

**Evaluating patient follow-up and complexity in cancer clinical trials:  
Development of an objective methodology to define and quantify trial  
complexity, intensity and workload to improve operational management and  
enhance models of trial delivery.**

**Short title:** Evaluating Patient follow-up And Complexity in Cancer clinical Trials  
(EFACCT)

**Protocol Version:** Version 3.0 Sep 4 2017

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**Funding Source:** United Lincolnshire Hospitals NHS Trust (through cancer charitable  
funds provided in the name of Roman Kopyt) and the University of  
Lincoln.

**Study Sponsor:** University of Lincoln.

**This protocol has regard for the HRA guidance and order of content.**

**SIGNATURE PAGE**

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor’s SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

**For and on behalf of the Study Sponsor:**

Signature:

Date:

...../...../.....

...../...../.....

Name Sara Owen

Position: Pro Vice Chancellor/Head of College of Social Science

**Chief Investigator:**

Signature:

Date:

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...../...../.....

Name: (please print): Helene Markham Jones

.....

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Funder(s)	United Lincolnshire Hospitals NHS Trust (through cancer charitable funds provided in the name of Roman Kopyt) and the University of Lincoln.
Key Protocol Contributors	<p>Helene Markham Jones. Professor Chris Bridle. Professor Tanweer Ahmed.</p>
Committees reviewing protocol (patient & public involvement)	Lincolnshire Research Patient and Public Forum

**STUDY SUMMARY**

Study Title	Evaluating patient follow-up and complexity in cancer clinical trials: Development of an objective methodology to define and quantify trial complexity, intensity and workload to improve operational management and enhance models of trial delivery.
Internal ref. no. (or short title)	Evaluating patient follow-up and complexity in cancer clinical trials. (EFACCT).
Chief Investigator	Helene Markham Jones
Study Design	Multi-centre study using mixed-methods.
Study Participants	Clinical research professionals and cancer patients.
Planned Size of Sample	<p>Study involves qualitative methods and grounded theory using theoretical sampling. The following are guides for the different work packages.</p> <p><u>Quota sample:</u> Documentation &amp; database analysis (n = 100).</p> <p><u>Purposive samples:</u></p> <p>Delphi study – professionals &amp; cancer patients (n = 15-20 each arm).</p> <p>Questionnaires - professionals &amp; cancer patient (n = 100).</p> <p>Semi-structured interviews - cancer patients (n = 15).</p> <p>Semi-structured interviews - professionals (n = 20-30).</p> <p>Trial sites (n = 12).</p>
Setting	NHS cancer trial centres, clinical trial units, clinics and R&D offices in the UK to include regional variations and a mix of acute, district general and teaching hospitals. Online Delphi Study.
Planned Study Period	July 2017 – June 2019
Research Question/Aim(s)	<p>Primary Objective:</p> <p>To define and quantify complexity and follow-up in cancer clinical trials.</p> <p>Secondary Objectives;</p> <ul style="list-style-type: none"> <li>• Develop trial rating and complexity assessment tool (TRACAT) based on protocol design, types of cancer, study phase, service delivery requirements and patient needs.</li> <li>• Conduct in-depth study to define variables and phenomena contributing to service pressures in trial delivery.</li> <li>• Optimise use of quantifiable clinical trial and performance data.</li> <li>• Identify and evaluate barriers to efficiency and</li> </ul>

	<p>quantifiable factors forming complex structures.</p> <ul style="list-style-type: none"> <li>• Obtain rich contextual data from trial participants and research professionals and investigate qualitative phenomena of trial delivery.</li> <li>• Provide mechanism for continual trial assessment &amp; enhanced reporting to support strategic planning.</li> <li>• Identify and report best practices in evidence at trial sites.</li> </ul> <p><u>Work Packages:</u></p> <p>Work Package No.1 – Documentation and database analysis</p> <p>Work Package No.2 – TRACAT tool</p> <p>Work Package No.3 – Qualitative Study (Phases 1-3)</p> <p>Work Package No.4 – Systematic Review</p>
<p>Key eligibility criteria</p>	<p><u>Sites</u></p> <p>Clinical trial centres and sites conducting cancer clinical trials in NHS secondary care settings in the UK.</p> <p><u>Cancer patients</u></p> <p>Patients with a diagnosis of cancer who have previously participated or are currently participating in a cancer clinical trial conducted at an NHS site.</p> <p>Cancer clinical trial patients who have completed one or more follow-up visit and are able to provide informed consent.</p> <p>Cancer patients over 18 (no upper age limit)</p> <p><u>Clinical Research Professionals</u></p> <p>Clinical research professionals with a minimum of 18 month’s experience in working within cancer clinical research.</p> <p>Clinical research professionals over 18 (no upper age limit)</p> <p>See individual work packages and section 7.1 for further details.</p>
<p>Description of interventions</p>	<p>Statistical data: Collation of local and national statistical data including performance, recruitment &amp; KPI data, follow-up and visit volumes, portfolio of studies at site, resource/head count delivering cancer studies (including role mix and study mix per resource capita where available).</p> <p>Documentation data: Collation of cancer clinical trials documentation to include protocols, schedule of activities, industry costing templates, pharmacy manuals, investigator</p>

	<p>brochures, REC &amp; IRAS forms, CRFs, questionnaires and participant documents (PIS, Consent forms, diaries etc.).</p> <p>Delphi study: Delphi questionnaire conducted in 3-4 rounds. Participants will be 'expert' research professionals and cancer patients. Part of the role of the Delphi study will be to define and rank trial attributes to support the creation of the TRACAT scoring model.</p> <p>Structured questionnaire (with free text addition) – sent to cancer patients and research professionals.</p> <p>Semi-structured interviews – conducted at relevant sites in a suitable private location with cancer patients and research professionals (initial structured questionnaire will inform the interview guide).</p>
<p>Outcome measures</p>	<p>Qualitative analysis of; Delphi round 1 survey, patient and professional questionnaires (with free text addition) and interviews.</p> <p>Quantitative analysis of; trial documentation and databases and rounds 2 and 3 of Delphi survey and questionnaires.</p> <p>Systematic review: Comparative analysis of commercial and non-commercial clinical trial interventions, follow-up and complexity.</p> <p>Development of a trial rating assessment tool – TRACAT. Tool evaluated through EDGE survey at the conclusion of the study.</p> <p>Development of grounded theory describing cancer clinical trial delivery.</p>
<p>Data analysis</p>	<p>Data analysis will include descriptive statistics, thematic content analysis, theoretical, open, axial and selective coding and constant comparison methods. Statistical summaries will use measures of central tendency and levels of dispersion.</p>

**FUNDING AND SUPPORT IN KIND**

<p><b>FUNDER (S)</b></p> <p>Main PhD project funder: The Lincolnshire Clinical Research Facility, United Lincolnshire Hospitals NHS Trust undertakes the role of funder for this PhD research study through cancer charitable funds provided in the name of Roman Kopyt.</p> <p>The University of Lincoln undertakes the role of joint funder of this study providing additional financial support for this PhD research in the</p>	<p><b>FINANCIAL AND NON FINANCIAL SUPPORT GIVEN</b></p> <p>Lincolnshire Clinical Research Facility,                  United Lincolnshire Hospitals NHS Trust                  Lincoln County Hospital, Greetwell Road                  Lincoln, LN2 5QY                  Tel: 01522 573941                  Email: <a href="mailto:Tanweer.Ahmed@ulh.nhs.uk">Tanweer.Ahmed@ulh.nhs.uk</a></p>
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## ROLE OF STUDY SPONSOR AND FUNDER

### Funding source

The main funding for the research is provided through cancer charitable funds in the name of Roman Kopyt through the United Lincolnshire Hospitals NHS Trust with additional funding support provided by the Lincoln Institute of Health at the University of Lincoln.

### Participant stipends and payments

Participants will not receive payment for their involvement but reimbursement will be made for travel where costs are incurred to attend an interview. Reimbursement will be made at the current rate as stated on gov.uk website, in line with HMRC mileage allowance payments.

## STUDY MANAGEMENT

### Study Management and Protocol contributors

The research is being undertaken as part of a PhD study. Helene Markham Jones, Chief Investigator will be the main study contact and will manage all study activities including study design, recruitment, data collection and analysis, tool design and dissemination of findings.

The protocol contributors include Professor Tanweer Ahmed and Professor Christopher Bridle, who act as academic supervisors and provide expertise, direction and guidance on the design and conduct of the research.

### Patient & Public Involvement Group

The Lincolnshire Research Patient and Public Forum (LRPPF) has been consulted in the preparation of this protocol to ensure that patient perspectives have been considered in the research design.

### CRN Coordinating Centre Leeds

Dr Clare Morgan, Research Delivery Director and Liz Gardner, Study Recruitment and Delivery Manager, CRN National Coordinating Centre (CRNCC) have been consulted during the development of this study in relation to possible collaborative areas of interest in patient follow-up.

### IT Partners

The EDGE Clinical Research Management System hosted by Southampton University Hospitals NHS Trust in conjunction with the University of Southampton will be supporting the study through the permission to host the TRACAT tool within the system and support in kind through system management knowledge and data expertise.

EDGE contact details; <http://www.edgeclinical.com/> Email: [edge@soton.ac.uk](mailto:edge@soton.ac.uk)  
Tel: +44 (0)23 82027 200

**Key Words:** Complexity, Cancer, Clinical Trial, Workload, Follow-up, Intervention

## ABBREVIATIONS

CI	Chief Investigator
CTU	Clinical Trials Unit
CPMS	Central Portfolio Management System
CRF	Case Report Form
CTMS	Clinical Trials Management System
CTUs	Clinical Trial Units
DMP	Data Management Plan
EORTC	European Organisation for Research and Treatment of Cancer
GCP	Good Clinical Practice
HRA	Health Research Authority
ICF	Informed Consent Form
KPI	Key Performance Indicators
LPMS	Local Portfolio Management System
LRPPF	Lincolnshire Research Patient and Public Forum
NHS	National Health Service
NIHR	National Institute for Health Research
ODP	Open Data Platform
PI	Principal Investigator at a local centre
PIS	Participant Information Sheet
REC	Research Ethics Committee
R&D	Research and Development
TRACAT	Trial Rating and Complexity Assessment Tool
ULH	United Lincolnshire Hospitals



UoL                      University of Lincoln

WP                        Work Package

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**Study Work Package (WP) Chart**

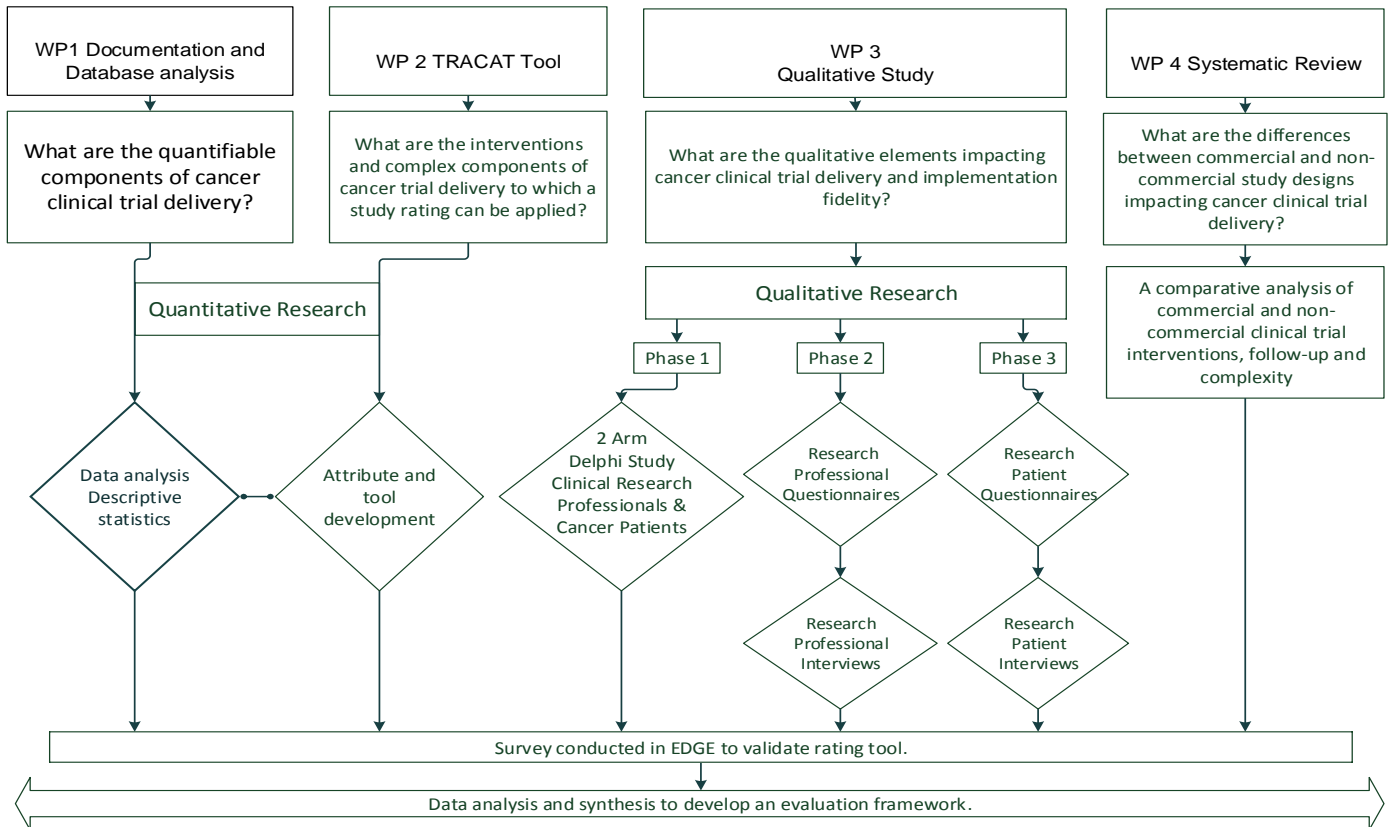


Fig 1.

**TIMELINE**

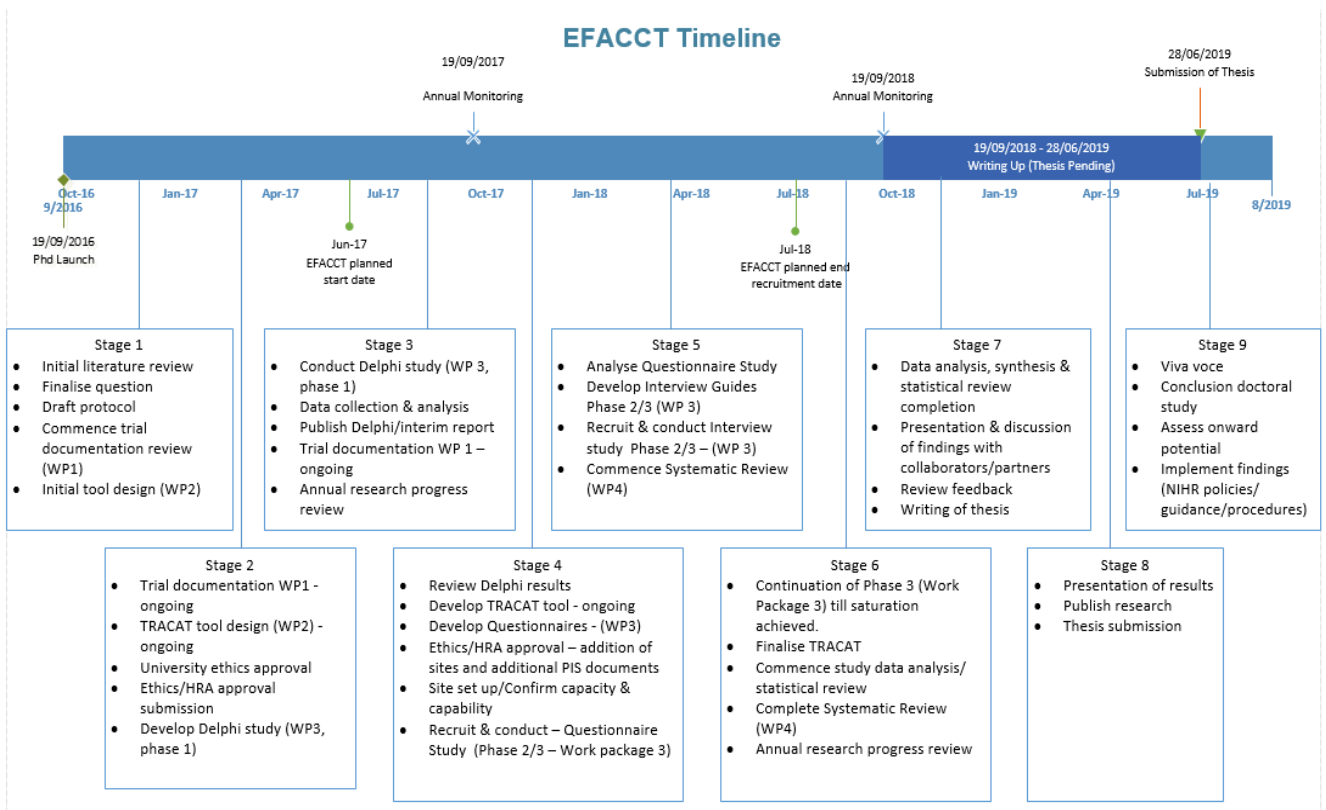


Fig 2.

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## STUDY TITLE

Evaluating patient follow-up and complexity in cancer clinical trials: Development of an objective methodology to define and quantify trial complexity, intensity and workload to improve operational management and enhance models of trial delivery.

## 1 BACKGROUND

There is a burgeoning problem in the management of cancer clinical trials. Cancer studies are amongst the most complex in design with detailed, prolonged follow-up and intricate protocols. Recent years have witnessed substantial growth in procedures per protocol (Getz et al., 2011). Amendments and complex designs place significant burden on participating sites and cancer, as a multi-factored disease, adds to the complexity. As researchers explore tailored treatments, evaluation of evolving protocols is required to understand operational implications. For trials delivered in NHS settings there are further levels of complexity of which financial, cultural and organisational factors are elements. Research should be at the fore of healthcare provision as it provides patient access to the latest treatments and drugs. Ameliorating trial recruitment comes with associated problems of managing increased volumes of patients in follow-up. The NIHR funding provision to service providers is a recruitment focussed model requiring researchers to meet specific targets including a 70 day first patient benchmark. As sites work to increase recruitment to time and target patient volumes in follow-up increase exponentially. Workload can vary dramatically between studies yet this is not monitored nationally. With a 70% increase in cancer incidence predicted within twenty years (World cancer report, 2014), improvements in survival rates and pressures on NHS funding, it is pertinent to evaluate trial interventions and their impact on research sites and patients. The need to evaluate cancer care and research delivery in the NHS is a perpetual process, as the disease, its treatments and the social environment evolves. Study into models of research delivery need to be undertaken to interpret the paradigm in the present era. Interpretation is needed that can map trial complexity and follow-up in 'real time' and over study lifetimes in an accessible manner, with data that can be reported locally, regionally and nationally and mapped into existing data systems, such as LPMS and CPMS applications. The unique nature of the NHS warrants in-depth study to comprehend variables and phenomena contributing to service pressures in trial delivery and to identify the changing needs of patients and research professionals.

## 2 RATIONALE

The EFACCT study will involve research professionals experienced in delivering cancer clinical trials and cancer patients who have previously or are currently participating in a trial. The key stakeholders involved in cancer clinical research are placed at the core of the study design. They are crucial in identifying issues in existing processes and invaluable in providing insight and perspective which can support the development of future research delivery models. The study will take a broad yet granular approach in describing cancer research delivery in context, and in identifying the constraints and facilitators to operational efficiency and patient-centred models of care at the micro, meso and macro levels. Through an analysis of the political, financial and cultural environments in which research is conducted, and a review of existing frameworks and models supporting cancer clinical

trials, it is anticipated mechanisms can be developed to optimise the capacity of organisations and research professionals to support the future demands for cancer research in the UK.

This research is directed at providing clear insight into the nature of cancer trials in terms of operational delivery thereby providing a platform for continual assessment and improvement of service solutions and patient outcomes. The aim of this study is to analyse elements of cancer clinical trial execution and quantifiable factors forming complex structures around core themes of follow-up, complexity, workload and barriers to efficient delivery through an analytical approach which is data, system and patient centred. With the introduction of the amendment ICH GCP (R2) the study also supports review into applicable areas covering trial efficiency, management of adequate resource, quality management and risk management as well as developing a tool which enhances the ability to monitor and measure trials. The complexities of trial protocol design, amendments and level of activities including follow-up can place a significant burden upon operational resources of participating sites. In order to fully understand the variations in complexity and follow-up this research study's intent is to develop an objective methodology and system based tool to enable the accurate evaluation of factors determining the overall model intensity, workload and resource impact on trial centres.

Studies analysing protocol complexity and clinical trial workload have predominately been conducted within the US and Canada, although a study to develop a workload measurement tool was undertaken in 2006 within the UK in conjunction with the EORTC Clinical Research Coordinators Group. The trial collected workload data for a six month period but excluded key investigator and pharmacist roles as difficulty was anticipated in collating accurate workload data for these roles (Lyddiard, J et al, 2010). Previous research has identified the need for qualitative evaluation of workload and complexity alongside the development of a rateable trial scoring model using 'experts' whose advice is "fundamental to the weighting and scoring" (Briggs, J, 2008). There is little evidence of subsequent studies being adopted in the UK to address complexity, follow-up and burden which incorporates both cancer patient and research professional perspectives, or of contextual analysis of the delivery of cancer clinical trials within NHS settings.

The EFACCT study therefore intends to address this gap through a mixed-methods study using grounded theory which will discover the unknown elements of trial delivery and develop an evaluative model which can support research at a local, regional and national level. The intended outcomes are the modelling of an operational framework and the provision of an instrument to support chief investigators, clinical trial units and trial sites, trusts and networks in study evaluation, monitoring and workforce management which provides enhanced outcomes for cancer patients within the NHS. Additionally the study seeks to bring greater focus and perspective to the feasibility stage of study adoption through the creation of a structured evaluative tool which will support practitioners in making sense of large volumes of data, recognising the difficulties of absorbing and critiquing protocols and other trial documentation at the same time as working in a fast-paced, time-pressured and patient-facing context. The TRACAT tool and the data knowledge it develops over time will assist investigators in the designing of trials and the development of research grants ensuring the appropriate financial support is incorporated into the study design to support all interventions and study stages including follow up.

### 3 THEORETICAL FRAMEWORK

The EFACCT study adopts a pragmatic approach and the use of mixed methods in the analysis of the complex area of cancer research delivery, bringing together large volumes of data, practices, inter-disciplinary teams and human experiences. Context is highly relevant to the study of practice and operational activity and requires qualitative analysis whereas data and metrics can be analysed quantitatively. Both qualitative and quantitative methods have important roles in understanding research data, systems, contexts and cultures. There are significant benefits to adopting mixed-methods within healthcare research, most crucially is it facilitates the adoption of a holistic approach, both in a philosophical and a medical sense. This 'third research paradigm' of mixed methodology is necessary in a research world which is 'interdisciplinary, complex and dynamic' (Johnson and Onwuegbuzie, 2004). Through a combination of objective and subjective approaches in examining patient follow-up and complexity in cancer clinical trials, the resultant data will provide a deep level of understanding of the phenomena. The study design also recognises the importance in obtaining patient perspectives in the design and delivery of research as defined in "the values and principles framework" (INVOLVE, 2015). Similarly the involvement of research professionals in the analysis and reflection on service delivery and care is critical from ethical, evaluative and research design perspectives as well as the important role staff engagement plays in development of a committed and motivated workforce. Research within the NHS has shown that involving staff in identifying the issues and challenges that the organisation faces leads to higher levels of staff engagement, improved strategic decision making and performance improvement where "initiative has to come from within the NHS" (Ham C, 2014).

The process of undertaking sociological research requires the adoption of an open mind (Denzin, 1989) so the impartiality of the researcher is crucial in this research activity. Whilst the paradigm illustrating cancer clinical research will not be defined in advance themes may emerge encompassing characteristics of organisational, open-systems or complexity theories as well as the role of health informatics in change theory. Cancer portfolios will be evaluated at participating sites with interventions analysed in relation to key participants and levels of interactions, the 'Conditional/Consequential Matrix' (Strauss & Corbin, 2008, 244). The interaction between research professionals and patients in the act of conducting and participating in cancer research will also form a substantive focus of study. Grounded theory will be used as it is well-suited to "capturing complexities of the context" (Locke K, 2001). A conceptual framework will be developed to describe the complex phenomena of trial delivery and to support enhanced models of delivery and improved outcomes for patients. At present there is no conceptual model to serve as an 'exemplar' as an operational model for cancer clinical trials other than the more generic models of adopting the principles of Good Clinical Practice.

An interactionist perspective is suited to the operational elements of clinical trial delivery but alongside that runs the concept of cancer as a 'complex disease' and of 'uncertainty in healthcare' (Han et al, 2011). Complexity and uncertainty straddle both the realms of social interaction involved with disease management and trial delivery and the nature of cancer

itself. Han et al describe three taxonomies in relation to uncertainty in healthcare; 1) sources of uncertainty; 2) substantive issues of uncertainty; 3) locus of uncertainty. They further separate substantive issues in uncertainty to form subcategories under the scientific (data-centred), practical (system-centred), and personal (patient-centred) (Han et al, 2011). In this study we can utilise these concepts to form a framework from which to study complexity and uncertainty in relation to cancer clinical trials. The trial design takes into account the disease-centred and patient-centred models of clinical trial delivery through the use of qualitative and quantitative methods.

#### **4 RESEARCH QUESTION/AIM(S)**

The key aims of the research are to evaluate and define patient follow-up and complexity and understand the elements contributing to trial complexity, intensity and workload. This requires analysis of study interventions across multiple types of cancer studies and a review of protocol designs affecting the capacity to deliver clinical research. In tandem the identification of research strategies in practice, and the elaboration of social contexts will support the development of theory targeted at realising efficiencies and sustainable procedural improvements. The aim is to identify methodologies and policies designed to improve patient experiences and outcomes. A key product of the research will be the design and implementation of a Trial Rating and Complexity Assessment Tool (TRACAT) which will be developed to provide a mechanism for continual trial assessment, enhanced reporting and to support strategic planning as well as improved feasibility assessment and implementation of pipeline studies.

The problems that the research intends to address is the;

- Lack of visibility of the volume of follow-up activity.
- Need for a comprehension of complexity and the burden these elements place on trusts and networks.
- Need for strategies in addressing these issues locally, regionally and nationally.
- A need to measure, report and forecast workloads and resource requirements systematically, thereby managing capacity issues.
- A need to ameliorate set-up of pipeline studies, increase recruitment and support the growing number of patients in follow-up.
- Lack of clarity from Chief Investigators in allocating research and service support costs to participating sites.

##### **4.1 Objectives**

###### **Primary Objective:**

The primary objective of the study is to define and quantify complexity and follow-up in cancer clinical trials conducted within the NHS.

###### **Secondary Objectives;**

The secondary objectives of this study are to;

- Develop trial rating and complexity assessment tool (TRACAT) based on protocol design, types of cancer, service delivery and patient needs. This should serve as an objective methodology to evaluate workload and complexity and leverage the benefits of health informatics in quantifying clinical trial and performance data.
- Conduct in-depth study to define variables and phenomena contributing to service pressures in trial delivery.
- Identify and evaluate barriers to efficiency and quantifiable factors forming complex structures.
- Obtain rich contextual data from trial participants and research professionals and investigate qualitative phenomena of trial delivery, exploring their perspectives in relation to trial delivery and understanding their priorities, needs and experiences.
- Provide a mechanism for continual trial assessment and enhanced reporting to support strategic planning.
- Identify and report best practices in evidence at trial sites.

## 4.2 Outcomes

The main outcomes of the study include;

- Qualitative analysis of Delphi round 1 survey, patient and professional questionnaires and interviews.
- Quantitative analysis of trial documentation, performance data and rounds 2 and 3 of Delphi survey.
- Development of a trial rating assessment tool – TRACAT.
- Development of theoretical model defining cancer clinical trial delivery.
- Systematic review providing a comparative analysis of commercial and non-commercial clinical trial interventions, follow-up and complexity.

## 5 STUDY DESIGN and METHODS of DATA COLLECTION AND DATA ANALYSIS

EFACCT is a collaborative multi-centre study using an inductive mixed-method approach and grounded theory to develop a holistic analysis of cancer research delivery in the United Kingdom in NHS secondary care settings. A matrix of methods will collect and synthesise data from quantitative analysis of multiple sources including trial documentation and databases and from qualitative investigation involving cancer patients and research professionals. Quantitative components will capture volumes and frequencies of interventions and attributes whilst qualitative study will explore perceptions and experiences of patients and professionals involved in delivering or participating in trials in order to elicit the contextual factors and experiential themes. A true workload measurement analysis would be limited without incorporating qualitative analysis (Gwede et al, 2001). Data triangulation will add validity to the study design as simultaneous collection, analysis and comparison will be drawn from four work packages. Through a data collection methodology combining multiple approaches, participants and materials it is argued that a strategy is created adding “richness, and depth to any inquiry” (Denzin N, 2012).

Research participant involvement will take place in Work Package 3 which consists of three phases. The following summary table details the separate work packages.

Work Package	Activity Description
Work Package 1	Documentation and Database analysis
Work Package 2	Trial Rating and Complexity Analysis Tool (TRACAT)
Work Package 3	Qualitative Study
	Phase 1. Delphi Study
	Phase 2. Clinical Research Professionals Questionnaires & Interviews
	Phase 3. Clinical Research Patient Questionnaires & Interviews
Work Package 4	Systematic Review

Fig 3.

### Grounded Theory

The study will adopt the use of grounded theory which is an inductive methodology developed in the United States 1960s by Barney Glaser and Anselm Strauss. Grounded theory is an approach which is detailed and pragmatic. Data collected from cancer clinical research documentation and participants via the multiple work streams will be drawn together through data triangulation. A constant comparison method is used to formulate conceptual categories and theory which is grounded in the data and “systematically obtained and analysed in social research” (Glaser and Strauss, 1967). A priori theory is not developed in advance but concepts, themes and theory are developed from the collected data making it highly sensitive to the context of the subject being researched. Through a ‘ground up’ approach the unknown elements within process and social relations in cancer trial execution will be drawn out from the research data and given conceptual meaning. The data sources are coded to form emerging themes and categories which will move through an analytical framework or “concept-indicator model” (Yates, S.J, 2004) incorporating open sampling and coding, axial coding, theoretical saturation and selective coding. Triangulation in data collection is a feature of grounded theory supporting reduction in bias and a “convergence upon the truth about some social phenomenon”, (Denzin, 1978, p14).

From a theoretical stance it is important to approach the research subject from the perspective of the clinical research professionals and cancer patients participating in clinical trials. Grounded theory is appropriate as the nature of the subject is problematic and highly dependent upon the social environment. My decision to adopt grounded theory was influenced by my concern to reflect the relevance of the conduct of clinical research to its context. Locke (2001) argues that ‘it is impossible to comprehend fully a phenomenon without understanding the context in which it is expressed’. Using this method the research will generate rich contextual data to conceptualise cancer trial complexity and the burden of follow-up. In a grounded theory study the data that is generated is constantly reviewed against literature, both theoretical and contextual, so the literature review will run concurrently with data collection throughout the life of the study.

### Reflexive journal

A reflexive journal will be kept by the Chief Investigator to record additional information in relation to the research process in keeping with the grounded theory methodology. The journal will be updated after each interview or data collection session and will form part of



the research evaluation. The diary will only be accessed by the Chief Investigator and the supervisors for the research study.

## Data Collection

Study data will be collected under the following categories; Delphi surveys, questionnaires, interviews, performance metrics, demographic data and sponsor trial documentation. Third party data will include data in the public domain (e.g. Office for National Statistics, NHS digital, Quality Health UK) and data requiring secure access (e.g. NIHR ODP, EDGE databases). Data will include audio recordings, transcribed notes in Word, coded transcriptions added to SPSS and reflexive journal data. Data formats may include; CSV files, Word and Excel documents, SPSS files and information stored in secure databases.

## Data analysis

Data from all workflows will be synthesised to develop grounded theory with sampling and collection continuing until theoretical saturation is achieved. Interviews will be recorded and the resultant data transcribed, compared and categorised. Data collection and analysis from the four work packages will also be used to inform trial ratings and create attributes within the TRACAT tool.

In a study using grounded theory data is coded and goes through the following stages;

- Open text coding – initial codes or concepts are developed from the research data
- Axial coding – the concepts are then linked into conceptual groups or families (coding paradigm)
- Selective coding – the conceptual groups are then selectively coded to form theoretical frameworks

The data from the Delphi study will involve both qualitative and quantitative data analysis methods using content analysis, descriptive statistics and statistical summaries. Further details are provided in section 5.3.1.

## Software Packages

NVivo 10 for Windows - NVivo software will be used to assist in the management of data and coding from qualitative elements and in development of grounded theory.

IBM SPSS Statistics Package Version 22.0 – SPSS will be used for statistical analysis of quantitative data.

EDGE Clinical Research Management System Version 2 – Trial monitoring and recruitment tracking (EFACCT study), attribute development for protocol, complexity, workload and follow-up analysis (cancer study samples), TRACAT tool hosting and workforce capacity management evaluation.

## 5.1 Work Package 1 - Documentation and Database analysis

A systematic analysis of documentation and databases will inform rateable and quantifiable elements of follow-up and complexity in cancer clinical trials both in terms of their design and delivery. As researchers develop new and tailored treatments the evolution of trial and protocol designs over time needs to be reviewed in combination with key operational performance metrics. The steps undertaken in this work package will include the following;

- Analysis of recruitment, visit and follow-up volumes at participating trial sites and nationally (where data is available). Key data sources will include the Clinical Research Network Open Data Platform (ODP) and the EDGE Clinical Research Management System.
- Applicable data sets providing demographic and health data including data in the public domain (e.g. Office for National Statistics, NHS digital, Quality Health UK), NIHR performance metrics, statistical analysis, and demographic data relevant to describing the research question obtainable through the ODP database, EDGE and published CRN or site data.
- Analysis of quantifiable elements of sponsor documentation using a quota sample (n=100) representing a comprehensive mix of study designs and disease sites will be reviewed. A separate convenience sample will be selected from centres participating in the qualitative study to compare delivery of the same study at different sites. This activity is aimed at developing a comprehensive understanding of the impact of protocol and study design on research sites and networks. Sponsor trial documentation will be obtained through participating sites and through open data platforms such as OpenTrials.net. Documents reviewed will include; cancer trial protocols, schedules of activity, industry templates, pharmacy manuals, investigator brochures, participant documents and CRFs.

## 5.2 Work Package 2 – Trial Rating and Complexity Analysis Tool (TRACAT)

One of the main study objectives is the creation of a trial rating and complexity analysis tool (TRACAT). The development of this evaluative instrument is aimed at supporting research professionals in the management and operational delivery of clinical trials. It will be developed to provide a mechanism for continual trial assessment, enhanced reporting and to support strategic planning as well as improved feasibility assessment and implementation of pipeline studies. The tool will be an attribute based system, initially designed to evaluate cancer study designs, but will be adaptable for use with other therapeutic areas. Consideration will be given to future-proof the tool to support the fluid nature of research methods and evolution of study designs. Data from all workflows will be synthesised to create attributes informing the trial rating. The tool aims to provide a protocol rating which truly reflects the nature and implications of the lifecycle of a study. The EDGE (EDGE Clinical Research Management System), a cloud-based software application created by the University of Southampton, will be used to host the tool but the TRACAT model will be replicable in other data forms or databases for use by sites which are not presently using EDGE as their LPMS system.

The tool design and development will be conducted in tandem with the other study work elements and outputs from work packages 1, 3 and 4 will feed into the rating and complexity analysis. Trials will be categorised based on protocol design, types of cancer, service delivery requirements and patient needs. The initial input received will be from the documentation, database analysis and the Delphi study and subsequently from the questionnaires and interviews in the qualitative phases of the study. The steps undertaken and the analysis will include the following;

- Stratify procedural and clinical study elements to develop a scoring model to fit all study phases, types of cancer and trial sites (adaptable to other therapeutic areas).
- Define and monitor elements deemed to be complex or adding to complexity through inter-dependence.
- Provide a model to consistently measure volumes of follow-up, study outcomes, recruitment and life-cycle study management from site to national level.
- Record and evaluate all study interventions and identify resource performing activity.
- Quantify resource elements, time and costs over the life of a study.
- Develop resources for CIs and CTUs.
- Provide a real-time workforce planning mechanism for trusts and networks to assess resource requirements and monitor delivery based on a rolling study portfolio.
- Define optimal resource service model to support complex trials and patient care.
- Allow flexibility in tool for re-assessment of study following substantial amendments.

On completion of the research and the analysis of all results the TRACAT tool design and trial rating format will be finalised. Arrangements will be made with the NIHR and the EDGE management team to discuss the potential for adopting the ratings into practice. The EDGE element will be trialled with existing end users and a survey conducted within EDGE to obtain collective feedback. End user survey evaluation is conducted as a standard business practice by the EDGE team.

### 5.3 Qualitative Study

Work Package 3 incorporates the qualitative elements of the study and is separated into the following phases;

- Phase 1 - A Delphi study involving two groups (cancer patients and research professionals);
- Phase 2 - Questionnaires and semi-structured interviews involving research professionals with knowledge of cancer trials.
- Phase 3 - Questionnaires and semi-structured interviews involving cancer patients.

The aims of the qualitative study are to;

- Evaluate facilitators, barriers and variables impacting efficiency such as; internal and external structures, resource and capacity, morale, design methods, cultural values, multi-disciplinary communication.
- Obtain rich descriptive participant content to gain insight and formulate theory on models of cancer research delivery.

- Gain in-depth insight into the phenomena of cancer clinical trial delivery and follow-up from the perspective of the key stakeholders.
- Involve stakeholders in the evaluation of trial rating and validation of emerging themes around follow-up, complexity and workload.

### **5.3.1 Phase 1 – Delphi Study**

An online Delphi study (e-Delphi) will be conducted using an expert panel adopting a classic approach to reach consensus in the trial rating and complexity assessment of cancer clinical trials. The two-armed Delphi study will include research professionals and cancer clinical trial patients (the experts), a stakeholder sample (n = 15-20 each arm), and produce both qualitative and quantitative data outputs. The Delphi technique is a method used for the purpose of achieving consensus through the use of sequential questionnaires answered by a panel of participants (expert panel) who have expertise or specialist knowledge in the field of the research subject. Using the e-Delphi technique allows participants from across the UK to provide expert input into the design of the TRACAT tool. Their input will also inform the subsequent questionnaire and interview stages creating a democratic review of cancer trial delivery. The participants will remain anonymous with the intention of facilitating freedom of expression and prevention of over dominance by participants who could direct or influence views within a group. This feature of Delphi studies is a particular strength in preventing bias. Participants have equal opportunity to express their views freely without domination from hierarchical individuals or bodies which may be experienced within an open group.

A series of questionnaires will be circulated commencing with open questions in the first round analysed qualitatively and then moving to a quantitative analysis in subsequent rounds using a 7-point Likert scale with the aim of reaching consensus. All responses are collated and analysed by the research team and feedback is given to participants on the previous round's data submitted by the group. These are reported as a statistical measure of the group response but individual responses remain anonymous. Once there is a convergence of opinion or an agreed consensus measure has been reached the process is complete. This method is widely used in healthcare, predominantly to identify priorities or gain consensus. Statistical analysis will look at measures of central tendency.

#### **Aim of the Delphi study**

The main aim of this Delphi study will be to identify the extent of agreement and disagreement across expert panelists on the factors contributing to the burden of follow-up and trial complexity within cancer clinical trials. It is anticipated that the research will identify the different research priorities and perspectives of research professionals delivering cancer clinical trials as well as those of cancer patients as service users. The Delphi study has been selected as a consensus method to elicit the opinions of experts on the importance and priority of trial delivery variables and as a method which is an effective process for the analysis of complex problems by a group (Linstone & Turoff, 1975). The data from the Delphi study will inform the creation of a trial ranking and provide a basis for the questionnaires to be sent to professionals and patients which in turn will inform the

interview guides to be used in the semi-structured interviews later in the study. The data produced from the Delphi element of the study will also contribute to the developing theory (grounded theory).

## Participants & sample size

There will be two different stakeholder groups participating in the Delphi study and each will answer slightly different questions relating to delivery of cancer clinical trials. Delphi participants will be purposively selected based on their knowledge of cancer clinical trials and meet specific selection criteria. Combining professionals and patients in a single Delphi study would make the group too heterogeneous. In a Delphi study there needs to be a balance between homogeneity and heterogeneity in order to ensure that a wide range of perspectives are considered. Patients' perspectives are important in understanding the impact of study design and their experience as participants so a separate arm was deemed necessary. If both groups were combined achieving consensus would be challenging and a much larger sample size would be required. Each group will therefore create their own list of topics covering issues and priorities and rate the emergent themes.

In order to achieve a sample of 15-20 panelists the study will aim to recruit 22-30 participants to each arm. Whilst this is a relatively small sample size, the importance in the selection of a Delphi sample is the knowledge and expertise of the participants in relation to the key topic being studied. If the sample of experts are similarly knowledgeable and expert in the field of study a small sample size can be deemed effective (Atkins et al, 2005). Within the research professional group the multi-disciplinary mix ensures that the panel is sufficiently heterogeneous not to produce bias. Within the patient group we will be seeking to recruit from a range of patients involved in cancer studies across the UK, study phases and cancer types.

## Demographic data

The Delphi survey will record core participant characteristics and demographics. For the professionals their role, site, gender, age group and years of experience in clinical trial delivery will be recorded. For patients their gender, age group, disease category, type of study and the length of participation on a clinical trial will be captured. If the patient has participated in more than one clinical trial this will also be recorded. Participant anonymity will be maintained in any study data analysis and reporting to protect participants. The following demographic data will be collected for each of the Delphi study arms;

### Clinical Research Professionals

- Name
- Present job role
- Name of department
- Name of employing NHS Trust
- Age
- How many years working in clinical research

- Most recent or current clinical research role

### **Cancer Patients**

- Name
- Age
- Type of cancer
- Time diagnosed
- Time participated on clinical trial
- Name of trial
- Phase of trial

### **Delphi Arm 1 - Research Professionals**

The Delphi professional panel will be a multi-disciplinary team to include research professionals working within the NHS or collaborating with NHS Trusts and networks who will be invited to participate in the Delphi study due to their knowledge of the delivery of cancer clinical trials and cancer patient care within in the United Kingdom.

### **Delphi Arm 1 eligibility criteria;**

- Aged 18 or over.
- Clinical research professionals with a minimum of 18 month's experience of working within cancer clinical research in an NHS secondary care setting.
- Are currently working within the field of cancer clinical research or have participated in delivery of a cancer clinical trial within the past 18 months.
- Are willing to participate in a Delphi study using consensus methods and have the capacity to complete all rounds.
- Are a member of one of the following professions or groups; Clinical/R&D directors, Chief Investigators, Principal/Co-Investigators, R&D Managers, Research Radiographers, Research Nurses/Officers. Data Managers/Research Assistants and Research Pharmacists.
- Are a member of an associated profession involved in supporting cancer clinical research within the NHS and may include professionals from the following groups; Governance bodies, network professionals (NIHR, HRA, Study Support Service, Research Design Service), Clinical Research Organisations (CROs), Sponsors – Commercial and Non-Commercial.
- All research professional participants should have 18 months experience of working within a relevant clinical research delivery or support role.

## Delphi Arm 2 - Cancer Clinical Research Patients

The Delphi cancer clinical research panel will be formed from cancer patient representatives who have previously participated in a cancer clinical trial or are currently a trial patient.

### Delphi Arm 2 eligibility criteria;

- Aged 18 or over.
- Are willing to participate in a Delphi study using consensus methods.
- Have access to the internet.
- Have had a diagnosis of cancer and have previously participated in a cancer clinical trial conducted at an NHS site.
- Have completed a cancer clinical trial or have attended at least one follow-up visit within the past 18 months.

### Delphi Method

In order to join the study participants will complete an online demographic questionnaire and consent form and email this back to the study team. Participants are advised in the Participant Information Sheet (PIS) that their involvement is entirely voluntary and they can withdraw at any time. Further study information and consent forms are available for participants to access online and download from the study website; <https://efacct.com>. Once a participant's consent form is received they will be provided with a Delphi study brief for the first Delphi round and confirmation of the start date and response timeframe. The value and importance in completing rounds in a Delphi study will be discussed but their right to withdraw at any time will also be highlighted. The Delphi panelists will answer a series of questionnaires circulated in rounds. The anticipated number of rounds is three but the process may progress to four rounds if required to achieve consensus. When each round is ready to start they will be sent a link to an online questionnaire survey and advised of the 14 day timescale for completion. Two weeks will be the response time allocated between iterations. Non-respondents will receive a follow-up call. The response rates throughout the study will be logged and reported in a table to be included in the chapter covering the Delphi study in the thesis. Twelve weeks is the anticipated timeframe for completion of the Delphi study.

An initial pilot will be conducted with a small group to test the first round questionnaire. The data and participants from the pilot will not be included in the final Delphi analysis. The purpose of the pilot is to test the questionnaire design.

### Round One

In the first round participants will be asked to provide responses to an open-ended questionnaire. Demographic data will also be collected in the initial questionnaire. This data is an important element of the study so that the nature of the experts and their views relative to role can be analysed. The data from all respondents in round one will be analysed and used to form the basis of the second round questionnaire.

## Round Two

In round two participants will be sent a second questionnaire which will include information summarised from round one. The questionnaire will include a Likert scale numbered 1 to 7 and panelists will be asked to rank items identified in round 1 as core priorities and categories. They will also have the option to add additional comments in the second survey which can be included as ranked value items in the third survey. Data from round two will be analysed using SPSS version 22.0 software.

## Round Three

Each participant will receive a third questionnaire which will also include a summary of the responses from round two and analysis of the level of consensus achieved on those items. Participants will see their own responses in relation to the group responses and will be asked to rate the final statements with a view to reaching consensus amongst the expert panel. All individual responses will remain anonymous.

## Round Four

A fourth round will be only be conducted if required in order to achieve consensus.

## Consensus Strategy & Likert Scale

Participants will be asked to rate the themes raised in round 1 in terms of their relative importance using the 7 point Likert scale. The final consensus will be achieved based on 70% of experts coming to an agreement on the rating of an item. All items achieving consensus in the final round to be put forward as items for review in phase 2 and 3 of the study and considered as TRACAT tool rateable values.

## Data Analysis

The Delphi study will involve both qualitative and quantitative analysis methods which will include content analysis, descriptive statistics and statistical summaries. Qualitative content analysis will be used for the data collected in round 1. NVivo software will be used to manage the responses. Open coding will be used and statements organised into themes. In the second and third rounds analysis will use descriptive statistics. The third round questionnaires will include all the items circulated in round 2 but alongside these the median response of the group will be shown along with the respondent's original score. The Delphi panelists will be asked to review the responses and consider their own selection in the light of the group rating for each item. They will be then asked to re-rate each item or leave their original response unchanged, based on their opinion. Where a participant has rated an item by more than two points from the median, they will be asked to provide comments on their reasons for their score. Descriptive statistics and statistical summaries will be produced using the median response as a measure of central tendency and the Inter-Quartile Range (IQR) for each topic. The IQR will show the clustering or scattering of the responses. Analysis of Likert scale responses will be performed in SPSS version 22.0.



# Delphi Study Design

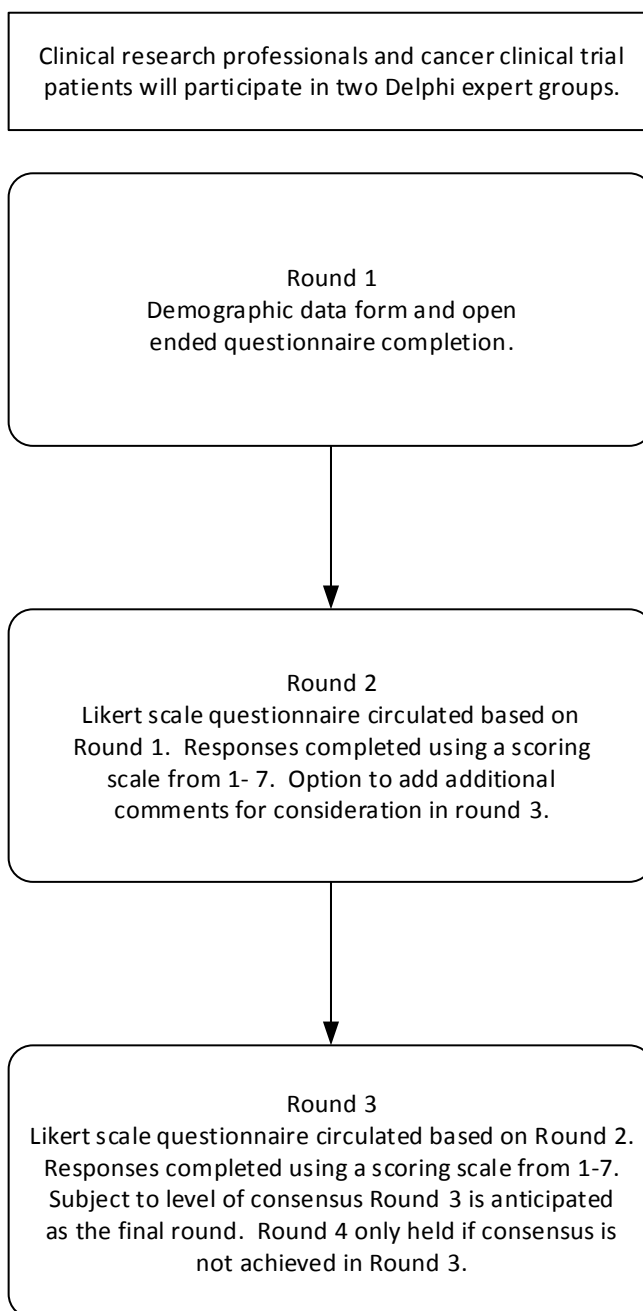


Fig 4.

## Questionnaires and Interviews – Phase 2 & 3

Following completion of the Phase 1 Delphi study structured questionnaires will be developed and sent to research professionals and cancer clinical trial participants. The questionnaires will inform the development of interview guides based on the previous study phases and allow participants who wish to take part in the interview stage time to consider aspects of cancer clinical trial delivery prior to the interview. The results of the questionnaire round will also provide additional data to inform the trial rating tool.

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The semi-structured interviews will be conducted with each cohort (clinical research professionals and cancer patients). It is proposed that participants will engage in one interview which will be approximately 60 minutes in duration. All interviews will be conducted by the Chief Investigator (CI) who will commence the interview by confirming with the participant that they have read and understood the patient information sheet, have completed the consent form and will reiterate that participation is entirely voluntary and that they are free to withdraw from the study at any time. Empathy will be demonstrated whilst conducting the interviews and participants made aware that they can stop the interview at any time, if they feel uncomfortable. The CI will confirm to participants where they can access support and this information will also be detailed in the Participant Information Sheets (PIS). A follow-up phone call or email communication may be arranged in agreement with the participant to check the information gathered and clarify any points raised. Interviews will be recorded on a mobile recording device and the data transcribed and coded. A reflexive journal will be kept to record interview observations.

### **5.3.2 Phase 2 - Research Professionals Questionnaires & Interviews**

The outcomes of the analysis of findings from Work Package 1 and Work Package 3 (phase 1) will be used to develop the structured questionnaires (with free text addition option) for research professionals active in cancer clinical trial delivery. The purpose of this activity is to take the findings from the Delphi study and test this with a wider group of professionals. The responses from the questionnaires will in turn lead to the development of themes for discussion in the interview study. Participants may select only to participate in the questionnaire study or the interviews. They also have the option to participate in both, should they wish.

### **5.3.3 – Phase 3 – Cancer Clinical Research Patient Questionnaires & Interviews**

Similarly as above, the outcomes of the analysis of findings from Work Package 1 and Work Package 3 (phase 1) will be used to develop the structured questionnaires (with free text addition option) for cancer clinical trial patients. The responses from the patient Delphi study will be used to develop patient questionnaires, gaining further analysis from a wider group. The sites involved in the trial will participate as recruiting centres to support the recruitment of appropriate cancer trial patients. Responses from the patient questionnaires will similarly be used to develop interview themes. Participants can opt in to either the questionnaire or interview study or both.

Whilst an estimated figure of 30 to 40 research professional participants and 15 cancer clinical research patients have been identified as a guide figure to recruit to the interview stages of the study, the use of grounded theory means that recruitment continues until saturation of themes is achieved and no new emergent categories arise in the data. Should it be determined that additional participants are necessary recruitment will continue through consultation with participating sites until theoretical saturation is achieved.

## 5.4 Work Package 4 - Systematic Review

A systematic review will be undertaken to answer the question, “What are the differences between commercial and non-commercial study designs impacting cancer clinical trial delivery”. This will be a comprehensive, comparative analysis of commercial and non-commercial cancer clinical trial interventions, follow-up and complexity based on protocol designs delivered in NHS settings. A separate protocol will be compiled for this research which will be conducted at the University of Lincoln, under the supervision of Professor Christopher Bridle and Professor Tanweer Ahmed and conducted in line with University ethical guidelines and policy.

## 6 STUDY SETTING

The research will be conducted as a multi-centre study with participants recruited via secondary healthcare cancer research centres across the United Kingdom. The research will be carried out online as well as at hospital sites relative to the study phase. The Phase 1 Delphi study will be undertaken online with participants remotely accessing the survey. The phase 2 & 3 questionnaires will be provided to professionals and cancer patients either directly via a participating research site or may be accessed online. All participant interviews will be conducted within NHS hospitals. Appropriate rooms will be identified at participating sites in which interviews can be conducted which may be located within outpatients, cancer clinics or R&D offices within NHS hospitals.

A mix of teaching, acute and district general hospitals hospital sites (n = 12), will be approached to participate in the study and will include variation in region and scale of site. The study seeks to obtain a comprehensive data set to ensure that all phenomena relating to trial delivery in the UK is gathered. It is important to have a distribution of hospital sites to avoid regional effects on the research results through involvement of participants from across a range of sites and trusts, incorporating both urban and rural settings. Organisational and cultural environments and the impact on cancer trial performance in addition to protocol designs is being studied and this therefore requires a diversity of settings and professionals to participate. The CI is also seeking to conduct a comparison of studies through the data analysis of selected cancer trials conducted at multiple sites and will be undertaking a small cohort analysis of these.

## 7 SAMPLE AND RECRUITMENT

The sample and recruitment steps specific to each of the study phases is detailed under the relevant headings in the following sections and in the flow chart in Fig. 9 in section 7.3.1. The summary table below details the separate work packages involving participant and site involvement.

Work Package	Activity Description
Work Package 3	Qualitative Study
	Phase 1. Delphi Study
	Phase 2. Research Professionals Questionnaires & Interviews
	Phase 3. Clinical Research Patient Questionnaires & Interviews

Fig 5.

## 7.1 Eligibility Criteria

The eligibility criteria listed below covers the core categories for participating sites, studies and participants. A further breakdown of eligibility criteria for the Delphi study is detailed in section 5.3.1.

### 7.1.1 Inclusion Criteria

- Cancer clinical trials Phases I to IV conducted in an NHS setting.
- NIHR portfolio studies only.
- Cancer clinical trials units/secondary care trial centres.
- Commercial and non-commercial cancer trials.
- All cancer types.
- Protocol within 5 years - analysis of protocols conducted at multiple sites for delivery/interpretation comparison.
- Research professionals with a minimum of 18 month's experience in working within clinical research.
- Patients with a diagnosis of cancer who have previously participated in a cancer clinical trial conducted at an NHS site.
- Patients who have completed one or more follow-up visits and able to provide informed consent.
- Cancer trial patients over 18 (no upper age limit)

### 7.1.2 Exclusion Criteria

- Clinical trials not conducted in an NHS setting.
- Non-UK sites.
- Primary care settings.
- Non-cancer clinical trial participants.
- Cancer patients whose disease has progressed to an advanced stage where the patient is too unwell to participate.
- Inability to understand and communicate in English spoken language (budgetary constraints would not allow for the translator/interpreter support).
- Inability to consent to their participation in the study.
- Cancer patients under the age of 18.

## 7.2 Sampling

### 7.2.1 Size of Sample

The size of the samples and sampling techniques in this study are relative to the different work packages. Recruitment to each phase of the study is guided by grounded theory where theoretical sampling will determine if the indicative sample is sufficient and relevant data is obtained to answer the research question. An initial guiding sample size has been identified for the purpose of coordinating and progressing the study, however, sampling will continue through constant comparative data analysis until theoretical saturation is achieved. Fig. 6 below provides an indicative guide for each of the work packages.

<b>Quota Sample</b>	<b>Sample</b>
Documentation and Database analysis	n = 100
<b>Purposive &amp; Snowballing Samples</b>	
Delphi Study - cancer patients.	n = 15-20
Delphi Study – research professionals	n = 15-20
<b>Purposive Samples</b>	
Questionnaires - cancer patients	n = 50
Questionnaires - research professionals	n = 50
Semi-structured Interviews - cancer patients	n = 15
Semi-structured interviews – research professionals	n = 20-30
Trial sites	n = 12

Fig. 6.

### 7.2.2 Sampling technique

The different work packages will incorporate a mix of sampling techniques to include; purposive sampling, quota, theoretical and snowball sampling. These choices are relevant to the methodology of each work package and are summarised below;

- Theoretical sampling - Grounded Theory involves the use of theoretical sampling where data is constantly compared between multiple phases of data collection to build categories and theory (Creswell, 2003). A sample therefore needs to include participants who have relevant experience and who can provide sufficient knowledge and description of the research subject to allow the researcher to form substantive theory. Data collection stops when no new categories emerge whereby an ‘end point called data saturation’ is reached (Sargeant, 2012).
- Data triangulation – Through the use of data triangulation and the extraction of data from varying sources and work packages a much more informed view of the phenomena being research is gained which in turn adds to the quality and sufficiency of the data samples.
- Quota sampling – A quota sample in relation to cancer clinical trials ensures that a representative selection of studies is obtained to be able to analyse study protocols and documentation in depth across a range of cancers and trial designs.

- Purposive sampling - Due to the specialised nature of the research question it is pertinent to adopt sampling methods which will ensure participants are experienced and qualified to answer the nature of the phenomena being investigated.
- Snowball sampling – As ‘experts’ are required to be identified to participate in the study, particularly in relation to the Delphi phase of the study the use of ‘snowball sampling is appropriate in combination with other methods. Known ‘experts’ (either research professionals or patient forum representatives) may be recruited or recommended to participate in the study. The use of online social media recruiting methods within the Delphi study will facilitate the use of ‘virtual snowball sampling’ Brunet, (2012) allowing recruitment of ‘experts’ from a wide geographical area.
- Delphi technique – The sample size in Delphi studies is also governed by the heterogeneity of the group and the potential for attrition. Further details in relation to Delphi recruitment and sample size are discussed in section 5.3.1.

### **Documentation and Database analysis (Work Package 1)**

A quota sample (n= 100) of cancer clinical trials will be identified within this work package and will involve the review and analysis of sponsor documentation to include; study protocols, IRAS forms, pharmacy manuals, schedules of activities, patient documentation and industry costing templates. Sampling for protocols and study documentation will be based on a quota. A selection will be made from each specialism and will aim to include a protocol from each type of cancer and from phase I-IV for portfolio studies which have been opened within the past five years. From this selection a separate convenience sample will be selected to compare interpretation and delivery of the same study protocol at multiple sites where a sufficient sample can be identified from multiple regions.

In order for the quota sample to cover a comprehensive mix of study types, phases, disease topics and range of sites approximately 100 study protocols and related documentation will be reviewed. This number would represent a 10% sample of recruiting studies listed on the UK Clinical Trials Gateway but a potential 100% sample of a cancer portfolio of a representative research site activity within a Trust. Protocols will be accessed, in agreement with study sponsors and Chief Investigators, and reviewed as part of a systematic analysis of cancer clinical trial protocols and trial documentation in relation to analysing complexity and follow-up in addition to protocol design.

### **Work Package 3 - Delphi, Questionnaires and Interviews**

A purposive research sample will be obtained in work package 3 and will include research professionals from a variety of roles as well as cancer patients.

<b>Research Participants</b>
Clinical & R&D Directors, Principal & Co-Investigators, Sponsors/Clinical Research Organisations
R&D Staff/Trial/Site Managers
Support Department Specialists (Radiographers, Pharmacists, Chemotherapists)
Research Nurses/Officers/Data Mgrs./Research Assistants
Cancer Clinical Trial Patients

Fig. 7.

**Trial sites**

Trial sites will be recruited from a cross-section of NHS secondary care sites across the UK, with a representative mix of regions involving trusts from the south, midlands and the north and ideally will include a range of teaching, acute and district general hospitals who are conducting cancer clinical trials.

Trust/Hospital	North	Midlands	South
Teaching Hospital (Large City)	1	1	1
District General Hospital (Medium/City)	2	2	2
District General Hospital (Small/Town)	1	1	1
			12

Fig. 8..

**Patient participants**

Cancer patients who have participated in a UK cancer clinical portfolio trial within the past 5 years at one of the participating sites will be invited to join the trial. Patients currently on trials may be included if they have attended a follow-up visit and are able to provide informed consent. Patients will be invited to complete questionnaires if they have previously participated in a cancer clinical trial. A sub-section of patients who have completed a questionnaire will be invited to participate in semi-structured interviews. Cancer patients under the age of 18 will not be included in this study due to the extended requirements for consent and limitation of the resources of the Chief Investigator to undertake this element. This does not however exclude obtaining qualitative data from research professionals and from the analysis of protocols to identify elements of complexity and follow-up in the conduct of paediatric cancer trials.

**Research professional participants**

The following roles will be approached to participate in the study; Clinical/R&D directors, Principal/Co-Investigators, R&D Managers, research nurses, officers and assistants, research pharmacists, radiographers as well as associated research professionals on site or externally. External professionals may include sponsors (commercial and non-commercial), governance

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bodies & network professionals (NIHR, HRA, Study Support Service, Research Design Service). All research participants should have over 18 months experience in clinical research.

### **Delphi study expert panel**

Delphi participants will be purposively selected based on their knowledge and experience of participating in cancer clinical research, either as a research professional or a cancer trial patient. The purpose of this element of the study is to involve key stakeholders with the aim of reaching a consensus in defining trial complexity and the selection of the panel is based on their status as an 'expert' in the research subject.

## **7.3 Recruitment**

Clinical research professional and patient participant involvement will take place in Work Package 3 which consists of three phases. The recruitment methods will be specific to each of the phases, as detailed under the relevant headings in the following sections and shown in Fig.9.

Sites across the UK are invited to participate in the recruitment of cancer patients and research professionals alike. The local site staff will be responsible for the identification of cancer research patients at their site and will make the initial approach to participants. They will also be involved in the identification of research professionals to invite to take part in the study in consultation with the Chief Investigator.

### **7.3.1 Recruitment of participants**

The Chief Investigator will identify sites and potential Delphi participants and sites will identify professional site participants and cancer clinical trial patients. The following list is a breakdown of the main methods of recruitment the research team will adopt to identify and invite participants;

- Conference recruitment (professionals)
- Through relevant literature and references (professionals)
- Email and social networking media (both groups)
- Via study website (both groups)
- Via NIHR/networks/existing contacts (both groups)
- Recommendations from invited participants - snowballing (both groups)
- Sponsors, CROs (professionals)
- Trusts/R&D Departments/Research sites & teams (both)
- PALS/Patient and Public Involvement Manager/Patient Forums (patients)

Study publicity will include the use of leaflets, posters and the EFACCT website.

An initial communication will be sent to the NIHR Central Coordinating Centre, local CRNs and Cancer Research Networks advising them of the study and inviting them to recommend potential sites and contacts. A list of potential sites will be compiled. Clinical trial centres, sites and contacts may also be identified by conference networking or via direct approaches to trust R&D departments or noted experts within the field of cancer research.



An introductory email will be sent to the identified sites along with an invitation to participate and supporting documents. The communication will be sent to a site’s R&D inbox or to a recommended contact. If the site is interested in participating arrangements will be made to issue the local document package to the R&D office and the Local Clinical Research Network. Only the clinical care team at the recruiting site will have access to patient records in order to identify potential participants and check whether they meet the inclusion criteria. The site will make the initial approach to patients.

Reimbursement for travel expenses will be provided in the case of a participant needing to make a special journey to attend an interview. Payments will be made in line with HMRC and gov.uk published mileage allowance payments.

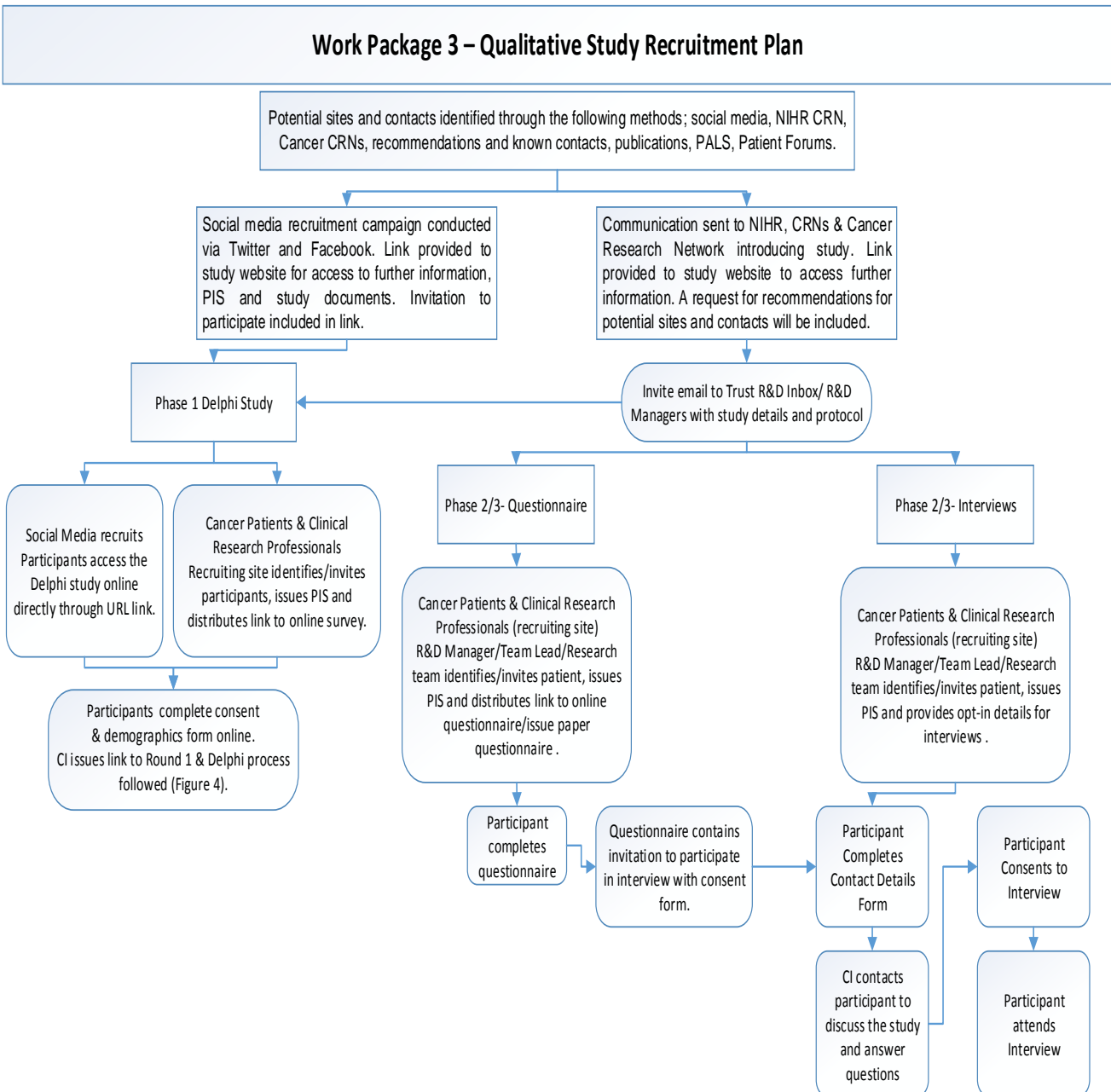


Fig. 9.

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## **Phase 1 - Two arm Delphi study**

Cancer patient recruitment to phase 1 of the qualitative study may be conducted through consultation with patient forums, through an online recruitment process or via recruiting sites.

Where a cancer patient approaches the study team or Chief Investigator requesting participation in the study, either directly through social media or via the study website, and they are receiving ongoing treatment in a clinical trial the trial site will be made aware of the patients' request.

The recruitment to the Delphi consensus activity will form the first phase of the study involving participants. The result of the Delphi exercise will then inform the development of the questionnaires to which a separate cohort of participants will be recruited. The questionnaires will also include an invite to participate in the final stage of recruitment, which is the interview phase. Participants may just participate in one element of the study, should they wish. The Chief Investigator will discuss with the sites a suitable location for consenting participants and conducting interviews.

## **Phase 2. Research Professionals Questionnaires & Interviews**

### **Structured questionnaires (professionals)**

For the recruitment of research professionals to phase 2 of the study the R&D team will be approached. The Chief Investigator will liaise with the site to identify potential participants. The R&D Manager/Team lead at site will be send an invitation to participate by letter/email to eligible staff and will be provide them with a Participant Information Sheet and a link to the online questionnaire. The PIS will contain contact details for the Chief Investigator. If they wish to discuss the study further before participating they can contact the CI directly, who can answer any questions that they may have. Questionnaires can also be provided in printed formats to sites/participants or emailed as a PDF document.

### **Semi-structured interviews (professionals)**

If participants wish to take part in the subsequent semi-structured interviews they will be provided with a PIS and a contact details form and copy of the consent form. Details regarding the interview phase of the study will be also be included in the questionnaire study. The PIS and consent forms will include contact details for the Chief Investigator and supervisors. In addition the Chief Investigator will liaise with the site to identify participants for this second stage. Following receipt of an expression of interest (contact details form/email) the Chief Investigator will follow-up with an introductory phone call to discuss the study, answer any questions and take verbal consent. If the participant wishes to proceed a convenient location and time to conduct the interview will be arranged. All interviews will be held at an NHS site in a suitable environment.

## **Phase 3. Research Patient Questionnaires & Interviews**

### **Structured questionnaires (patients)**

For the recruitment of cancer patients to phase 3 of the study the research team at the participating site will be involved in identifying and making the initial approach to patients. The Chief Investigator will liaise with the site who will identify potential participants and provide them with a Participant Information Sheet and a link to the online questionnaire. The PIS will contain contact details for the Chief Investigator. If they wish to discuss the

study further before participating they can contact the CI directly, who can answer any questions that they may have. Questionnaires can be also be provided in printed formats to sites/participants or emailed as a PDF document.

### **Semi-structured interviews (patients)**

If cancer participants wish to take part in subsequent interviews they will be provided with a PIS and a contact details form and copy of the consent form. Details regarding the interview phase of the study will be detailed on the questionnaire and will include contact details for the Chief Investigator and supervisors. In addition the Chief Investigator will liaise with the site to identify participants for this second stage. As described above a contact details form will be provided to patients along with the PIS. If they return the contact form/email the CI expressing interest in the interview phase the Chief Investigator will follow-up with an introductory phone call to discuss the study, answer any questions and take verbal consent. If the participant wishes to proceed a convenient location and time to conduct the interview will be arranged. All interviews will be held at an NHS site in a suitable environment.

## **7.4 Consent**

Valid informed consent will be obtained prior to undertaking any activities. The consent process relates to each of the respective study phases and is specific to the participant type. A proportionate approach to consent has been adopted within the study, ensuring participants to have sufficient and clear information to allow them to make an informed decision as to whether they wish to participate. The different phases of the study involving participants have specific documents, see appendix 11.1.

### **Delphi Study (Clinical research professionals and patients)**

Participants will be provided with a Participant Information Sheet (PIS) for the Delphi study for consideration. This will advise that their involvement is entirely voluntary and they can withdraw at any time. Participants will complete an online demographic questionnaire and consent form and email this back to the study team. Further study information, the first round study brief and consent forms will be available for participants to access online and download from the study website; <https://efacct.com>. Once a participant's consent form is received they will be provided with an email including the first round study brief, confirmation of the start date and response timeframe and link to the survey. Contact details for the study team will be included and participants will be encouraged to raise any questions they may have prior to completing the survey. If participants wish to discuss the study further the Chief Investigator will follow up with a telephone call at a time convenient to them. Completion of the subsequent rounds of the Delphi study will infer implied consent to continue. This will be indicated in the communication provided for each of the Delphi rounds and feedback.

### **Questionnaire study.**

A Participant Information Sheet relative to the questionnaire study will be provided online or handed to potential participants directly. Participants will complete the questionnaire study online or in paper format (if preferred). There will be no separate consent form for this study phase. By completing and returning the questionnaire the participant implies consent. The questionnaire and PIS will clearly indicate this and advise that participation is entirely voluntary.

## Interview study

Informed consent will be obtained for interview participants. A Participant Information Sheet will be provided to each potential participant (which they may keep) and copies will be available online. Following receipt of an expression of interest the Chief Investigator will make contact with the participant by telephone, answer any preliminary questions they may have and arrange a convenient date and time to conduct the interview, if they still wish to continue. Verbal consent will be obtained over the telephone but written consent will be obtained prior to conducting the interview. Participants will be given the opportunity to ask questions and to withdraw from the study at any time.

The following principles will be followed in relation to obtaining ethical and valid informed consent:

- Participants will receive full information on the study which will describe the research, the rights of the participants and the consent process. Participant information sheets and consent forms with full REC approval will be provided. These leaflets are specific to the different phases of the study and types of participants. See Appendix 11.1 for examples.
- Valid informed consent will be obtained from each participant on consent forms appropriate to each study phase in which a participant is involved.
- Participants will have a minimum of 48 hours to decide if they wish to participate in the study.
- The study will not involve participants lacking capacity to consent for themselves nor include prisoners or young offenders.
- The full nature and purpose of the research will be described with the potential participant and a detailed explanation given of what involvement in the study will entail.
- The benefits of conducting the research will be explained and any potential burden to participants of their involvement described.
- As there are no medical interventions in the study the risk to participants is considered to be low but a clear explanation will be given prior to taking consent that they may withdraw from the study at any time should they feel uncomfortable or no longer wish to participate.
- Full details of where participants can access additional support, information or raise concerns about the conduct of the study will be provided. This will be detailed in the participant information sheet. The sheets also contain a link to the website which will detail this information.
- Participants will be given the opportunity to ask questions and time to consider participation in the study. They will be encouraged to ask questions if they are unclear on any elements of the study and further explanation will be provided.
- Information leaflets and forms can be taken away by patients who are provided with details on the study so that they can discuss this with relatives or their care team.

- Clinical research professionals can similarly take the information away for consideration of discussion with colleagues. They will be advised that participation is entirely voluntary and there will be no consequences to their employment and role whether they decide to participate or not.
- Once a potential participant has received the Participant Information Sheet and has had the opportunity to discuss this and ask questions they will be asked to sign a consent form for the relevant part of the study in which they wish to participate. Prior to obtaining their signature participants will be asked if they have understood the inclusion and exclusion criteria, the purpose of the study and if they have any further questions.
- It will be emphasised that all personal information provided during the research is confidential and individual data will be anonymised. Audio recordings will be made of the interviews subject to participant consent.
- If participants consent and then no longer wish to take part in the study they can withdraw at any time. If the participant loses capacity after giving consent they will be withdrawn from the study.

## 7.5 Withdrawal

Participation in the study is entirely voluntary and the right to withdrawal from the study at any time will be emphasised at all stages and within the study documentation. Interview data can be withdrawn up to two weeks after the data collection. After this time the data will have been processed and analysed. As the Delphi survey design and grounded theory are iterative processes the data that has already been incorporated into analysis of previous Delphi rounds or used to form theoretical categories will be used in overall study analysis. All data however is anonymised once received so participants' identity will be protected at all times.

## 8 ETHICAL AND REGULATORY CONSIDERATIONS

We do not anticipate any ethical issues, adverse effects or risk to participants arising from this research and the study does not involve any medical interventions. There are no conflicts of interest in conducting the research and the researchers will act with integrity and diligence in relation to all ethical and regulatory matters. All appropriate approvals will be in place prior to the commencement of any research.

### 8.1 Assessment and management of risk

This study involves interviews and questionnaires relating to participant knowledge and experiences of processes and phenomena surrounding clinical trials and does not involve clinical interventions. The researchers will be sensitive to the participants, their needs and understanding of the study and ensure that they are comfortable with the process at all times. Involvement for research participants in the study includes describing or answering questions relating to their experience of working on cancer trials (research professionals) or

participating in a cancer clinical trial (patient). For desk-based research involving a systematic review, analysis of databases and clinical trial documentation, the accuracy of data will be systematically and rigorously checked.

The following steps and considerations support the management of risk within the study;

- University, NHS ethics and HRA study approval will be obtained prior to any data collection or research activity.
- A risk assessment template has been completed and the study risk was rated low.
- There are no medical procedures involved in the study.
- A data management plan (DMP) has been developed and will be maintained throughout the study to ensure the secure and ethical handling of research data and to mitigate any risk or loss to confidential information. All data handling, storage and transfer will be according to the strict rules set out in participating organisations' security policy and Information and Governance policies. All research data relating to sites and individual participants will be anonymised.
- The study will not involve participants lacking the capacity to consent for themselves nor include children, prisoners or young offenders.
- Participation in the study is entirely voluntary and participants have the right to withdraw at any time.
- Cancer patients will be invited to participate in the questionnaire study and interviews if they have completed a follow-up visit and are able to provide informed consent. To minimise risk for patients the clinical research team at participating sites will be involved in screening and approaching patients, so that patient data can be checked to ensure no patients who have died are contacted.
- To avoid potential distress cancer patients whose disease has progressed to an advanced stage will not be included to avoid any negative impact of participating in interviews reflecting on their treatment and illness.
- Patients will be provided with the contact details of their local research care team, Chief and Principal Investigator details and PALS contact information.
- Professional participants will be provided with the contact details of the Chief Investigator, Principal Investigators and details of the university ethics lead.
- Relevant support will be identified to provide to participants if they found that reflection on their role or involvement in previous research studies was distressing.
- If any clinical questions are raised during the course of the interview process by a cancer patient participant, they will be referred back to the staff involved in their clinical care/research team for appropriate advice.

- To mitigate all risks a comprehensive review of all methodologies will be undertaken prior to commencement of the study. A version controlled risk register and issue log will be maintained throughout the study and shared with the immediate study team ensuring any issues are acted upon and addressed in a timely manner.

## 8.2 Research Ethics Committee (REC) review & reports

This research is being undertaken in partial fulfilment of the requirements of the University of Lincoln for the degree of Doctor of Philosophy. In order to undertake this research ethical approval will be sought from the University of Lincoln Research Ethics Committee and the NHS Research Ethics Committee (REC).

- Before the commencement of the study UoL and NHS REC approval will be obtained to cover all relevant documentation including the study protocol, informed consent forms, participant information sheets and any other relevant forms.
- Substantial amendments that require review by REC will not be implemented until the REC grants a favourable opinion for the study.
- All correspondence with the REC will be retained.
- The Chief Investigator's will prepare an annual progress report (APR) which will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the study is declared ended.
- The Chief Investigator will also notify REC of the end of the study.
- If the study is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination.
- Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the REC.
- The study will be conducted in accordance with the guiding ethical principles of the Declaration of Helsinki, 2013; the principles of Good Clinical Practice, and the Department of Health Research Governance Framework for Health and Social Care, 2005.

## 8.3 Peer review

The study design and protocol has been peer reviewed by academic supervisors to ensure that it is scientifically sound and is a valid research question.

The results of the trial shall be exposed to rigorous peer review and subject to examination by the University of Lincoln exam board in part fulfilment of a PhD award. The results of the study will also be submitted to the NIHR CRN Coordinating Centre in Leeds for review. Findings and articles arising from the research will be submitted for publication in peer reviewed journals.

## 8.4 Patient & Public Involvement

This protocol is the confidential property of the University of Lincoln. No part may be transmitted, reproduced, published, or used by others persons without prior written authorisation from the University of Lincoln.

The aims of the research are to understand cancer clinical research delivery in order to realise benefits, efficiencies and improve outcomes for researchers and cancer patients alike. This study supports the initiatives of the NHS (National Health Service) and NIHR (National Institute for Health Research) to involve the public in health and social care research.

This study has been designed to involve the patient view of cancer clinical trial delivery and the protocol has been reviewed by the Lincolnshire Patient and Public Forum and perspectives incorporated. The study seeks to benefit patients and research staff involved in cancer clinical trials as well as considering wider benefits for other therapeutic areas.

## 8.5 Regulatory Compliance

The study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, 1996; the principles of Good Clinical Practice, and the Department of Health Research Governance Framework for Health and Social Care, 2005.

The Chief Investigator will apply for approval/favourable opinion from the Research Ethics Committee (REC) and Health Research Authority (HRA). No research or enrolment activities will be undertaken prior to approvals being granted for all activities and study documentation including the protocol, consent forms and participant information sheets.

Confirmation of capacity and capability will be obtained before commencing activities at research sites.

Should a protocol amendment be made that requires REC approval the changes in the protocol will not be instituted until the amendment and revised informed consent forms and participant information sheets (if appropriate) have been reviewed and received approval/favourable opinion from the REC and HRA.

## 8.6 Protocol compliance

The interventions within this study are conducted by the Chief Investigator and author of the protocol. As the author is fully involved in the design of the study protocol compliance will be rigorous.

- Accidental protocol deviations will be adequately documented and reported by the Chief Investigator to the Sponsor immediately.

## 8.7 Data Policy

The sponsor and funding organisations overseeing the study have established policies and procedures in relation to data protection and handling to ensure high standards are met and to protect research integrity. These policies will be adhered to throughout the study and in addition the following principles will apply.



### 8.7.1 Data Management & Handling

The Chief Investigator (CI) as the data custodian for the study will be responsible for new data collected specifically for the purposes of answering the research question and will implement and maintain the Data Management Plan (DMP). All data activities and responsibilities in this area will be undertaken by the CI.

Data will be obtained from the four work packages described in section 5 and may include records in the following formats; csv files, audio files, Word, Excel, txt, SPSS files, jpegs, pdfs and other relevant formats.

Study data will include the following; interview transcripts, questionnaire responses, performance metrics, database extracts, participant demographic data, sponsor documentation and third party data. Data will include both confidential data (e.g. NIHR ODP and EDGE data) and information in the public domain (e.g. Office for National Statistics, NHS digital and Quality Health UK).

Access to full details on the study will be available online through the study website at <https://efacct.com/>. Sources of advice, support and key study contacts will be clearly highlighted in all participant information sheets and on the study website at <https://efacct.com/>.

### 8.7.2 Data Protection, Access & Security

The investigators will ensure that all information collected during the course of the research will be kept strictly confidential and handled in accordance with the Data Protection Act 1998 and the Caldicott principles. NHS staff accessing patient data are guided by Trust policies and UK legislation in relation to data handling. In addition the following principles and measures are applicable to the conduct of the study;

- ULH NHS Trust and University of Lincoln policies and training ensure that data information is handled confidentially, securely and in compliance with applicable legislation.
- Only authorised members of the research team at the University of Lincoln and United Lincolnshire Hospitals Trust will access the research data and the Chief Investigator will be responsible for access and security.
- Electronic data will be stored on University of Lincoln or NHS secure network drives which requires system user log in to access or stored within the secure EDGE database and will only be accessible by the immediate study team. Out of date electronic records will be deleted. All digital files will be encrypted.
- All paper documentation, study files and the Trial Master File (TMF) will be stored in locked cabinets in a locked office at the University of Lincoln with the key held only by the Chief Investigator. Analogue data no longer required will be shredded.

- Personal data will be stored in linked anonymised form on a secure database on a password protected computer and will be kept for 3 months after the end of the study after which it will be disposed of securely.
- Research data and meta-data will be stored for 5 years and in accordance with university and NHS regulations. After this time data will be disposed of securely.
- Interview recordings will be transferred from the mobile recording device and stored on a secure password protected computer at the University of Lincoln. The audio files will be imported into an NVivo software account only accessible by the Chief Investigator.
- Data may be saved in Word, Excel, and SPSS or in secure databases. For remote working by the Chief Investigator remote logins will be used to access NHS and University desktops.
- Where data is required to be exported to a different application this work will be undertaken by the Chief Investigator and an encrypted memory stick used for transporting data between computers.
- Data collected by sites will be stored within their LPMS instance and will comply with their standard data collection and reporting procedures and will remain the responsibility of those parties.
- The data resulting from the thesis is the property of the Chief Investigator, United Lincolnshire Hospitals Trust and the University of Lincoln.
- Necessary access by the CI in relation to recruitment and performance data required for the purpose of answering the research question will be discussed with the NIHR, participating CRNs and sites.

### **EDGE Data Handling**

- The EDGE database will be used to host the TRACAT (Trial Rating and Complexity Assessment Tool) which will create a new dataset. A data sharing agreement will be discussed with the EDGE team in Southampton in relation to data created as a result of the tool development, should this become relevant.
- This EDGE database is a secure online application which has undergone secure black box penetration testing (certificate dated 2016). The database is backed up by the service provider. Details of the EDGE security and data protection policies are available in the following links;

This protocol is the confidential property of the University of Lincoln. No part may be transmitted, reproduced, published, or used by others persons without prior written authorisation from the University of Lincoln.

<http://www.edgeclinical.com/security/>  
<http://www.edgeclinical.com/data-protection/>

EDGE contact details [Email: edge@soton.ac.uk](mailto:edge@soton.ac.uk) , Tel: +44 (0)23 82027 200

- A written contract is in place between the CRN East Midlands and EDGE, encompassing the lead site. Data is handled securely and in compliance with the Data Protection Act 1988.
- The EDGE database will also be used for tracking recruitment and visit data within the study. NHS staff accessing patient data in EDGE are guided by NHS and trust policy in relation to data protection, the principles of the Caldecott guardian and UK legislation.
- Data extracts may be taken from the EDGE database for the purpose of analysis by the immediate research team. Such data will be stored on University of Lincoln NHS secure network drives which can only be accessed by members of the research team who have secure access.
- The Chief Investigator will take a weekly data-back up of the local instance of the EDGE database which will be stored securely on a University or NHS secure network drive which is password protected.
- Should the EDGE database no longer be an accessible product the key study data, in relation to the developed TRACAT tool, will have been stored in an alternative format and analogue and digital copies saved.

### 8.7.3 Patient Confidentiality

All study staff, investigators and local collaborators will protect the study participant's rights to privacy and valid informed consent, and will adhere to the Data Protection Act, 1998. As detailed in section 5 participant information leaflets will describe the study, participant rights and how the information produced by the study will be preserved and shared. Consent forms will be completed by participants and will cover data handling and sharing.

The EDGE database will be used for tracking recruitment in the study. NHS staff accessing patient data are guided by NHS and trust policy in relation to data protection, the principles of the Caldecott guardian and UK legislation.

All participant research data will be anonymised. Where it is deemed to be appropriate to use quotations obtained through interviews or questionnaires, the identity of the author and participant will be protected. For research professional quotes, the role will be removed from any texts, if this would potentially identify the individual participant, and they will in place be described as 'research professional'. Research professionals will not be affected

in their relationship with their employer if they opt to participate in the study or not. Participation in the study is entirely voluntary.

The anonymity of panel participants is an important part of the Delphi process to ensure that each panel member has the opportunity to contribute insights freely. Participants will remain anonymous to the other members of the group. Answers will be fed back to the group but the analysis will not reveal the identity of the contributors. Direct quotations may be reported in Delphi rounds or as part of the research analysis but these will not be traceable to the author.

Audio recordings will be made of interviews subject to participant consent and will remain confidential.

The source documents and individual participant personal information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited with the exception of the immediate study team and inspection by relevant regulatory authorities.

If information is disclosed during the study that could pose a risk of harm to the participant or others, the Chief Investigator will discuss this with the study team and where appropriate report accordingly.

Data generated as a result of this study will be available for inspection on request by the NIHR, the United Lincolnshire Hospitals Trust, the University of Lincoln representatives, the REC, local R&D Departments and the regulatory authorities.

## **8.8 Indemnity**

University of Lincoln indemnity arrangements will apply to meet the potential legal liability of the sponsor for harm to participants arising from both the design and management of the research. NHS indemnity will apply to meet the potential legal liability of investigators/collaborators arising from negligent harm to participants in the conduct of the research at NHS sites.

There are no special compensation arrangements in place in the unlikely event of harm to research participants where no legal liability arises (i.e. non-negligent harm). This is explicit within the participant information sheets.

If any patient participant wishes to make a complaint about any aspect of the study they will be provided with information regarding the Trust Complaints Procedure by the responsible investigator. Full details of the Patient Advice and Liaison Service (PALS) is detailed in the participant information sheets. Research professional participants who may wish to complain formally can contact the Chair Professor for the School of Health and Social Care Research Ethics Committee at the University of Lincoln, whose details are provided in the participant information sheets.

The Chief Investigator responsible for all data collection, recruitment, study interventions and analysis will conduct the research in accordance with Trust policy for Research Governance and the EU Directives (Good Clinical Practice). The study will be subject to monitoring in accordance with Trust policy.

The Chief Investigator responsible for the study is employed by the United Lincolnshire NHS Hospitals Trust and will ensure that all guidelines, policies and procedures are followed as required by the Trust and study funder.

## 8.9 Amendments

If a substantial amendment is required the Chief Investigator will submit a notice of amendment in writing to the REC for consideration along with relevant supporting documents.

The HRA and participating sites will be notified about the amendment and submitted in IRAS.

The protocol is version controlled and the amendments will be highlighted in the protocol version amendment history section 13.3.

The Chief Investigator will make the decision as to whether the amendment is substantial or non-substantial.

## 8.10 Access to the final study dataset

The following will have access to the final dataset;

- The Chief Investigator
- The Co-Investigators & Supervisors
- The University examiners conducting the viva for the study.
- The NIHR or relevant regulatory authorities.

## 8.11 Intellectual Property Rights (IPR) and Copyright Management

- Where Intellectual Property Rights and Copyright are developed as a product of this research appropriate arrangements will be made between EDGE Clinical Research Management, the University of Lincoln, the United Lincolnshire Hospitals Trust and the Chief Investigator and any other relevant parties.
- The EDGE Clinical Research Management System, a cloud-based software application created by the University of Southampton, will be used to host the TRACAT tool (Trial Rating and Complexity Assessment Tool). Whilst the EDGE data base and the performance related data generated are managed as part of their existing structures and agreements within the NHS, the TRACAT model however will be the product of this doctorate and will be replicable in other data forms or databases. The data resulting from the thesis is the property of the Chief Investigator and the University of Lincoln.
- Data collected within EDGE as part of the trial will remain the responsibility of each local research site where this relates to their individual site performance data. The data stored under the lead site's instance of EDGE will remain the property and

responsibility of the CI, study team and university. The metadata collected in the study will remain the responsibility of the Chief Investigator.

## 9 Dissemination & Authorship

### 9.1 Dissemination policy

The following principles apply to the dissemination of the results of this research study;

- On completion of the study, the data will be analysed and tabulated and a final study report published in the form of a doctoral thesis following academic and peer review.
- The data arising from the study will be owned jointly by the Chief Investigator, the University of Lincoln and United Lincolnshire Hospitals Trust.
- The University of Lincoln will be acknowledged within the publications, however the chief investigator and principal investigators will have review and publication rights of the data from the study.
- The results of this study will be presented in the form of abstracts, posters and oral presentations at conferences and seminars and submitted for publication in peer-reviewed journals.
- The full study report will be available on the study website and via the University of Lincoln repository following completion and publication. The proposed submission date of the thesis is highlighted in the study timeline in figure 2. The thesis will be available via open data access.
- The progress and outcome of the study will be available on the study website; [www.efacct.com](http://www.efacct.com)
- A copy of the lay protocol will also be made available on the study website along with all participant documentation such as example consent forms, participant information sheets and questionnaires.
- Feedback will be provided to participants and staff involved in the study. Participants may also request a copy of the final study report from the Chief Investigator following completion and publication of the doctoral thesis.
- Anonymised summary data will be made publicly available on the study's website following completion of the doctoral thesis and subject to any editorial or journal data embargos.
- Before any dissemination of findings all data will be anonymised. The anonymity of participants will be maintained in any reports and data kept secure and confidential. No sensitive or participant identifying data will be shared. Due to the anonymous nature of the data, participant level data such as individual interview transcripts will not be made public.

- Arrangements will be made with the NIHR to present the study's findings and discuss impact of potential implementation of initiatives.
- Data which is specific to the NIHR performance will only be shared in agreement with CRN networks, trusts and research teams. Should the Network and NHS agree to individual trust performance data reporting within CRN networks the format of this will be agreed with relevant parties in advance of circulation.
- The TRACAT tool rating system will be discussed with the NIHR for potential adoption into practice. The developed tool will be trialled and evaluated through the platform and feedback obtained from end users.

## 9.2 Authorship eligibility guidelines and any unintended use of professional writers.

The chief and principal investigators and lead statistician will be granted authorship.

## 10 REFERENCES

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## 11. APPENDICIES

### 11.1 Appendix 1 – Screening Log

A screening log will be added to EDGE for the Chief Investigator and sites to complete with drop down menus to select relevant options e.g. participant type (cancer clinical trial patient or clinical research professional).

Screening Log (owner: United Lincolnshire Hospitals NHS Trust)		
✓	Site Code	RWD
✓	Participant ID	EFCLN001
✓	Participant Type	Clinical Research Professional
✓	Date Screened	08/05/2017
✓	Eligible	Yes
✓	PIS Given	Yes
✓	PIS Type Issued	Delphi Study
✓	Contact Form Issued (Interview Study)	N/A
✓	Contact Form Completed at Site (Interview Study)	N/A
✓	Screening Comments	Email invite issued with Delphi PIS and link to online survey

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## 12.0 - Appendix 2 – Schedule of Procedures

<b>Procedures</b>	<b>Total Number</b>	<b>Average time in minutes per procedure</b>	<b>Conducted by and where</b>
Delphi demographic and consent form completion by Delphi participant (both arms).	1	20	Delphi participants complete consent form online or complete printed form and return to Chief Investigator.
Completion of Delphi questionnaire by participant.	3-4	30	Self-administered Delphi questionnaire completed remotely online by participant. Completed at participant's office location (clinical professionals) or from personal computer.
Completion of structured questionnaire by phase 2/3 study participant.	1	30	Self-administered structured questionnaire completed remotely online by participant. Completed at participants office location (clinical professionals) or from personal computer.
Telephone call to prospective patient participant to discuss research, answer questions, and arrange first interview (where written informed consent will be obtained).	1	20	Chief Investigator, Helene Markham-Jones from NHS/University premises.
Semi-structured interview consent form completion by phase 2/3 study participant.	1	20	Semi-structured interview consent by study participant (phase 2/3) completed at agreed location convenient to the participant prior to the commencement of the interview.
One-to-one semi-structured interview with participant.	2	60	Chief Investigator, Helene Markham-Jones from NHS premises.
Site meeting to review TRACAT tool development and analysis of follow-up and recruitment data for participating sites.	4	60	Chief Investigator, Helene Markham-Jones meeting with participating site representative conducted at NHS site or via remote meeting.

### 13.0 Appendix 3 – Amendment History

Protocol amendments will be submitted to the Sponsor for approval prior to submission to the REC committee.

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
1	2.0	01/06/2017	H M Jones (CI)	<p>Updates made to;</p> <p>p3- sponsor contact details</p> <p>p7 –study management and protocol contributors</p> <p>p16 – additional text ‘research evaluation’ under reflexive journal</p> <p>p26,32,33 – changed ‘PIC’ to ‘recruiting’</p> <p>p30 –additional text and rewording ‘in agreement with study sponsors and Chief Investigators’</p> <p>p36 – time to consider study updated to minimum 48 hours</p> <p>p42 – additional text ‘encompassing lead site’</p> <p>p43 – weekly back-up location added</p> <p>p46 – wording amended from study to ‘lay’ protocol</p> <p>‘Research professional’ replaces ‘clinical research professional’ throughout protocol.</p>
2	3.0	04/09/2017	H M Jones (CI)	<p>p7 &amp; p33 – reference to no payments updated to state reimbursement will be provided in cases where special journey made by participant.</p> <p>p37 – in section 7.5 reference to data ‘cannot be erased’ and changed to confirm data will still be used.</p>