neo-bladder reconstruction) was not available from our data sources and no replacement was available. One secondary outcome for OG cancer – surgical complications defined as anastomotic leak – was identified in the national audit data, but as explained above these data were not available to researchers. Our patient co-applicant led the process of identifying items in the NCPES for analysis, covering e.g. patient choice of treatment, confidence in staff, communication, effectiveness of teamwork and opportunity to participate in research.

Table 3. Summary of primary and secondary outcomes, process measures, and mediating factors for each cancer: initial and final measures

Type of cancer and outcomes	Initial variables from Protocol v1.0 13 July 2015	Changes to Protocol v1.2 9 August 2018 (Yes/No)? If yes, reason	Changes to Protocol v1.3 July 2019 (Yes/No)? If yes, reason	Variables included in the final analysis
Prostate cancer				
Primary outcome	• Proportion of men treated by primary surgery who remain continent (pad free) at 12 months	• Yes. The measure was not available for the 'before' reconfiguration period in London Cancer and the rest of England as it was	• No	• Proportion of men with length of stay longer than 3 days (as in Protocol v1.2 9 August 2018)
			• No	• Proportion of men readmitted as an emergency within 90 days of surgery (as in Protocol v1.2 9 August 2018)

		not collected. It was replaced with two other measures.		
Secondary outcomes	• Proportion of men treated by surgery with pre-operative erectile function who have erections sufficient for penetration at 12 months	• Yes. The measure was not available for the 'before' reconfiguration period in London Cancer and the rest of England as it was not collected. This measure was removed.	• No	• Removed (as in Protocol v1.2 9 August 2018)
	• Length of stay	• No	• No	• Length of stay
	• Readmission	• No	• No	• Readmission
	• Surgical complications specifically: • conversion to open surgery • rectal injury • small bowel injury • injury other than rectal • blood transfusion	• No	• No	• Surgical complications, specifically: • conversion to open surgery • rectal injury • small bowel injury • injury other than rectal • blood transfusion
	• Post-operative complications, specifically: • Anastomotic leak • Prolonged dependence on a drain, • ileus, • deep vein thrombosis, • compartment syndrome (in particular related to length of procedure)	• Yes, the list of measures was expanded, in accordance to data collected in the BAUS Audit	• No	• Post-operative complications, specifically (as in Protocol v1.2 9 August 2018): • wound infection, • chest infection, • sepsis, • haematuria, • urine leak, • anastomotic leak, • haemorrhage / bleeding, • ileus, • pelvic haematoma, • return to theatre, • lymphocele
	• Diagnostic outcomes: proportion of men diagnosed with clinically significant prostate cancer	• No	• Yes, split into **'over-treatment'** and **'under-treatment'**	• 'Over-treatment' – proportion of men with low-risk localised prostate cancer undergoing radical prostate cancer therapy • 'Under-treatment' – proportion of men with locally-advanced prostate cancer undergoing radical prostate cancer therapy

	• Patient experience, including choice of treatment, access to services, confidence in staff, communication, effectiveness of teamwork and opportunity to participate in research	• No	• Yes, the list of measures was specified, in accordance to data collected in the NCPES.	• Patient experience, specifically: • Choice of different types of treatment; • Confidence and trust in doctors; • Who to contact if worried; • GP given enough information about condition/treatment; • Whether team worked well together; • Ease of contacting clinical nurse specialist; • Explained what operation would entail; • Doctors had right documents/notes.
Bladder cancer				
Primary outcome	• 30 day post-operative mortality [national figure (2012)=2.4%][39]	• No	• No	• 30 day post-operative mortality
Secondary outcomes	• Length of stay	• No	• No	• Length of stay
	• Proportion of patients offered neo-bladder reconstruction	• Yes, this measure was removed, as not available in the data sources.	• No	• Removed (as in Protocol v1.2 9 August 2018)
	• Proportion of patients receiving neo-bladder reconstruction	• No	• No	• Proportion of patients receiving neo-bladder reconstruction
	• Surgical complications (measured by Clavien-Dindo grading)	• No	• No	• Surgical complications (measured by Clavien-Dindo grading)
	• Patient experience, including choice of treatment, access to services, confidence in staff, communication, effectiveness of teamwork and opportunity to participate in research	• No	• Yes, the list of measures was specified in accordance to data collected in the NCPES	• Patient experience, specifically: • Choice of different types of treatment; • Confidence and trust in doctors; • Who to contact if worried; • GP given enough information about condition/treatment; • Whether team worked well together; • Ease of contacting clinical nurse specialist; • Explained what operation would entail; • Doctors had right documents/notes
Renal cancer				
Primary outcome	• 30 day post-operative mortality	• No	• No	• 30 day post-operative mortality

	(anticipated figure=10.5%)[40]			
Secondary outcomes	• 30 day readmission	• No	• No	• 30 day readmission
	• % of cases of T1a tumours having nephron sparing surgery	• No	• No	• % of cases of T1a tumours having nephron sparing surgery
	• Length of stay	• No	• No	• Length of stay
	• Surgical complications (measured by Clavien-Dindo grading)	• No	• No	• Surgical complications (measured by Clavien-Dindo grading)
	• Conversion from laparoscopic (including robotically assisted) to open surgery	• No	• No	• Conversion from laparoscopic (including robotically assisted) to open surgery
	• Patient experience, including choice of treatment, access to services, confidence in staff, communication, effectiveness of teamwork and opportunity to participate in research	• No	• Yes, the list of measures was specified in accordance to data collected in the NCPES	• Patient experience, specifically: • Choice of different types of treatment; • Confidence and trust in doctors; • Who to contact if worried; • GP given enough information about condition/treatment; • Whether team worked well together; • Ease of contacting clinical nurse specialist; • Explained what operation would entail; • Doctors had right documents/notes.
OG cancer				
Primary outcome	• 30 day post-operative mortality [national figure (2013)=1.7%][41]	• No	• Yes, 90-day post-operative mortality has been added following the suggestion from the Study Steering Committee participants and consultations with clinical collaborators, as these are widely used benchmark measures.	• 30 day post-operative mortality • 90 day post-operative mortality
Secondary outcomes	• % of patients offered	• No	• Yes. This measure was	• % of patients receiving endoscopic resection for

	endoscopic resection for tumours staged as T1a		changed from 'offered' to 'receiving', as the former was not available in the data sources	tumours staged as T1a
	• Length of stay	• No	• No	• Length of stay
	• % Complete R0 resection (i.e. full removal of tumour)	• No	• No	• % Complete R0 resection
	• Surgical complications – anastomotic leak	• No	• Yes. This measure was originally identified from the National OG cancer audit data that was not available to researchers, thus removed.	Removed (as in Protocol v1.3 July 2019)
	• Patient experience, including choice of treatment, access to services, confidence in staff, communication, effectiveness of teamwork and opportunity to participate in research	• No	• Yes, the list of measures was specified in accordance to data collected in the NCPES.	• Patient experience, specifically: • Choice of different types of treatment; • Confidence and trust in doctors; • Who to contact if worried; • GP given enough information about condition/treatment; • Whether team worked well together; • Ease of contacting clinical nurse specialist; • Explained what operation would entail; • Doctors had right documents/notes.
Process measures (all)				
	• Waiting times (within 62 days of referral, 31 days of decision of treatment)	• No	• No	• Waiting times (within 62 days of referral, 31 days of decision of treatment)
	• Number of patients seen by surgeon • Case volume per surgeon	• Yes, these two measures were combined into one - number of procedures per surgeon per year	• No	• Number of procedures per surgeon per year
	• Proportion of cases where surgery is an emergency procedure	• No	• No	• Proportion of cases where surgery is an emergency procedure
Mediating factors (all)				

	• Patient characteristics (age, gender, ethnicity, socioeconomic status)	• No	• No	• Patient characteristics, specifically: • Age • Gender • Ethnicity • Index of multiple deprivation quantiles
	• Cancer stage	• No	• Yes, tumour, mode, metastasis (TNM) stage and Grade were added.	• Cancer stage, specifically: • TNM stage • Grade
	• Whether procedure is a salvage procedure	• No	• Yes, this measure was removed, as not available in the data sources.	• Removed (as in Protocol v1.3 July 2019)

Note: Protocol version 1.0 dated 13th July 2015 was the original protocol submitted to funder; version 1.2 dated 9th August 2018 was the revised version submitted to funder in August 2018; version 1.3 was the subsequent revised version submitted to funder in July 2019.

Table 4 presents the datasets we will access, the time period covered, and the numbers of cancer patients likely to be available per year in these datasets. The True NTH UK – Post Surgical Follow up dataset and the National Prostate Cancer Audit dataset were originally included to analyse prostate cancer outcomes but have been replaced by NCRAS because the latter is available for all study periods, is more inclusive, and can be linked with data from the National Cancer Register, HES and mortality data and NCPES. NCRAS has also been included for the other cancers. National OG Cancer Audit data were not available to researchers as outlined above.

Table 4. Summary of datasets to be sampled

Dataset	Year and month change occurs	Years sampled	Approximate mean number of patients per year, by area	Notes
Prostate cancer				
National cancer registration and analysis service	April 2016	2012-2017	*Incidence of prostate cancer* in 2016 (England) =40,489	Cancer Registration Statistics, England, 2016 (First Release)
Hospital Episode Statistics	April 2016	2012-2017		
BAUS Radical prostatectomy dataset	April 2016	2014-2017	BAUS audit participation (national)=2093	BAUS Radical Prostatectomy Audit report (2012)[42]
National Cancer Patient Experience Survey	April 2016	2014-2017	London Cancer=276 Rest of England=5002	National Cancer Patient Experience survey (2013)[43]
Bladder cancer				

National cancer registration and analysis service	April 2016	2012-2017	*Incidence of bladder cancer* in 2016 (England) =9,244	Cancer Registration Statistics, England, 2016 (First Release)
Hospital Episode Statistics	April 2016	2012-2017	Patients undergoing cystectomy (national)=1360 *Incidence of bladder cancer:* London Cancer=628 Rest of England=7895	From NCIN analysis of 2005-2007 bladder cystectomies[44] Mean annual incidence of bladder cancer from UK Cancer Atlas data 2008-2010[26]
BAUS audit of cystectomies	April 2016	2014-2017	BAUS audit participation (national)=5763	BAUS Cystectomies Audit report (2012)[42]
National Cancer Patient Experience Survey	April 2016	2014-2017	London Cancer=321 Rest of England=6327	National Cancer Patient Experience survey (2013)[43] NB these are overall figures for urological cancers – will be disaggregated by ICD10 code.
Renal cancer				
National cancer registration and analysis service	April 2016	2012-2017	*Incidence of renal cancer* in 2016 (England) =9,883	Cancer Registration Statistics, England, 2016 (First Release)
Hospital Episode Statistics	April 2016	2012-2017		
BAUS audit of nephrectomies	April 2016	2012-2017	BAUS audit participation=5851 *Incidence of renal cancer:* London Cancer=282 Rest of England=5930	From BAUS nephrectomy Audit report (2012) Mean annual incidence of renal cancer from UK Cancer Atlas data 2008-2010[26]
National Cancer Patient Experience Survey	April 2016	2014-2017	London Cancer=321 Rest of England=6327*Incidence of renal cancer* in 2016 (England) =9,883	National Cancer Patient Experience survey (2013).[43] NB these are overall figures for urological cancers – will be disaggregated by ICD10 code.
OG cancer				
National cancer registration and analysis service	December 2015	2012-2017	*Incidence of OG cancer* in 2016 (England) =12,879	Cancer Registration Statistics, England, 2016 (First Release)
Hospital Episode Statistics	April 2016	2012-2017		
National Cancer Patient Experience Survey	December 2015	2014-2017	London Cancer=221 Rest of England=3860	National Cancer Patient Experience survey (2013).[43] NB these are overall figures for upper GI cancers – will be disaggregated by ICD10 code.

Note: patient-level data from the National OG Cancer Audit and the National Prostate Cancer Audit, as mentioned in Protocol versions 1.0 and 1.2, were not available to researchers, and have therefore been removed from the analyses. Years sampled were extended for two additional years for NCRAS, HES and BAUS (renal cancer) to include two additional years for the 'before' period (previously 2014, now 2012). We will use 2015-2017 data from the National Cancer Patient Experience Survey, we will use the 2014 if it is made available to us.

Sample size calculations for this study are fraught with difficulty for several reasons: there are uncertainties about the event rate in the unexposed groups; we have little or no information about the expected effect size of the reconfiguration on the outcomes; we are using a difference-in-differences design; and, while we have selected primary outcomes for each type of cancer being considered based on expert clinical opinion, it was acknowledged that other outcomes could have been selected instead. Bearing this in mind, based on the figures in Table 4, in order to study the impact on clinical processes, patient experience, clinical outcomes and cost-effectiveness on the changes in London Cancer, we ideally require the following number of cases in London during the post-reconfiguration period: prostate cancer 1000; bladder cancer 192; kidney cancer 496; OG cancer 264. These figures have been discussed with our clinical colleagues and compared with available data on the numbers being treated to ensure that our sample sizes are feasible and would be sufficient to study the impact on clinical processes, patient experience and clinical outcomes on the changes in London Cancer. The implementation timeline was identified based on the planning documents (mainly Gateway 4) and divided into three periods: 'before' - the period before the reconfiguration was agreed and the services' infrastructure was completed; 'during'- the transition period when the reconfiguration was officially signed off and first patients started to be transferred to the centralised centres; and 'after' - the period when all patients were expected to receive care under the new system. These time periods are different for each cancer type. Table 5 summarises the dates for the 'before', 'during' and 'after' periods that we are studying.

Table 5. Implementation timelines in London Cancer

Cancer type	Before		During		After	
Bladder	01/01/2012-30/06/2015	42 months	01/07/2015-31/03/2016	9 months	01/04/2016-31/12/2017	21 months
Prostate	01/01/2012-30/06/2015	42 months	01/07/2015-31/03/2016	9 months	01/04/2016-31/12/2017	21 months
Renal	01/01/2012-31/12/2014	36 months	01/01/2015-31/03/2016	15 months	01/04/2016-31/12/2017	21 months
OG*	01/01/2012-31/12/2015	36 months	-	-	01/01/2016-31/12/2017	24 months

* For OG cancer there was no "during" period.

Cost-effectiveness (RQ6) (LC only)

Using our links with providers and commissioners, we will obtain information on the costs associated with the process of centralisation and implementing changes. Although some of these costs may represent one-off, sunk costs to providers and commissioners, they will be important in informing other organisations as to what the potential cost of centralisation might be. We will also attempt to quantify any impact on cost per procedure and in-patient hospital costs that may have occurred as a result of the centralisation, for example as a result in change in patient case-mix and complexity, changes in bed management practices or as a result of the way theatres are being booked and used. The cost-effectiveness of the centralisations will then be reported as an incremental cost per quality-adjusted life-year gained and incremental cost per outcome gained as informed by the DCE.

5. DATA COLLECTION

Discrete Choice Experiment (RQ1) (LC, GMC, national)

We will establish preferences for the scenarios included in the analysis by asking respondents in our selected stakeholder groups to complete a survey.

The survey tool will be designed as follows:

1. We will identify key attributes for cancer surgery services that may be affected by centralisation. A long list of attributes will be drawn from the published literature. The final list of attributes to be included in the analysis will be derived from focus groups with patients, the public and professionals. Potential attributes will include clinical outcomes and care processes as described above, plus travel distance, frequency, time, and cost, NHS cost per patient and potential unit closures. Attribute descriptions will undergo plain English review by the Plain English Campaign (http://www.plainenglish.co.uk/services/editing-services.html).
2. We will assign levels to these attributes based on clinically feasible ranges derived from systematic literature reviews.
3. We will design the DCE questionnaire. At this stage we will use a pairwise choice framework and will compile a set of pairwise scenarios that describe the feasible combinations of levels and attributes of centralised versus non-centralised cancer surgery services. The number of pairwise choices will be reduced to a practical number for participants to answer using an orthogonal fractional main effects design[45].
4. The DCE questionnaire will undergo plain English review by the Plain English Campaign, to ensure its accessibility for all stakeholders.
5. We will pilot the DCE questionnaire with patient representatives, including cancer patients. We will use stakeholder feedback to identify the strengths and weaknesses of the tool, and edit it accordingly.
6. The questionnaires will be available both as online survey tools and hard-copy postal questionnaires.
7. Quality Health (an organisation specialising in the design, implementation, and analysis of surveys in healthcare settings, and which runs the NCPES) will assist in the distribution and will be in charge of data collection, data entry, and preparation of the dataset.
8. All data collected will be anonymised, and demographic details will be categorised such that participants cannot be identified.
9. Further information on how the different stakeholder groups will be approached is provided under *Recruitment*.

Documentary analysis, stakeholder interviews and non-participant observations (RQ2,3) (LC, GMC)

Much of the documentation covering development and implementation of the centralisations will be obtained through engagement with Greater Manchester Cancer and London Cancer, and staff in other participating organisations. We will supplement these data with online searches for local and national documentation, including relevant policy, guidance and media reports. Physical documents will be stored for analysis in locked cupboards in a secure, pass-protected environment, while electronic documents will be stored on a secure server on password-protected computers.

Semi-structured interviews will be conducted with a range of stakeholders (including NHS staff, wider context, and patient and carer representative groups). Topic guides will be developed in collaboration with patient and clinical team members to focus on key aspects

of the centralisations, including the decision to change, selection of the model, processes of planning and implementing the changes, perceived impact and sustainability of changes (e.g. on ways of working, service quality, continuity of care, and patient choice and experience), and influential factors (such as local and national context). Interviews will only be conducted with written, fully informed consent. All interviews will be digitally recorded for professional transcription in full.

Non-participant observations of meetings (related to planning of the changes, oversight, and management of the centralised systems) will be recorded as fieldnotes. These will be recorded using a semi-structured template, in order to describe setting (e.g. room layout, communication systems), agenda/meeting structure, Chairing (including who acts as Chair and their style, e.g. approach to opening up meeting to discussion); attendees; process for discussing topics (e.g. pathway strategy, system performance, patient cases), and researcher reflections on interactions observed.

All interview and observation data will be stored securely and fully anonymised for analysis.

Impact on clinical processes, clinical outcomes, and patient experience (RQ4, 5) (LC only)

Formal requests for national datasets will be made through the relevant organisations (specified in Table 3). These requests have been accounted for both in terms of time and funding. The research team is experienced in successfully obtaining data of this kind, and has already contacted several of these organisations to confirm how best to obtain the data.

Cost-effectiveness (RQ6) (LC only)

We will use clinical process and clinical outcomes data along with data from published sources and data from costing the design, planning and implementation of the changes to populate the cost-effectiveness models described in Section 6. Additional data to be collected will include:

- Probabilities and disease progression (obtained from systematically reviewing epidemiological and other literature)
- Unit costs (obtained from NHS Reference Costs, previous studies http://www.crd.york.ac.uk/CRDWeb/), British National Formulary (http://www.bnf.org/bnf/index.htm), Unit Costs of Health and Social Care (http://www.pssru.ac.uk/project-pages/unit-costs/2013/)
- Utilities (obtained from CEA registry https://research.tufts-nemc.org/cear4/)

Combining the methods

Combining our evaluation methods throughout the lifespan of the study will benefit the research in terms of data collection, analysis, and the resultant lessons. In terms of data collection, interview topic guides will in the first instance be informed by the documentary analysis and primary measures used in the process, outcome and patient experience analyses, and latterly incorporate issues identified through our ongoing observations (e.g. system responses to new contextual challenges). The process and outcome analyses will in part be guided by documentary analysis (e.g. in terms of specifying when centralisation took place and identifying relevant measures). Potential sources of cost data will be partly identified through interviews and documentary analysis (e.g. issues related to staffing and resource use), while the focus of the cost-effectiveness analysis will be guided by the results of the outcomes analysis. The attributes used in the DCE will be informed by documentary analysis and further confirmed with professionals, patients and the public.

6. RECRUITMENT

Discrete Choice Experiment (RQ1) (LC, GMC, national)

Recruitment to the DCE will be arranged by the research team and Quality Health (Quality Health administer the NCPES in England).

The DCE questionnaire (whether postal or online) will include a cover letter and a summary sheet informing potential participants about the study, what participating will entail, how data will be managed and stored, and who they can contact if they have questions or encounter any issues.

We will recruit the three stakeholder groups as follows:

- ***Patients (postal or online survey)***. Quality Health will recruit patients, using the NCPES database to identify cancer patients who have agreed to take part in further research. A sample of these patients will be sent a copy of the DCE questionnaire and study information by post. Patients will be invited to return the questionnaire by post or online. Quality Health will send patient participants two reminders to complete the survey.
- ***General public (online survey)***. Quality Health will recruit members of the public by advertising the survey through health-related (but non-cancer) charities' websites, newsletters, and email listservs. The advertisements will include a link to the online questionnaire and associated study information.
- ***Professionals (online survey)***. The research team will identify groups and organisations associated with relevant professionals (including surgeons, nurses, dieticians, physiotherapists) in London, GM and nationwide. Organisations identified include Royal Colleges and professional organisations, e.g. BAUS, the Association of Upper Gastrointestinal Surgeons (AUGIS), UK Oncology Nursing Society, relevant NCRI Clinical Studies Groups, the British Dietetic Association Oncology Specialist Group, and the Association of Chartered Physiotherapists in Oncology and Palliative Care. We will advertise the study through these organisations' websites, newsletters, and email listservs. The advertisements will include a link to the online questionnaire and associated study information.
- Finally, we will provide links to the online questionnaires for our different stakeholder groups in the RESPECT-21 newsletter.

Recruitment documentation:

- Information sheets will be developed in collaboration with patient and clinical team members. Copies of all recruitment documentation will be submitted as part of a substantial amendment for REC approval.
- These forms will describe clearly the purpose of the DCE, how long completing the questionnaire is estimated to last, and state that any (personal or research) data will be stored securely and not used for any purpose beyond this analysis.
- The forms will also state that participation is entirely voluntary, that participants may withdraw at any time, and that completion of the survey tool implies consent to participate.
- For the online survey tool, an opening page will provide equivalent information and consent details; to begin the survey, participants will have to press a button stating "I understand - click here to take the survey".

Stakeholder interviews and non-participant observations (RQ2, 3) (LC, GMC)

All potential interviewees (e.g. NHS staff, wider context, and patient and carer representative groups) will be approached by a study researcher: in the first instance, contact, including provision of information sheets, will be made through e-mail and telephone. Potential interviewees will have at least 48 hours to consider the contents of information sheets and will be free to ask any questions about the research. Participants will only be interviewed once they have given written, fully informed consent and will be free to withdraw at any time, up to and including the actual interview.

We aim to observe relevant meetings and events in participating services. We anticipate that staff participants are unlikely to experience any risks from this component of the study. When visiting NHS sites, researchers will not directly observe patients at any time. Permission to observe meetings will be obtained from the Chair in advance of the meeting taking place. The participant information sheet will be circulated with meeting papers to all attendees. On the first attendance, the researcher will brief attendees on the study's aims, what participation entails, and that they may decline to participate at any time; at subsequent meetings, the researcher will announce him/herself as a non-participant observer, and confirm that he/she is happy to answer any questions in relation to the research. Agreement for observation to proceed will be recorded in meeting minutes. If participants do not agree to participate, any contributions they make to the meeting will be excluded from the researcher's field notes, or the researcher will withdraw from the meeting if more appropriate. Staff participants will be granted anonymity, and will not be identified by name in any reports.

7. DATA ANALYSIS

Discrete Choice Experiment (RQ1) (LC, GMC, national)

The DCE will allow estimation of the preferences held in pre-defined populations and the weighting of the relative value attached to attributes determining these preferences. It will also provide an indication of people's willingness to trade between attributes. We will analyse preference data using conditional logit regression analysis. The results will indicate which attribute is most important to respondents and how this compares with the other attributes. Data will be analysed for all respondents jointly and separately for each of the three subgroups. To explore the trade-offs participants were willing to make between attributes, we will calculate the marginal rates of substitution. We will also use the regression results to calculate the predicted probability that different combinations of the attribute levels used in the experiment would be selected. This allows us to rank centralised versus non-centralised services in terms of their order of preference by the participants[46], and to explore how this ranking varies by sub-group.

Documentary analysis, stakeholder interviews and non-participant observations (RQ2,3) (LC, GMC)

To interpret these data, we will use a case study approach[47-49]. As discussed under 'sampling', in each area we will analyse the overarching governance, pathway-specific governance, and for each cancer a specialist unit, a local unit, and a hospital that no longer provides services. We will draw on findings from a recent review of evidence on large-scale transformation initiatives, which identified five 'simple rules' likely to enhance 'successful' implementation. These rules suggest the importance of blending designated and distributed leadership approaches; supporting feedback and learning; awareness of history of change;

engagement of professionals; and inclusion of patients and families[2]. We have developed these 'rules' further through our study of centralisations of acute stroke services in London and Greater Manchester. Our analysis has drawn out the importance of combining 'bottom up'-led change with 'top down' central leadership, and of understanding of the social and political context of the changes and their impact on outcomes.

The documentary analysis will draw on our conceptual framework (Figure 2) and reflect key processes related to changes of this kind (agreeing the case for change, planning the changes, implementation), and influential factors (e.g. governance structure, local and national policy context). This information will be used to produce detailed timelines of the changes and narrative summaries of centralisations based around this framework.

Interview transcripts and observation field notes will be managed with NVIVO software. Ongoing iterative and thematic analysis of all data will be undertaken concurrently, following established procedures of constant comparative analysis [50].

Initial analysis and category building will be led by the London and Manchester qualitative researchers and will include category mapping and constant comparison; the analysis will be developed with a subgroup of co-investigators who have qualitative expertise; and interpretation of findings will be contributed to by the whole research team. Validity will be assessed in relation to Patton's four criteria of validity in qualitative research: verification, rival explanations, negative cases and triangulation[51].

Impact on clinical processes, clinical outcomes, and patient experience (RQ4, 5) (LC only)

We will aggregate risk-adjusted patient level data by Trust and time (quarter) and use between-region difference-in-differences regression analysis to investigate the impact of the centralisation in LC on the clinical process, clinical outcome, and patient experience measures described above.

We will risk-adjust the observed patient outcomes using expected outcomes that are obtained from patient level regression models. In the case of the primary outcomes (length of stay longer than 3 days, emergency readmissions within 90 days of surgery, 30 day mortality) we will use patient level logistic regressions. For each type of cancer, the binary outcome at the patient level will be regressed against a series of covariates including: gender; age (measured in five year bands); interactions between age and gender; cancer diagnosis using the first four digits of the full primary ICD-10 diagnosis code; Charlson index derived from secondary ICD-10 diagnostic codes; presence of 16 comorbidities included in the Charlson index; ethnic group; deprivation quintile based on area of residence; and rural Urban classification based on area of residence. The patient-level regressions will be run only on patients who had surgery before the reorganisations so that the risk adjustment will not be contaminated by the changes. The regression coefficients (derived from the logistic regressions for the pre-implementation periods) will then be used to predict the probability of the outcome for every patient (in both pre- and post-implementation periods). These will then be aggregated to create a dataset of the actual outcomes (actual percentage of patients who had a length of stay of over 3 days, emergency readmission within 90 days or who had died by 30 days) and the expected outcomes by admitting hospital and quarter (from the logistic regressions).

For each outcome and type of cancer we will construct a Trust-by-quarter dataset covering the whole of England where possible containing data on the clinical outcomes and care processes plus covariates. We will then regress the risk adjusted outcomes (actual minus expected outcomes), measured at the Trust level in each quarter, against a variable

denoting cancer surgery service centralisations, controlling for Trust and time fixed effects. This two stage approach (patient level risk adjustment followed by between-region difference-in-differences analysis on aggregate Trust-by-quarter data) is consistent with Medical Research Council guidelines for using natural experiments to evaluate population health interventions[52] and has been used previously in the evaluation of the Advancing Quality initiative in the North West of England[51], and the centralisation of stroke services in Greater Manchester and London[5]. In the regression analysis of the aggregate data the regression model is

$$y_{jt} = \alpha_1 + u_j + v_t + \delta_1 D^1_{jt} D^2_{jt} + \delta_2 D^1_{jt} D^3_{jt} + e_{jt}$$

where *y* is the risk-adjusted outcome of interest (e.g., mortality, readmissions, length of stay; actual minus expected values with expected values based on the aggregated patient level risk adjustment model), *j* indicates Trust, *t* indicates quarter, α is a constant term, *u* are Trust fixed effects and *v* are time (quarter) fixed effects. D^1 is a variable taking the value 1 if the provider Trust is in London Cancer and 0 otherwise, D^2 is a variable which equals 1 if the observation belongs to the time period after the reconfiguration and 0 otherwise, D^3 equals 1 if the observation belongs to the time period during the reconfiguration and 0 otherwise. Sample weights based on patient numbers in each Trust/quarter will be used. We are particularly interested in the sign and statistical significance of the coefficient δ_1, which quantifies the changes in risk-adjusted outcomes over time in London Cancer controlling for the changes over time in the rest of England. We will run pre-trends tests to examine whether the outcomes had a different linear trend in London Cancer compared with the rest of England before centralisation.

We will undertake a secondary analysis using a synthetic control, defining a control group that closely resembles London Cancer in terms of the outcomes in the period before the reforms. We will create the synthetic control [53-56] using a weighted combination of Trusts from the rest of England to approximate pre-centralisation outcomes in London Cancer. Trends in outcomes between London Cancer and the synthetic control will then be compared over time using an adapted version of the regression model described above.

We will also use patient-level regression analysis to relate the care processes (independent variables) to the clinical outcomes (dependent variables).

Cost-effectiveness (RQ6) (LC only)

We will construct de novo cost-effectiveness models to test whether centralisations reflect good value for money 30 days and 1 year post-surgery. A before and after decision analytic model will be constructed for London Cancer, with a different model for each type of surgical cancer centralisation. Where possible we will construct a decision analytic model of an urban region in England that has not been centralised as a control comparator to determine what change may have occurred if no centralisation had taken place. The models will be constructed using data described above along with data from published sources to calculate NHS and personal social services costs and outcomes of surgery pre and post-centralisation, with the aim of providing policy makers, commissioners and providers with information on the value for money of centralisation in surgical cancer as described above. We will include information and descriptive statistics on surgery, in-patient stay, follow-up, readmission, centralisation and implementation resource use and costs. Where possible we will report costs available from providers or commissioners. If this information is not available costs will be based on national published sources. Special attention will be paid to

specific analysis of fixed and variable costs and where assets have been purchased versus staff costs so as to provide an accurate assessment of mean cost per patient before and after.

Outcomes will be modelled as quality-adjusted life years (QALYs). We will assess the feasibility of calculating QALYs from patient level patient reported and clinical outcome measures. If this information is not available utility scores of health states for calculating QALYs will be obtained from the CEA registry (https://research.tufts-nemc.org/cear4/). Cost-effectiveness will be calculated as mean cost difference between before and after centralisations, divided by mean difference in outcomes before and after, to give incremental cost-effectiveness ratios. In addition to reporting the mean incremental cost per QALY we will report the mean incremental cost per outcome gained as informed by the DCE described above. We will conduct probabilistic and deterministic sensitivity analyses to explore effects of uncertainty. Where provider or commissioner costs have been used and national published values are available, we will conduct sensitivity analyses of the impact on the results of using national versus local values. Cost-effectiveness acceptability curves will be created comparing the net monetary benefit (the willingness to pay for an outcome gained multiplied by the incremental increase in outcome minus the incremental cost), for each of the centralisation options after compared to before. We will assess the feasibility of constructing before and after life-time models for each cancer centralisation, extrapolating the results of survival and re-admission data described above, collected as part of the evaluation. We will also assess the feasibility of calculating the cost to primary care of the different centralisation models. However, this is unlikely to be viable, owing both to issues associated with accessing the necessary data, and to the additional resources that would be required to collect this information.

Combining the data

We will conduct a mixed-method case study approach to combine the above methods, with cases defined as governance of the changes in both areas (overarching and at pathway level), and for each cancer pathway a specialist centre, a local centre, and a centre that no longer provides services (see Figure 3). The case study method permits development and testing of theories on how change processes interact with the context in which they take place; a multiple case study approach – in this case, the overarching governance and implementation of change and the impact on organisation of services in Greater Manchester Cancer and London Cancer – allows the analysis to be conducted in different organisational contexts[47-49,57]. The analysis will present rigorous quantitative data on the impact of the London Cancer centralisations on provision of care, clinical outcomes, cost-effectiveness, and patient experience. However, such findings alone are of limited benefit, as they leave unanswered the important questions of how these impacts were achieved, and what factors were influential. In-depth qualitative analysis of approaches taken in planning, implementing, and sustaining these changes will be used to develop potential explanations of their impact on quality of care, while the focus on contextual influences will support generalisability beyond the specialist cancer surgery settings under investigation. Finally, the DCE will provide valuable insights on the priorities of a range of key stakeholders in relation to changes of this kind, which will guide the cost-effectiveness and qualitative analyses. Taken together, we will generate compelling lessons for future centralisations of specialist services, in terms of engaging key stakeholders, planning and implementing change, and potential impact on quality and outcomes of care.

8. STUDY ADMINISTRATION AND ETHICAL ISSUES

ETHICS

Discrete Choice Experiment

The DCE may raise issues for our anticipated participant groups in different ways. For members of the public, and especially patients who have previous experience of cancer services, the hypothetical situations described in relation to care preferences (e.g. distance to services versus care options) may cause distress, as individuals revisit previous experiences of cancer care. For staff respondents, 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 cancer care. To address this concern, our patient and clinical team members will review the survey tools, to ensure that the hypothetical scenarios are presented in a sensitive fashion. Further, the participant information sheets will make clear the (hopefully minimized) risk of distress, and make clear that participation is voluntary, and that participants may withdraw at any stage.

Interviews

When interviewed, staff engaged in planning and delivering specialist cancer services may feel reluctant to raise criticisms of services provided, while patient and carer representatives may find it stressful to discuss how they have been involved in planning and overseeing specialist cancer surgical services. The Participant Information Sheets make clear the independence of the researcher conducting interviews, the importance of identifying challenges as well as successes, and that any information will be anonymised fully; they also make clear that participation is entirely voluntary, and that participants may withdraw from the study at any time.

Non-participant observations

The non-participant observation component of this research will allow some understanding of how these new specialist cancer services operate in practice (e.g. by observing SMDT meetings). We recognise that meeting attendees (including NHS staff and patient and carer group representatives) may be sensitive about being observed, and that they may be concerned that observations may interfere with provision of high quality care. Following the approach taken in an observational study of maternity services (NHS REC reference: 08/H0808/178) and a study of 24/7 working in London Hyperacute Stroke Units (NHS REC reference: 14/LO/0355), we will seek to ensure that staff are fully aware of the research both before and during these observations (e.g. through presentations to staff meetings), that staff have the opportunity to provide informed consent, and that they are assured that the researcher will withdraw from any situation where it is felt that observation is not appropriate or might interfere with provision of care.

MANAGEMENT ARRANGEMENTS

As Chief Investigator, NF will provide overall leadership of the project team, lead the qualitative analysis, manage the London-based qualitative research team, and provide expertise on healthcare policy and evaluation. SM will lead the quantitative analysis and DCE, manage the quantitative and DCE teams, and provide expertise on health economics and statistical methods. RH will lead the cost-effectiveness analysis, manage the health economist working on this analysis, and provide expertise on health economics and statistical methods. RB will manage the Manchester-based qualitative researcher, and

provide expertise on organisational change and evaluation. KPJ will provide expertise on the LC centralisations. JH will provide expertise on the LC centralisation of urological services. DS will provide expertise on the GMC centralisations. NC and our patient collaborators will provide patient expertise on all aspects of the study. AR will provide expertise on healthcare evaluation and will support fieldwork and analysis of qualitative, quantitative, and DCE elements.

To ensure effective management across the different institutions, formal project management will be provided by London Cancer, Greater Manchester Cancer, and UCL (further detail on how they will contribute is provided under 'expertise and justification of support required').

The research team will meet on a monthly basis throughout the study to discuss the status of the centralisations, support progress with data collection and analysis, and to ensure effective dissemination of findings and stakeholder engagement. These meetings will be chaired by NF; administration will be provided by a project manager; teleconference facilities will be used to optimise participation. The research team meeting will take place in person once per year.

Ad hoc subgroups of the project group will be formed to lead on particular aspects of data collection and analysis. For example, NF, RB, AR, and the qualitative researchers will form a qualitative subgroup to support development of interview topic guides and coding frameworks, for final approval by the wider research team.

This is to be a rigorous, independent evaluation, conducted by a team that includes clinicians and others involved in the changes in LC and GMC. While a co-production research approach can offer important benefits at all stages of a study, it can also represent a risk to maintaining 'critical distance' – that is, ensuring the research remains independent and the findings unbiased. To address this, all team members have made a joint commitment to understanding the process and impact of the changes, whether positive or negative; any potential conflicts of interest will be discussed openly amongst colleagues and disclosed in any publication of findings. This commitment will be revisited over the course of the study, and inform all stages of the evaluation, e.g. in ensuring we recruit a wide range of participants (including people with less positive views of changes studied) and ensuring our interpretation of findings reflect the evidence obtained.

STUDY STEERING COMMITTEE

During the 6 months preceding project launch, the research team will recruit members of the Study Steering Committee (SSC). The SSC will have an independent Chair. In addition to members of the research team, the SSC will be composed of a wide range of stakeholders from London and Greater Manchester, including patient and carer representatives, commissioners, and academics with expertise in qualitative and quantitative methods (including health economics).

PATIENT AND PUBLIC INVOLVEMENT

Patient representatives played a significant role in developing this study, for example in terms of discussing the research questions and identifying items in the NCPES for analysis. Patient and public involvement will continue to benefit the study in the following ways: ensuring the research focuses on issues that are of importance to service users; 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.

Our patient collaborators will participate in quarterly team meetings, attend the annual SSC meetings, and comment on study documents such as participant information sheets, interview topic guides and summaries of findings. Our patient collaborators will provide expertise on all aspects of the project, e.g. commenting on study documents, and will be invited to attend annual SSC meetings. In addition, we will engage with service user groups in London and Greater Manchester to share our research findings and to obtain feedback on the focus and dissemination of our study.

We have budgeted to support our patient representatives in all these activities. To support effective participation, we will ensure that documents relating to meetings and events are distributed in a timely fashion (e.g. a week in advance) and that both paper and electronic versions of these documents are made available. Also, a member of the team will be identified as primary contact with whom patient representatives may raise any issues or concerns. Recommendations on effective involvement and payment of patients and the public will be followed.[58-61]

9. INSURANCE

UCL's insurance policy provides for negligent and non-negligent harm for all studies but in line with current sponsor's arrangements, non-negligent harm insurance is only covered for Clinical Trials of Investigational Medicinal Product (CTIMPs) and other non-CTIMP interventional studies. All other studies will be covered for negligent harm cover only. 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. University College London 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. DATA MANAGEMENT

DATA TRANSFER (HANDLING, PROCESSING AND STORAGE)

Quantitative data (DCE, HES, audits, patient experience)

Electronic data drawn from national datasets (e.g. HES, national clinical audits, National Cancer Registry, NCPES) will be transferred securely in accordance with the systems approved by the data owners. These data will be analysed within the UCL Data Safe Haven (DSH - see https://www.ucl.ac.uk/isd/services/file-storage-sharing/data-safe-haven-dsh). DSH 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.

Any paper-based quantitative data – such as completed hard copy surveys – will be stored in a locked filing cabinet in security card protected office space at the UCL Department of Applied Health Research (1-19 Torrington Place, University College London WC1E 7HB). These data will be transferred to electronic format and also stored and analysed within the DSH.

Professor Steve Morris (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 UK Data Protection Act 2018 which implements the General Data Protection Regulation (EU) 2016/679 (GDPR), 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' consent.

Qualitative data (interviews and observations)

In the study, interview data will be collected from participants in accordance with the participant consent forms, participant information sheets and Section 6 of this protocol (under *Recruitment*). Interviews will be recorded on an encrypted, password-protected digital audio recorder to which only the researcher knows the password. Data collected by the London researcher will be taken directly to the UCL Department of Applied Health Research (1-19 Torrington Place, University College London WC1E 7HB); data collected by the Manchester researchers will be taken directly to Alliance Manchester Business School, University of Manchester (Booth Street West, Manchester M15 6PB). The data will be anonymised and stored securely for analysis, and the data will be cleared from the digital audio recording device when it has been transferred. Participant identifier codes will be stored in a password-protected file on a secure network to which only named team members have access via password-protected computers at the UCL Department of Applied Health Research. These data will be kept completely separate from study data: interview data will be anonymised and organised by participant codes. Data will be shared between London and Manchester qualitative researchers using the UCL Data Safe Haven (discussed above).

Digital audio recordings of interviews will be appropriately sent to Essential Secretary (http://www.essentialsecretary.co.uk/) for transcription using a secure FTP system. Digital audio recordings of interviews, anonymised interview transcripts, and data for the documentary analysis will be stored for analysis on a secure computer network to which only named team members have access via password-protected computers at the UCL Department of Applied Health Research and Alliance Manchester Business School. Only the research team will have access to participants' personal data (i.e. name and status). Any paper-based data – such as signed consent forms – will be stored in locked filing cabinets. Greater Manchester data will be stored in a locked office space; in London, they will be stored in security card protected office space at the UCL Department of Applied Health Research.

Professor Naomi Fulop (UCL Department of Applied Health Research) will act as the data controller for the qualitative study. She will process, store and dispose of all qualitative data in accordance with all applicable legal and regulatory requirements, including the UK Data Protection Act 2018 which implements the General Data Protection Regulation (EU) 2016/679 (GDPR), 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' consent.

DATA ARCHIVING

Each participating site recognises that there is an obligation to archive study-related documents at the end of the study (as such end is defined within this protocol). The Chief Investigator confirms that she will archive the study master file at UCL for 20 years from the study end.

11. DISSEMINATION

To ensure that learning is shared rapidly and effectively, we will employ a similar range of approaches to those employed successfully in our study evaluating the centralisation of

stroke services in London and Greater Manchester[3]. The research team will provide regular feedback to stakeholders, including London Cancer, Greater Manchester Cancer, local commissioners, NHS England, and patient and carer representative groups. For example, project researchers will provide verbal updates at meetings in London and Manchester. In addition, accessible briefings covering specific findings will be produced and shared electronically with local stakeholders through key contacts, the SSC, and local Clinical Research Networks, for wider distribution. These briefings will be made available on the project website and the websites of London Cancer and Greater Manchester Cancer. We will also engage with people who are leading or developing similar changes in other parts of the country. A key example of such dissemination is the stakeholder workshop, which will be attended by people involved in planning centralisations of specialist cancer services elsewhere, and for people centralising or planning to centralise other types of 'non-cancer' specialist services. Participants will include providers, commissioners, and patient and carer representative groups.

We anticipate that our findings will influence approaches to planning, implementing and evaluating centralisations of this kind. Key beneficiaries are likely to include those who commission, organise, and manage healthcare services at national and regional level, healthcare staff working in relevant care domains, and patient and carer groups. With their consent, stakeholders will be added to a dissemination database, which will be regularly updated so that our findings can be shared as rapidly and effectively as possible. A number of key stakeholders, including the National Director for Cancer and representatives of local Clinical Commissioning Groups, Commissioning Support Units, and NIHR CLAHRCs, have indicated support for the research and interest in the findings; further, several have volunteered to join our SSC (see under *Study Administration*).

The final report to NIHR HS&DR will present the overall evaluation, along with lessons and recommendations tailored to relevant stakeholders, for example those who organise healthcare at national and regional level and the national Clinical Reference Groups that advise on specialist services.

Research articles based on key findings will be published 'open access' in high impact peer-reviewed journals related to surgery, organisation and management, and health economics, in order to reach the relevant academic audiences (see *Timeline* for submission dates).

12. INTELLECTUAL PROPERTY

The research team possesses substantial know-how relating to novel analytic techniques and models including a proprietary framework for analysing reconfigurations (see Figure 2, under 'Design'). The existing framework has been developed by the Chief Investigator (Fulop) and other members of the research team (Morris, Ramsay, Hunter) during their employment at UCL. As such the model is proprietary to UCL and the research team have full rights to use and develop the model over the course of the proposed research and beyond. The project team are familiar with this field of research, and are confident that no freedom to operate issues exist.

This research may generate new intellectual property. Any such product will be dealt with appropriately with guidance from UCL's technology transfer company, UCL Business PLC, and in partnership with the research team's host organisations. During the project we anticipate producing the following:

1. Survey tools for evaluating the preferences of key stakeholder groups (patients and carers, members of the public, and healthcare professionals) for changes of this kind;

2. Topic guides for in-depth interviews that explore the barriers and facilitators to changes of this kind among users and providers;
3. Short, accessible summaries of lessons on centralising services derived from our findings.

The above 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.

Intellectual property 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. Should the interventions prove effective and cost effective we anticipate they will be adopted by NHS commissioners across the UK as new models for cancer service delivery.

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.

13. TIMELINE

The timelines below represent a no-cost extension approved by the funder on 9th May 2019 for 13 months. The no-cost extension was requested due to delays in the availability of national datasets required for quantitative and cost-effectiveness analyses.

TASK	**MONTHS**
ORGANISING the EVALUATION	
Set up SSC	-6 to 3
NHS ethics approval	-6 to 1
NHS local research governance	-6 to 6
Recruit 2 qualitative researchers, DCE researcher, 0.5 quantitative researcher)	-6 to -1
Recruit 0.5 health economist	22 to 27
SSC meetings	14, 29, 42, 51, 63
Project meetings	Monthly
DISCRETE CHOICE EXPERIMENT	
Developing attributes for DCE	1 to 6
Survey distribution and collection	7 to 12
Data analysis	13 to 18
DOCUMENTS, INTERVIEWS, and OBSERVATIONS	
Topic guide development	1 to 6
Data collection - Greater Manchester Cancer	4 to 36
Data collection - London Cancer	4 to 42
Data analysis - Greater Manchester Cancer	10 to 40
Data analysis - London Cancer	10 to 46
PROCESSES, OUTCOMES, COSTS, and PATIENT EXPERIENCE	
Develop analysis plan	1 to 9

Specifying dataset	10 to 16
Data requests	30 to 47
Process analysis	48 to 64
Patient experience analysis	48 to 64
Outcome analysis	48 to 64
Cost analysis	48 to 64
STAKEHOLDER WORKSHOP	63
DISSEMINATION[1]	
Progress reports to HS&DR	6, 12, 18, 24, 30, 36, 42, 48, 54, 60
Stakeholder newsletters	Quarterly
Article: DCE scoping	18
Article: DCE results	20
Article: Network-led implementation of change in London Cancer	41
Article: Implementing change in GMC	53
Article: Inter-organisational collaboration in London Cancer	55
Article: Effect of losing specialist cancer surgery provision	55
Article: The cost of implementing reconfiguration	54
Article: Impact on outcomes, interventions, and patient experience	63
Article: Cost-effectiveness of centralisations in London Cancer area	64
Final report	65+ 2 weeks

Note. We have planned a 6 month lead-in, covering months -6 to -1, with launch at month 1.

[1.] Months specified under Dissemination represent anticipated submission dates.

14. ACKNOWLEDGEMENTS

We would like to acknowledge the contribution to this study made by our patient co-investigator, Neil Cameron, who died in May 2017. Neil contributed a great deal to the study, from the development of our proposal onward. We will continue to acknowledge Neil's contribution to our study in any future outputs.

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NHS National Institute for Health Research