Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)
SWEET

1. Is your project research?

(●) Yes ( ) No

2. Select one category from the list below:

( ) Ionising Radiation for combined review of clinical trial of an investigational medicinal product

( ) Ionising Radiation and Devices form for combined review of combined trial of an investigational medicinal product and an investigational medical device

( ) Clinical investigation or other study of a medical device

(●) Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice

( ) Basic science study involving procedures with human participants

( ) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology

( ) Study involving qualitative methods only

( ) Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)

( ) Study limited to working with data (specific project only)

( ) Research tissue bank

( ) Research database

If your work does not fit any of these categories, select the option below:

( ) Other study

2a. Will the study involve the use of any medical device without a UKCA/CE UKNI/CE Mark, or a UKCA/CE UKNI/CE marked device which has been modified or will be used outside its intended purposes?

( ) Yes (●) No

2b. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation? ( ) Yes (●) No

b) Will you be taking new human tissue samples (or other human biological samples)? ( ) Yes (●) No

c) Will you be using existing human tissue samples (or other human biological samples)? ○ Yes ◉ No

3. In which countries of the UK will the research sites be located? *(Tick all that apply)*

- ☑ England
- ☑ Scotland
- ☑ Wales
- ☑ Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- ◉ England
- ○ Scotland
- ○ Wales
- ○ Northern Ireland
- ○ This study does not involve the NHS

4. Which applications do you require?

- ☑ IRAS Form
- ☐ Confidentiality Advisory Group (CAG)
- ☐ HM Prison and Probation Service (HMPPS)

5. Will any research sites in this study be NHS organisations?

◉ Yes ○ No

5a. Are all the research costs and infrastructure costs (funding for the support and facilities needed to carry out the research e.g. NHS support costs) for this study provided by a NIHR Biomedical Research Centre (BRC), NIHR Applied Research Collaboration (ARC), NIHR Patient Safety Translational Research Centre (PSTRC), or an NIHR Medtech and In Vitro Diagnostic Co-operative (MIC) in all study sites?

Please see information button for further details.

○ Yes ◉ No

Please see information button for further details.

5b. Do you wish to make an application for the study to be considered for NIHR Clinical Research Network (CRN) Support and inclusion in the NIHR Clinical Research Network Portfolio?

Please see information button for further details.

◉ Yes ○ No

The NIHR Clinical Research Network (CRN) provides researchers with the practical support they need to make clinical studies happen in the NHS in England e.g. by providing access to the people and facilities needed to carry out research "on the ground".

If you select yes to this question, information from your IRAS submission will automatically be shared with the NIHR CRN. ***Submission of a Portfolio Application Form (PAF) is no longer required.***

6. Do you plan to include any participants who are children?

○ Yes ◉ No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

○ Yes ◉ No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

○ Yes ◉ No

9. Is the study or any part of it being undertaken as an educational project?

○ Yes ◉ No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

○ Yes ◉ No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

○ Yes ◉ No

Integrated Research Application System
Application Form for Other clinical trial or investigation

IRAS Form (project information)

Please refer to the E-Submission and Checklist tabs for instructions on submitting this application.

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting Help.

Please define any terms or acronyms that might not be familar to lay reviewers of the application.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
SWEET

Please complete these details after you have booked the REC application for review.

REC Name:
South Central - Hampshire B Research Ethics Committee

REC Reference Number:
23/SC/0254

Submission date:
30/06/2023

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

Supporting Women with adhErence to hormonE Therapy following breast cancer (SWEET)

A3-1. Chief Investigator:

	Title	Forename/Initials	Surname
	Professor	Linda	Sharp
Post	Professor of Cancer Epidemiology/Honorary Research Contract (NuTH)		
Qualifications	PhD, Cancer Epidemiology, University of Aberdeen MSc, Medical Statistics, London School of Hygiene and Tropical Medicine BSc (HONs), Mathematical Sciences, Strathclyde University		
ORCID ID			
Employer	Newcastle Univeristy		
Work Address	Level 5, Sir James Spence Institute Royal Victoria Infirmary Queen Victoria Road		
Post Code	NE1 4LP		
Work E-mail	linda.sharp@ncl.ac.uk		
* Personal E-mail	linda.sharp@ncl.ac.uk		

Work Telephone	00000000000
* Personal Telephone/Mobile	01912086275
Fax	00000000000

** This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*
A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?
This contact will receive copies of all correspondence from REC and HRA/R&D reviewers that is sent to the CI.

	Title	Forename/Initials	Surname
	Ms	Laura	Frisby
Address	The Newcastle upon Tyne Hospitals NHS Foundation Trust		
	Regent Point, Regent Farm Road, Gosforth		
	Newcastle		
Post Code	NE3 3HD		
E-mail	tnu-tr.sponsormanagement@nhs.net		
Telephone	0191 2825959		
Fax			

A5-1. Research reference numbers. *Please give any relevant references for your study:*

Applicant's/organisation's own reference number, e.g. R & D (if available):	
Sponsor's/protocol number:	1.0
Protocol Version:	1.0
Protocol Date:	28/06/2023
Funder's reference number (enter the reference number or state not applicable):	NIHR200098
Project website:	

Registry reference number(s):
The UK Policy Framework for Health and Social Care Research sets out the principle of making information about research publicly available. Furthermore: Article 19 of the World Medical Association Declaration of Helsinki adopted in 2008 states that "every clinical trial must be registered on a publicly accessible database before recruitment of the first subject"; and the International Committee of Medical Journal Editors (ICMJE) will consider a clinical trial for publication only if it has been registered in an appropriate registry. Please see guidance for more information.

International Standard Randomised Controlled Trial Number (ISRCTN):
ClinicalTrials.gov Identifier (NCT number):

Additional reference number(s):

Ref.Number Description	Reference Number

A5-2. Is this application linked to a previous study or another current application?

(●) Yes ( ) No

Please give brief details and reference numbers.
This application is linked to IRAS293238 (SWEET), which is a qualitative study exploring pre-user testing of the digital component of the prototype intervention (web app), and to explore target audience views and experiences of using the

digital component in real life context. It is also linked to IRAS 307011, the follow on feasibility study. This application is linked the main Randomised controlled trial under the same Sponsor (NuTH) and NIHR funding programme (Ref: NIHR200098)

2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. *Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. Where the research is reviewed by a REC within the UK Health Departments' Research Ethics Service, this summary will be published on the Health Research Authority (HRA) website following the ethical review. Please refer to the question specific guidance for this question.*

In 2016, 11,563 women died from breast cancer in the UK. Most would have been prescribed hormone therapy (HT); sometimes known as endocrine therapy, which blocks the effect of oestrogen on breast cancer cells. HT is prescribed as a daily tablet, usually for at least five years and often up to 10 years. When women stop taking HT prematurely, or don't take it as prescribed (known as "poor adherence"), they have up to a three times higher chance of the cancer returning and dying from cancer. At least 20% of women have poor adherence after two years and around 50% by five years.
Our previous research has identified reasons for poor adherence, including: feeling negative or concerned about HT; not fully understanding its importance; side-effects; feeling unsupported; and forgetfulness. SWEET is an NIHR funded a research programme, which supported by a Patient Advisory Group and Clinical Reference Group, will develop and test a support package to support women take ET as recommended. SWEET will be delivered over 6 workstreams.

This application refers to workstream 3, the randomised controlled trial. It will involve 1460 women, treated with adjuvant endocrine therapy. Women will be randomised to received either:
1. HT&Me support package: Initial and follow up appointment with a trained SWEET nurse, to discuss concerns and beliefs about endocrine therapy, access to the HT&Me web app with information, tips & tools to support adherence, and strategies for managing side effects. Regular motivational messages to encourage use of web-app and continue on AET.
2. Usual care (as per their site practices)

The study will test whether the HT&Me support package can improve endocrine therapy adherence, and cancer specific health related quality of life.

A6-2. Summary of main issues. *Please summarise the main ethical, legal, or management issues arising from your study and say how you have addressed them.*

Not all studies raise significant issues. Some studies may have straightforward ethical or other issues that can be identified and managed routinely. Others may present significant issues requiring further consideration by a REC, HRA, or other review body (as appropriate to the issue). Studies that present a minimal risk to participants may raise complex organisational or legal issues. You should try to consider all the types of issues that the different reviewers may need to consider.

Confidentiality: Trial staff will ensure that participants' anonymity is maintained. Participant identifiable information will be stored securely on the electronic database and when in paper form, will be stored separately from CRFs using only the individual's participant ID number. All documents will be stored securely and will only be accessed by trial staff and authorised personnel. The study will comply with relevant UK data protection legislation, which requires data to be pseudo-anonymised as soon as it is practical to do so.

Interview data and recordings of appointments will be recorded using audio devices or using Microsoft Teams. Recordings will be downloaded as soon as possible to encrypted university laptops and subsequently to the secure study area on the university servers, and then deleted from their original source. Any data that are transferred out of the secure environment (for example audio
files of interviews for transcription) will adhere to University of Warwick SOPs. All third party vendors will be subjected to an approved supplier review processes

3. PURPOSE AND DESIGN OF THE RESEARCH

A7. Select the appropriate methodology description for this research. *Please tick all that apply*:

- [ ] Case series/ case note review
- [ ] Case control
- [ ] Cohort observation
- [ ] Controlled trial without randomisation
- [ ] Cross-sectional study
- [ ] Database analysis
- [ ] Epidemiology
- [x] Feasibility/ pilot study
- [ ] Laboratory study
- [ ] Metanalysis
- [x] Qualitative research
- [x] Questionnaire, interview or observation study
- [x] Randomised controlled trial
- [ ] Other (please specify)

A10. What is the principal research question/objective? *Please put this in language comprehensible to a lay person.*

To determine the clinical effectiveness of the trial intervention in reducing poor adherence to AET and improving cancer specific HRQoL.

A11. What are the secondary research questions/objectives if applicable? *Please put this in language comprehensible to a lay person.*

To compare between arms:
• AET-specific HRQo
• Cost-effectiveness
(Additional outcomes)
• Extent of adherence
• Suboptimal implementation
• Non-persistence: >180 days gap in AET prescriptions; self-report
• Satisfaction with decision of non-adherence

A12. What is the scientific justification for the research? *Please put this in language comprehensible to a lay person.*

Breast cancer is the most common cancer in women in the UK. Although survival rates are high, in 2016, 11,600 women died from the disease. Most women with breast cancer (~80%) have estrogen receptor (ER)-positive disease. These women are usually recommended to take adjuvant endocrine therapy (AET - also known as hormone therapy) in the form of a daily tablet following surgery and/or radiotherapy or chemotherapy. AET significantly reduces the risks of recurrence, death from breast cancer, and (hence) death from any cause when taken for five years. Extending therapy beyond five years further reduces recurrences. In light of this, the recently-published NICE breast cancer diagnosis and management guidelines recommend extending AET use beyond five years.
Despite these recognised benefits, there is good evidence that many women do not take AET as recommended. Suboptimal implementation (taking less than the recommended dose of a medication) and early discontinuation (stopping taking the medication before the end of the recommended treatment period) are forms of medication nonadherence. Twenty to 40% percent of women display suboptimal implementation of AET, which is generally defined in this context as taking <80% of the recommended dose. In terms of early discontinuation, around 20% of women stop taking AET completely by two years and up to 50% do so by five years. In addition, our data indicate that women who display suboptimal AET implementation in the first year of therapy are more likely to discontinue therapy in the future.

To date no effective intervention to improve AET adherence exists. This full-programme of research will address this gap by testing an evidence-based, theoretically-informed, intervention to support women with AET adherence.

A13. Please summarise your design and methodology. *It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.*

SWEET is a multi-centre, unblinded, pragmatic randomised controlled trial (RCT) of HT&Me intervention + usual care Vs usual care alone. The aim is to determine the clinical effectiveness of the trial intervention in reducing poor adherence to AET and improving cancer specific HRQoL.

SWEET plans to recruit 1460 women, across up to 80 sites. Patients who are confirmed to be eligible will be invited to take part in the study and if, following review of the patient information sheet, they decide to participate, written, or remote verbal informed consent will be obtained. The target population will be women with invasive ER+ve breast cancer, stages 1 – 3 treated with curative intent, who have been prescribed adjuvant endocrine therapy (AET) within the past 3 months.

Baseline: Prior to randomisation, participants will be issued with a baseline questionnaire and health resource use questionnaire, as well as providing clinical information. Personal information (name, contact details and NHS number) will be collected for the purpose of creating HT&Me accounts where required, and for data linkage.

Particpants will be randomised on a 1:1 basis to recieve either;
HT&Me intervention, which includes:
1. Initial consultation with a SWEET nurse/practitioner (either at site, or remotely via Breast Cancer Now) to introduce the HT&Me intervention, discuss the patient's beliefs and concerns about AET, and experiences of AET.
2. Access to the HT&Me web-app which contains a short animation, information, tips & tools to support adherence including optional daily reminders to take AET or order repeat prescriptions, strategies for managing side-effects, and signposting to further support
3.Follow up consultation with a SWEET nurse/ practitioner (either at site, or remotely via Breast Cancer Now) to discuss any new concerns and review use of the HT&Me web app. Participants will also be asked to complete a feedback questionnaire on their experience of the HT&Me support pacakage
4. Regular motivational messages delivered by email or text, promoting adherence and encouraging use of the web-app.

Usual care: Participants randomised to usual care alone will continue to access AET as per institutional guidelines and will continue to be followed up (either at site or through their GP) as per institutional guidelines and follow up processes.

Follow up: Patients will be followed up by questionnaire at 6months, 12months and 18months for adherence and HRQoL. Sites will be responsible for distribution of questionnaires to participants. Participants may be followed up for up to 15years longer term data linkage (subject to additional funding).

Process evaluation: A parallel process evaluation will be undertaken, using a mixture of qualitative and quantitative methods. The aims of the process evaluation are to:
• Explore fidelity of the intervention as delivered, received and enacted
• Assess whether the intervention worked as hypothesized by the logic model
• To identify any moderating contextual factors and/or unintended consequences of the intervention.
Semi-structured telephone interviews will be conducted throughout the trial with participants (Arm A- HT&Me intervention, n=25-30; Arm B (control), n=10-15) to discuss their experience of the study. Interviews with SWEET study practitioners (n=20-25) will also take place. These interviews will explore:
• Views and experiences of the trial, intervention and Behaviour Change Techniques (BCTs) (as appropriate)
• Intervention fidelity and quality
• Potential contamination
• Contextual factors

A14-1. In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?

☑ Design of the research

- [x] Management of the research
- [ ] Undertaking the research
- [ ] Analysis of results
- [x] Dissemination of findings
- [ ] None of the above

Give details of involvement, or if none please justify the absence of involvement.
A Patient Advisory Group (PAG) has been established. Two user co-applicants co-chair the PAG group and also sit on the study Programme Management Committee. These user co-applicants have been actively involved from the start by commenting on iterations of the proposal. PAG members have assisted with co-designing the digital component, and have helped develop patient facing materials for the study. PAG members who wish involvement in analysis of study data will be given relevant training by team members.

4. RISKS AND ETHICAL ISSUES

RESEARCH PARTICIPANTS

A15. What is the sample group or cohort to be studied in this research?

Select all that apply:

- [ ] Blood
- [x] Cancer
- [ ] Cardiovascular
- [ ] Congenital Disorders
- [ ] Dementias and Neurodegenerative Diseases
- [ ] Diabetes
- [ ] Ear
- [ ] Eye
- [ ] Generic Health Relevance
- [ ] Infection
- [ ] Inflammatory and Immune System
- [ ] Injuries and Accidents
- [ ] Mental Health
- [ ] Metabolic and Endocrine
- [ ] Musculoskeletal
- [ ] Neurological
- [ ] Oral and Gastrointestinal
- [ ] Paediatrics
- [ ] Renal and Urogenital
- [ ] Reproductive Health and Childbirth
- [ ] Respiratory
- [ ] Skin
- [ ] Stroke

Gender: Male and female participants

Lower age limit: 18	Years
Upper age limit:	No upper age limit

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

1. Aged 18+
2. Female
3. Diagnosis of ER positive invasive breast cancer, stages 1-3 and treated with curative intent;
4. Completed surgery for breast cancer;
5. Within 3 months of first oral AET prescription (tamoxifen or aromatase inhibitor) post breast cancer completion surgery;

6. Completed chemotherapy (if applicable)
7. Able to access the internet
8. Has an email address
9. Are willing to use a support package with a web-based component

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

1. Male
2. Evidence of metastatic disease i.e. stage 4 disease (M1 regardless of T and N status)
3. Have cognitive impairment sufficient to preclude participation, as judged by the clinical team;
4. Had previous AET (for another breast cancer);
5. Are unable to read and understand English;

RESEARCH PROCEDURES, RISKS AND BENEFITS

A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. *These include seeking consent, interviews, non-clinical observations and use of questionnaires.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days)
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Discussion of SWEET study and provide Patient Information Sheet	1	0	20	Potential participants will be told about the study by a delegated member of staff, either in person at a clinic visit or via letter, and provided with a Patient Information Leaflet
Questions followed by written/ remote verbal informed consent	1	0	10	The Principal Investigator or delegated individual at each hospital sites
Baseline questionnaires	1	0	30	Following recruitment women will be asked to complete the baseline questionnaire
Collection of clinical information	1	0	10	Relevant medical details for each woman will be abstracted from medical records by the Research Nurse or a delegated member of the hospital team.
initial consultation (Arm A- HT&me intervention)	1	0	30	Recruited women will have initial consultation with the SWEET study nurse from their hospital site, or through Breast Cancer Now. The appointment may take place face-to-face or by

				telephone/video-conferencing.
Email/Text message reminder(s) (Arm A- HT&me intervention)	14	0	2	As part of the intervention, women will receive a routine email/text messages reminding them they can log in to the web-app.
Follow-up consultation with SWEET study nurse after approximately 12 weeks (Arm A- HT&me intervention)	1	0	30	Follow up consultation with the SWEET study nurse from their hospital site, or through Breast Cancer Now. The appointment may take place face-to-face or by telephone/video-conferencing.
Feedback question (Via SMS) on HT&Me support package (Arm A- HT&me intervention)	2	0	5	Women on Arm A will be asked to feedback on the HT&Me appointment via SMS (1 question- 1-5 scale)
Follow up questionnaires at 6months, 12months and 18months	3	0	30	Women will be asked to complete a follow-up questionnaire.
Interviews with a sub-set of women who have consented to the process evaluation interviews	1	0	60	A central researcher will interview a sub-set of women about their experience of the study
Informed consent- health care professionals process evaluation interviews	1	0	10	If a health professional is happy to take part in the study, an appropriately trained delegated member of staff will take consent for the interview
Health care professionals process evaluation interviews (n=25)	1	0	60	Central member of research team will conduct interview with health professional.

A19. Give details of any clinical intervention(s) or procedure(s) to be received by participants as part of the research protocol. *These include uses of medicinal products or devices, other medical treatments or assessments, mental health interventions, imaging investigations and taking samples of human biological material. Include procedures which might be received as routine clinical care outside of the research.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days).
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4

A20. Will you withhold an intervention or procedure, which would normally be considered a part of routine care?

○ Yes ◉ No

A21. How long do you expect each participant to be in the study in total?

18months for main study follow up. Up to 15 years for longer term follow up subject to additional funding.

A22. What are the potential risks and burdens for research participants and how will you minimise them?

For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.

Participating in process evaluation research and completing questionnaires may have emotional consequences for the participant and may involve them considering and discussing potentially upsetting issues related to their own experiences.
Interested women will have full study details and be given time to consider their participation prior to agreeing/consenting to take part, and participants will be able to choose how they are interviewed - face-to-face or remotely. Women will be informed that they do not have to answer any questions they do not feel comfortable answering and they can take a break during consultations or interviews if they wish.
Women will be informed that they can withdraw from the study at any point.

Should any element of the study raises any questions or concerns for participants, appropriate signposting is in place.

A23. Will interviews/ questionnaires or group discussions include topics that might be sensitive, embarrassing or upsetting, or is it possible that criminal or other disclosures requiring action could occur during the study?

(●) Yes ( ) No

If Yes, please give details of procedures in place to deal with these issues:

Participating in process evaluation research and completing questionnaires may have emotional consequences for the participant and may involve them considering and discussing potentially upsetting issues related to their own experiences.
Interested women will have full study details and be given time to consider their participation prior to agreeing/consenting to take part, and participants will be able to choose how they are interviewed - face-to-face or remotely. Women will be informed that they do not have to answer any questions they do not feel comfortable answering and they can take a break during consultations or interviews if they wish.
Women will be informed that they can withdraw from the study at any point.

Should any element of the study raises any questions or concerns for participants, appropriate signposting is in place.

A24. What is the potential for benefit to research participants?

We do not know whether the HT&Me support package will be effective in helping women to continue taking their hormone therapy as prescribed or in improving quality-of-life, however women in Group A, who receive the intervention will receive more information and support whilst taking their hormone therapy and they may find this helpful.
Women may not directly benefit from taking part in this research, but participation will help guide support for women with breast cancer taking hormone therapy in the future.

A25. What arrangements are being made for continued provision of the intervention for participants, if appropriate, once the research has finished? *May apply to any clinical intervention, including a drug, medical device, mental health intervention, complementary therapy, physiotherapy, dietary manipulation, lifestyle change, etc.*

Access to the HT&Me web app will continue to 18month follow up (for those participants on the intervention arm).

A26. What are the potential risks for the researchers themselves? *(if any)*

Very low risk other than a small chance that researchers to be alone with research participant, where researchers will be subject to lone working policy.

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used?*For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).*

Potentially eligible women will be identified at an appropriate MDT after their breast cancer surgery, or using hospital records. A member of hospital staff will review women's medical records to confirm eligibility. Members of the research team are considered as embedded within the clinical care team, it is expected that no one outside of the direct care team should have access to patient information prior to informed consent.

A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?

◉ Yes ○ No

Please give details below:
Potential participants will be identified by clinical teams involved in the participants care including research staff who are considered as embedded within the direct care team. Following identification of a potential participant, a suitably trained member of the research team at each site will be contacted to undertake eligibility checks in conjunction with the treating clinical team.

A27-3. Describe what measures will be taken to ensure there is no breach of any duty of confidentiality owed to patients, service users or any other person in the process of identifying potential participants.*Indicate what steps have been or will be taken to inform patients and service users of the potential use of their records for this purpose. Describe the arrangements to ensure that the wishes of patients and service users regarding access to their records are respected. Please consult the guidance notes on this topic.*

Potential participants will be identified by clinical teams involved in the participants care. All screening and identification will be undertaken by trained NHS research staff within the hospital facility at each site, using approved clinical systems and medical notes. All staff will abide by existing NHS and GDPR regulations

A27-4. Will researchers or individuals other than the direct care team have access to identifiable personal information of any potential participants?

◉ Yes ○ No

A27-5. Has prior consent been obtained or will it be obtained for access to identifiable personal information?

◉ Yes ○ No

If Yes, please give details below.
This is described in full detail in the patient information leaflet and consent is specifically requested for this on the consent form. The central research team require access to PID for the purpose of creating accounts on the HT&Me website, contacting participants for interviews (where they consent to this), and for longer term data linkage.

A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?

○ Yes ◉ No

A29. How and by whom will potential participants first be approached?

Potential participants who meet the eligibility criteria will be approached about the study via their clinical team at participating sites. This will either be in person (during a clinic visit) or via letter posted out directly to them. A follow-up phone call may also be made by NHS staff to find out if the person has received and been able to consider the study information.

A30-1. Will you obtain informed consent from or on behalf of research participants?

◉ Yes ○ No

If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

Each potential participant will be given an information sheet explaining the rationale of the study, what their involvement will entail and what the potential benefits and risks of the study are.
The delegated member of staff will explain to participants what the study involves, ask if they have any questions and ensure that the participant has full comprehension of what is being asked of them before obtaining consent.
When in person, written consent will be recorded on a form in which the participant will be asked to initial each point to show agreement, and then sign their name and date at the bottom.
When receiving consent from participants over the phone or video-call, the researcher will read out a verbal consent form to the participant. The researcher will read out each point and ask the participant if they agree or not; if yes, the researcher will add their own initials at that point on the form. The researcher will then sign this form to declare that they have read out all of the points and that the participant has verbally consented to take part in the study. This process should be overseen by a witness who should countersign the consent form.

For both methods, the researcher will be able to offer an explanation of any points included in the consent form

If you are not obtaining consent, please explain why not.

Please enclose a copy of the information sheet(s) and consent form(s).

A30-2. Will you record informed consent (or advice from consultees) in writing?

(●) Yes ( ) No

A31. How long will you allow potential participants to decide whether or not to take part?

Patients will be given sufficient time from being provided with the participant information sheet to consider their involvement. A member of the study team will offer to follow-up a day later to confirm whether patient wishes to proceed or not. If a patient requires more time to consider taking part in the study then this will be taken into account and a further follow-up call will be made within the time-frame requested by the potential participant.
Patients will be made fully aware that their routine clinical care will not change regardless of their decision to join the study, and that they are under absolutely no pressure to take part. However, if a patient states they are happy to take part and don't need any additional time to consider their involvement, and the person taking consent is satisfied they have fully understood what is being asked of them, then consent can be obtained immediately

A32. Will you recruit any participants who are involved in current research or have recently been involved in any research prior to recruitment?

(●) Yes
( ) No
( ) Not Known

If Yes, please give details and justify their inclusion. If Not Known, what steps will you take to find out?

Patients randomised into SWEET can be enrolled into other studies as long as this has been agreed with the TMG and they do not affect the study outcomes. This will be done on a case-by-case basis, with a rolling log of trials permitted for co-enrolment kept by the trial management team

A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs?*(e.g. translation, use of interpreters)*

Unfortunately, we will not be able to accommodate patients that do not fully comprehend English. We aim to recruit an ethnically diverse sample, but women will be excluded if they are unable to read, understand and be interviewed in English. The reason for this is that the content of the digital component of the intervention is only available in English.

A33-2. What arrangements will you make to comply with the principles of the Welsh Language Act in the provision of information to participants in Wales?

We will liaise with the Welsh Cancer Research Network who will use their own standard procedures to comply with the Welsh Language Act. Translations will be made available, where required, for study documents to be translated into Welsh.

A34. What arrangements will you make to ensure participants receive any information that becomes available during the course of the research that may be relevant to their continued participation?

In the event of new information becoming available, investigators will contact patients and explain the new information. Patients will have the opportunity to withdraw from the study at any time; however, should they wish to continue, further consent will be obtained following the patient's review of an updated version of the patient information sheet, approved by the ethics committee where required.

A35. What steps would you take if a participant, who has given informed consent, loses capacity to consent during the study? *Tick one option only.*

- ○ The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.
- ◉ The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.
- ○ The participant would continue to be included in the study.
- ○ Not applicable – informed consent will not be sought from any participants in this research.
- ○ Not applicable – it is not practicable for the research team to monitor capacity and continued capacity will be assumed.

Further details:

If you plan to retain and make further use of identifiable data/tissue following loss of capacity, you should inform participants about this when seeking their consent initially.

CONFIDENTIALITY

In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.

Storage and use of personal data during the study

A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)?*(Tick as appropriate)*

- ☑ Access to medical records by those outside the direct healthcare team
- ☐ Access to social care records by those outside the direct social care team
- ☐ Electronic transfer by magnetic or optical media, email or computer networks
- ☑ Sharing of personal data with other organisations
- ☐ Export of personal data outside the EEA
- ☑ Use of personal addresses, postcodes, faxes, emails or telephone numbers
- ☐ Publication of direct quotations from respondents
- ☐ Publication of data that might allow identification of individuals
- ☑ Use of audio/visual recording devices

- [x] Storage of personal data on any of the following:
  - [x] Manual files (includes paper or film)
  - [x] NHS computers
  - [ ] Social Care Service computers
  - [ ] Home or other personal computers
  - [x] University computers
  - [ ] Private company computers
  - [ ] Laptop computers

Further details:
All information will be entered onto a secure online database, set up by the University of Warwick Clinical Trials Unit (WCTU), that only authorised personnel with have access to. Only authorised individuals that require access to PID hosted on the secure online database will have access to this section of the database.
The Trial Master File (TMF), and any paper Case Report Forms (CRFs) that may be received, will be kept in locked filing cabinets in a designated archive room at WCTU; only authorised personnel with have access to this room.
Electronic documents for the TMF are stored on on the network drive with restricted access.
Qualitative interviews will be recorded and transcribed - both the recording and the transcription will be fully anonymised.
All electronic devices will be password protected as per NHS and WCTU SOPs, and in accordance with the UK General Data Protection Regulation (UK GDPR)

A37. Please describe the physical security arrangements for storage of personal data during the study?

Personal data collected during the trial will be handled and stored in accordance with UK GDPR.
Disclosure of confidential information will only be considered if there is an issue which may jeopardise the safety of the participant or another person, according to WCTU SOPs and the UK regulatory framework.
The database will be developed by the Programming Team at WCTU and all specifications (i.e. database variables, validation checks) will be agreed between the programmer and the appropriate trial staff, including the trial statistician.
All essential documentation and trial records will be stored at WCTU in conformance with the applicable regulatory requirements and access to stored information (paper and electronic) will be restricted to authorised personnel. All paper data will be stored within a restricted access archive room at WCTU, electronic data will be stored on password protected computers at WCTU, in a restricted access building

A38. How will you ensure the confidentiality of personal data?*Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.*

All data will be pseudo-anonymised after the collection of the baseline demographic data for each participant. Confidentiality will be strictly maintained and names or addresses will not be disclosed to anyone other than the staff involved in running the trial. All electronic participant-identifiable information will be held on a secure, password protected database accessible only to essential personnel. Paper forms with participant-identifiable information will be held in secure, locked filing cabinets within a restricted area of WCTU. Direct access to source data/ documents will be available for trial-related monitoring or audit by UHCW or Warwick CTU for internal audit, regulatory authorities or ethics committees. The principal investigator will arrange for retention of trial records on site in accordance with GCP and local Trust's policies

A40. Who will have access to participants' personal data during the study? *Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.*

Participants will consent to providing the trial management team and those conducting the process evaluation interviews (where participants have consented to this) with personal information for the purpose of conducting interviews and collecting prescription data.
Requests for data sharing will be managed in accordance with University of Warwick/WCTU policy on data sharing.
The datasets generated during and/or analysed during the current study are/will be available upon request. The publication of a trial protocol, trial results and trial data will be in line with the NIHR standard terms and will follow WCTU SOPs

Storage and use of data after the end of the study

A41. Where will the data generated by the study be analysed and by whom?

Data analysis will be undertaken by the University of Warwick Clinical Trials Unit Statistical team, and Health economic team at the University of Oxford

A42. Who will have control of and act as the custodian for the data generated by the study?

	Title	Forename/Initials	Surname
	Prof	Linda	Sharp
Post	Professor of Cancer Epidemiology/Honorary Research Contract (NuTH)		
Qualifications			
Work Address	Level 5, Sir James Spence Institute		
	Royal Victoria Infirmary		
	Queen Victoria Road		
Post Code	NE1 4LP		
Work Email	Linda.Sharp@newcastle.ac.uk		
Work Telephone	01912086275		
Fax			

A43. How long will personal data be stored or accessed after the study has ended?

- ○ Less than 3 months
- ○ 3 – 6 months
- ○ 6 – 12 months
- ○ 12 months – 3 years
- ◉ Over 3 years

If longer than 12 months, please justify:

A44. For how long will you store research data generated by the study?

Years: 10
Months:

A45. Please give details of the long term arrangements for storage of research data after the study has ended. *Say where data will be stored, who will have access and the arrangements to ensure security.*

As per Warwick Clinical Trial Policy, once the trial has come to an end and the analysis has taken place, trial documentation will be held for approximately 10 years. Data will be stored securely by a third party and will be easy to retrieve, if required. All electronic patient identifiable information will be held on a secure, password protected database, which will be archived and will accessible only to essential personnel.

INCENTIVES AND PAYMENTS

A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?

○ Yes ◉ No

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

○ Yes ◉ No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

○ Yes ◉ No

NOTIFICATION OF OTHER PROFESSIONALS

A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?

◉ Yes ○ No

If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.

A49-2. Will you seek permission from the research participants to inform their GP or other health/ care professional?

◉ Yes ○ No

It should be made clear in the participant's information sheet if the GP/health professional will be informed.

PUBLICATION AND DISSEMINATION

A50. Will the research be registered on a public database?

The UK Policy Framework for Health and Social Care Research sets out the principle of making information about research publicly available. Furthermore: Article 19 of the World Medical Association Declaration of Helsinki adopted in 2008 states that "every clinical trial must be registered on a publicly accessible database before recruitment of the first subject"; and the International Committee of Medical Journal Editors (ICMJE) will consider a clinical trial for publication only if it has been registered in an appropriate registry. Please see guidance for more information.

◉ Yes ○ No

Please give details, or justify if not registering the research.
ISRCTN
UKCRN portfolio adoption
University of Warwick Website

Please ensure that you have entered registry reference number(s) in question A5-1.

A51. How do you intend to report and disseminate the results of the study? *Tick as appropriate:*

☑ Peer reviewed scientific journals
☐ Internal report
☑ Conference presentation

- [x] Publication on website
- [ ] Other publication
- [x] Submission to regulatory authorities
- [ ] Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- [ ] No plans to report or disseminate the results
- [ ] Other (please specify)

A52. If you will be using identifiable personal data, how will you ensure that anonymity will be maintained when publishing the results?

Identifiable information will not be used during the analysis of trial data. The data will be pseudoanonymised to facilitate the analysis of the data and no identifiable data will be published, only anonymised data

A53. How and when will you inform participants of the study results?

If there will be no arrangements in place to inform participants please justify this.
A patient friendly summary of the trial findings at the end of the study will be developed. Patients will be asked on the Informed Consent Form, whether they wish to receive a copy of this summary directly. Those patients who consent to this option will also receive a copy of the summary by post (or by email if requested). This will be sent out by local hospital sites

5. Scientific and Statistical Review

A54. How has the scientific quality of the research been assessed? *Tick as appropriate:*

- [x] Independent external review
- [ ] Review within a company
- [ ] Review within a multi−centre research group
- [ ] Review within the Chief Investigator's institution or host organisation
- [ ] Review within the research team
- [ ] Review by educational supervisor
- [ ] Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:
This research was subjected to two rounds of peer review via the funders(NIHR). This involved their funding panel and external reviewers. The review process involved stage 1 preliminary application stage and a stage 2 full application stage. Feedback was received and appropriate actions undertaken, which were accepted by the funder.

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.

A56. How have the statistical aspects of the research been reviewed? *Tick as appropriate:*

- [x] Review by independent statistician commissioned by funder or sponsor
- [ ] Other review by independent statistician
- [ ] Review by company statistician
- [ ] Review by a statistician within the Chief Investigator’s institution

☑ Review by a statistician within the research team or multi−centre group

☐ Review by educational supervisor

☐ Other review by individual with relevant statistical expertise

☐ No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

	Title	Forename/Initials	Surname
	Dr	Louise	Hiller
Department			
Institution	University of Warwick		
Work Address	Warwick Clinical Trials Unit		
	Warwick Medical School		
	University of Warwick, Coventry		
Post Code	CV4 7AL		
Telephone			
Fax			
Mobile			
E-mail	L.Hiller@warwick.ac.uk		

Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

•Adherence using Combined self-report (Medical Adherence Report Scale (MARS-5) and prescription encashment records (Medication Possession Ratio (MPR).
•Cancer-specific HRQoL: Functional Assessment of Cancer Therapy scale- General (FACT-G) [56]

A58. What are the secondary outcome measures?*(if any)*

• AET-specific HRQoL: Breast Cancer Trialist Prevention checklist (BCPT)
• Cost-effectiveness: Within trial cost per quality-adjusted life year (QALY); and EQ-5D
Additional outcomes:
• Extent of adherence: MPR (continuous); encashment records
• Suboptimal implementation: self-reported: MARS-5
• Non-persistence: >180 days gap in AET prescriptions; self-report
• Satisfaction with decision of non-adherence: SWD scale

A59. What is the sample size for the research? *How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.*

Total UK sample size: 1460
Total international sample size (including UK):
Total in European Economic Area:

Further details:

A60. How was the sample size decided upon? *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

A sample size of 730 patients in each arm (1460 in total), assuming 15% loss to follow-up in both arms and thus the final sample size with adherence data available will be 620 per arm. Based on reported data, we assume 10% of

women in the usual care alone arm will have poor adherence at 18 months. There is no evidence on how high adherence needs to be to maintain the full clinical benefit of AET for an individual woman, so the clinically important difference is unknown. However, reducing poor adherence across the patient population to around 5% is considered achievable. With a 5% two-sided significance level, 620 women in each arm will provide 90% power to detect as statistically significant a difference of 5% in poor adherence rates (e.g. consistent with a reduction from 10% to 5%). Based on our own data, we assume that the mean FACT-G score will be 83.9 in the usual care arm (sd=15.9). Allowing for up to 20% non-completion/lost-to-follow-up, randomising 730 women to each arm will provide at least 99% power to detect a difference of 4 points in FACT-G scores between arms; and at least 89% power to detect a difference of 3 points (α=0.05, two-sided test).

A61. Will participants be allocated to groups at random?

(●) Yes ( ) No

If yes, please give details of the intended method of randomisation:
Trial arms will be allocated randomly using a computer minimisation algorithm held centrally at the Warwick Clinical Trials Unit and stratified by the following variables
1. Age: <50, 50+
2. AET: Tamoxifen/AI
3. Treatment complexity
i. No chemotherapy, no anti-HER2, no abemaciclib
ii. Chemotherapy, no anti-HER2, abemaciclib
iii. Chemotherapy, anti-HER2, no abemaciclib
iv. No chemotherapy, no anti-HER2, abemaciclib

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

The MARS-5 consists of five general statements about suboptimal adherence behaviour answered on a 5-point scale where 1 represents always and 5 represents never. It has been widely used, including by ourselves, to measure self-reported AET adherence. Our own data (co-applicant Hughes, suggests that a MARS-5 score of ≤23 (out of a possible 25) represents poor adherence to AET.
For the primary endpoint of poor adherence, women will be classified as having poor adherence if they have a (MPR<80%) OR (a MPR ≥80% and a total MARS-5 score of ≤23). Women who have a MPR ≥80% AND a total MARS-5 score of >23 will be classified as having adequate adherence.
For the primary endpoint of cancer-specific HRQoL, the FACT-G questionnaire contains 27 statements; respondents indicate the extent to which each has applied over the past 7 days on a 5-point Likert-type scale ranging from 0 (not at all) to 4 (very much) and question responses are summed.
Poor adherence rates at 18 months will be assessed across randomised arms using logistic regression methods to adjust for stratification variables. For the cancer-specific HRQoL assessment at 18 months, each randomised arm's point estimate (and 95% confidence interval) will be reported, and linear regression methods used to assess across randomised arms, with adjust for stratification variables. Appropriate longitudinal analyses will also be utilised for assessment of AET adherence and HRQoL over time.

6. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. *Please include all grant co−applicants, protocol co−authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.*

	Title	Forename/Initials	Surname
	Professor	Eila	Watson
Post	Professor in Supportive Cancer Care		
Qualifications	PhD, BSc		
Employer	Oxford Brookes University		
Work Address			

Post Code	OX3 0BP
Telephone	
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Title	Forename/Initials	Surname
Miss	Alice	Longe

Post	Clinical Trial Manager
Qualifications	
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Post Code	CV4 7AL
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Title	Forename/Initials	Surname
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Post	Statistician
Qualifications	
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Title	Forename/Initials	Surname
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	Title	Forename/Initials	Surname
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Post	Collaborator		
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	Title	Forename/Initials	Surname
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Post	Collaborator		
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	Title	Forename/Initials	Surname
	Dr	Sarah-Jane	Stewart
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	Title	Forename/Initials	Surname
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Post			
Qualifications			
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Title	Forename/Initials	Surname
Ms	Sue	Thompson

Post Qualifications	
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Title	Forename/Initials	Surname
Prof	Mary	Wells

Post Qualifications	Co-investigator
Employer	Imperial College Healthcare NHS Trust
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Title	Forename/Initials	Surname
Prof	Rob	Horne

Post Qualifications	Co-investigator
Employer	University College London
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	Title	Forename/Initials	Surname
	Prof	Janet	Dunn
Post	Co-investigator		
Qualifications			
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	Title	Forename/Initials	Surname
	Dr	Adam	Todd
Post	Co-Investigator		
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	Title	Forename/Initials	Surname
	Dr	Catriona	Cahir
Post	Co-investigator		
Qualifications			
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	Title	Forename/Initials	Surname
	Dr	Lyndsay	Hughes
Post	Co-ivestigator		
Qualifications			
Employer	King’s College London		
Work Address			

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	Title	Forename/Initials	Surname
	Prof	Andrew	Wardley
Post	Co-investigator		
Qualifications			
Employer	Outreach Research and Innovation Group		
Work Address			

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	Title	Forename/Initials	Surname
	Dr	Brian	Nicholson
Post	Co-investigator		
Qualifications			
Employer	University of Oxford		
Work Address			

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Work Email

	Title	Forename/Initials	Surname
	Mr	Peter	Donnelly
Post	Co-investigator		
Qualifications			
Employer	South Devon Healthcare NHS Foundation Trust		
Work Address			

Post Code
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Fax
Mobile
Work Email

	Title	Forename/Initials	Surname
	Mr	Henry	Cain
Post	Co-investigator		
Qualifications			
Employer	Newcastle-upon-Tyne Hospitals NHS Foundation Trust		
Work Address			
Post Code			
Telephone			
Fax			
Mobile			
Work Email			

	Title	Forename/Initials	Surname
	Dr	Farah	Rehman
Post	Co-investigator		
Qualifications			
Employer	Imperial College Healthcare NHS Trust		
Work Address			
Post Code			
Telephone			
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Mobile			
Work Email			

	Title	Forename/Initials	Surname
	Ms	Jan	Rose
Post	PPI		
Qualifications			
Employer	National Cancer Research Institute & Independent Cancer Patients' Voice		
Work Address			
Post Code			
Telephone			
Fax			
Mobile			
Work Email			

	Title	Forename/Initials	Surname
	Ms	Lesley	Turner
Post	PPI		
Qualifications			
Employer	National Cancer Research Institute & Independent Cancer Patients' Voice		
Work Address			

Post Code
Telephone
Fax
Mobile
Work Email

A64. Details of research sponsor(s)

A64-1. Sponsor

Lead Sponsor

Status:
- (●) NHS or HSC care organisation
- ( ) Academic
- ( ) Pharmaceutical industry
- ( ) Medical device industry
- ( ) Local Authority
- ( ) Other social care provider (including voluntary sector or private organisation)
- ( ) Other

Commercial status: Non-Commercial

If Other, please specify:

Contact person

Name of organisation	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Given name	Laura
Family name	Frisby
Address	Regent Point, Regent Farm Road, Gosforth
Town/city	
Post code	NE3 3HD
Country	United Kingdom
Telephone	0191 2825959
Fax	
E-mail	tnu-tr.sponsormanagement@nhs.net

Legal representative for clinical investigation of medical device (studies involving Northern Ireland only)
Clinical Investigations of Medical Devices that take place in Northern Ireland must have a legal representative of the sponsor that is based in Northern Ireland or the EU

Contact person

Name of organisation
Given name
Family name
Address

Town/city
Post code
Country
Telephone
Fax
E-mail

A65. Has external funding for the research been secured?

Please tick at least one check box.

- [x] Funding secured from one or more funders
- [ ] External funding application to one or more funders in progress
- [ ] No application for external funding will be made

What type of research project is this?

- ○ Standalone project
- ◉ Project that is part of a programme grant
- ○ Project that is part of a Centre grant
- ○ Project that is part of a fellowship/ personal award/ research training award
- ○ Other

Other – please state:

Please give details of funding applications.

Organisation	National Institute for Health Research (NIHR)
Address	Central Commissioning Facility Grange House, 15 Church Street Twickenham
Post Code	TW1 3NL
Telephone	02088438000
Fax	
Mobile	
Email	

Funding Application Status: ◉ Secured ○ In progress

Amount: £2,538,229.00

Duration
Years: 9
Months:

If applicable, please specify the programme/ funding stream:

What is the funding stream/ programme for this research project?
NIHR Programme Grants for Applied Research reference number (NIHR200098)

A66. Has responsibility for any specific research activities or procedures been delegated to a subcontractor (other than a co-sponsor listed in A64-1) ? *Please give details of subcontractors if applicable.*

○ Yes ◉ No

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?

○ Yes ◉ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.

A68-1. Give details of the lead NHS R&D contact for this research:

Title	Forename/Initials	Surname
Miss	Laura	Frisby

Organisation	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Address	The Newcastle upon Tyne Hospitals NHS Foundation Trust
	Regent Point, Regent Farm Road, Gosforth
	Newcastle
Post Code	NE3 3HD
Work Email	tnu-tr.sponsormanagement@nhs.net
Telephone	0191 2825959
Fax	
Mobile	

Details can be obtained from the NHS R&D Forum website: http://www.rdforum.nhs.uk

A68-2. Select Local Clinical Research Network for NHS Organisation identified in A68-1:

North East and North Cumbria

For more information, please refer to the question specific guidance.

A69-1. How long do you expect the study to last in the UK?

Planned start date: 01/01/2024
Planned end date: 30/06/2027
Total duration:
Years: 3 Months: 5 Days: 30

A71-1. Is this study?

○ Single centre
◉ Multicentre

A71-2. Where will the research take place? *(Tick as appropriate)*

- [x] England
- [x] Scotland
- [x] Wales
- [x] Northern Ireland
- [ ] Other countries in European Economic Area

Total UK sites in study 80

Does this trial involve countries outside the EU?

○ Yes ◉ No

A72. Which organisations in the UK will host the research?*Please indicate the type of organisation by ticking the box and give approximate numbers if known:*

☐ NHS organisations in England	65
☐ NHS organisations in Wales	5
☐ NHS organisations in Scotland	5
☐ HSC organisations in Northern Ireland	5
☐ GP practices in England	
☐ GP practices in Wales	
☐ GP practices in Scotland	
☐ GP practices in Northern Ireland	
☐ Joint health and social care agencies (eg community mental health teams)	
☐ Local authorities	
☐ Phase 1 trial units	
☐ Prison establishments	
☐ Probation areas	
☐ Independent (private or voluntary sector) organisations	
☐ Educational establishments	
☐ Independent research units	
☐ Other (give details)	
Total UK sites in study:	80

A73-1. Will potential participants be identified through any organisations other than the research sites listed above?

○ Yes ◉ No

A74. What arrangements are in place for monitoring and auditing the conduct of the research?

The study will be monitored by Warwick Clinical Trials Unit (WCTU) Quality Assurance team, to ensure the study is being conducted as per protocol, adhering to Research Governance and GCP. The approach to, and extent of, monitoring will be specified in a trial monitoring plan determined by the risk assessment undertaken prior to the start of the study. A Trial Monitoring Plan will be developed and agreed by the Trial Management Group (TMG), based on the

trial risk assessment, including on-site monitoring if applicable. The sponsor will ensure investigator(s) and/ or institutions will permit trial-related monitoring and audits, providing direct access to source data/documents as required. Monitoring will be performed by exploring the trial data set or performing central monitoring procedures and/or site visits, as defined in the trial monitoring plan.

A75-1. What arrangements will be made to review interim safety and efficacy data from the trial? Will a formal data monitoring committee or equivalent body be convened?

An independent data monitoring committee (DMC), of clinicians and statisticians, will be established in line with the charter set by Warwick Clinical trials Unit and follow University of Warwick SOP's. The DMC will be independently chaired and will monitor interim safety and efficacy data. The DMC will feed back their findings to the Trial Steering Committee (TSC). The DMC will advise the TSC if there is evidence to suggest amending or terminating the trial, based on recruitment rates, allocation compliance, interim analysis results or data from other studies

If a formal DMC is to be convened, please forward details of the membership and standard operating procedures to the Research Ethics Committee when available. The REC should also be notified of DMC recommendations and receive summary reports of interim analyses.

A75-2. What are the criteria for electively stopping the trial or other research prematurely?

This is a non-CTIMP and as such we do not propose to electively stop the trial prematurely

A76. Insurance/ indemnity to meet potential legal liabilities

***Note:* in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland**

A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? *Please tick box(es) as applicable.*

Note: Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.

- [x] NHS indemnity scheme will apply (NHS sponsors only)
- [ ] Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

A76-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? *Please tick box(es) as applicable.*

Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.

- [x] NHS indemnity scheme will apply (protocol authors with NHS contracts only)
- [x] Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

A76-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?

Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.

- [x] NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)
- [ ] Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

Please enclose a copy of relevant documents.

A77. Has the sponsor(s) made arrangements for payment of compensation in the event of harm to the research participants where no legal liability arises?

- ○ Yes
- ◉ No

Please enclose a copy of relevant documents.

A78. Could the research lead to the development of a new product/process or the generation of intellectual property?

- ◉ Yes
- ○ No
- ○ Not sure

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. *For further information please refer to guidance.*

Investigator identifier	Research site		Investigator Name	
IN1	(●) NHS/HSC Site ( ) Non-NHS/HSC Site		Forename Middle name Family name Email	Mr Zacharioudakis
	Organisation name	WRIGHTINGTON, WIGAN AND LEIGH NHS FOUNDATION TRUST	Qualification (MD...)	Consultant breast surgeon
	Address	ROYAL ALBERT EDWARD INFIRMARY WIGAN LANE WIGAN	Country	United Kingdom
	Post Code	WN1 2NN		
	Country	ENGLAND		
IN2	(●) NHS/HSC Site ( ) Non-NHS/HSC Site		Forename Middle name Family name Email	Abigail Evans
	Organisation name	UNIVERSITY HOSPITALS DORSET NHS FOUNDATION TRUST	Qualification (MD...)	Consultant breast surgeon
	Address	MANAGEMENT OFFICES POOLE HOSPITAL LONGFLEET ROAD POOLE	Country	United Kingdom
	Post Code	BH15 2JB		
	Country	ENGLAND		
IN3	(●) NHS/HSC Site ( ) Non-NHS/HSC Site		Forename Middle name Family name Email	
	Organisation name	UNIVERSITY HOSPITALS DORSET NHS FOUNDATION TRUST	Qualification (MD...)	
	Address	MANAGEMENT OFFICES POOLE HOSPITAL LONGFLEET ROAD POOLE	Country	
	Post Code	BH15 2JB		

	Country	ENGLAND		

IN4

◉ NHS/HSC Site
○ Non-NHS/HSC Site

		Forename	Karen
		Middle name	
		Family name	De Souza
		Email	
Organisation name	WHITTINGTON HEALTH NHS TRUST	Qualification (MD...)	Consultant oncologist
Address	THE WHITTINGTON HOSPITAL MAGDALA AVENUE LONDON	Country	United Kingdom
Post Code	N19 5NF		
Country	ENGLAND		

IN5

◉ NHS/HSC Site
○ Non-NHS/HSC Site

		Forename	Lee
		Middle name	
		Family name	Min
		Email	
Organisation name	WEST HERTFORDSHIRE TEACHING HOSPITALS NHS TRUST	Qualification (MD...)	Consultant surgeon
Address	TRUST OFFICES WATFORD GENERAL HOSPITAL VICARAGE ROAD WATFORD	Country	United Kingdom
Post Code	WD18 0HB		
Country	ENGLAND		

IN6

◉ NHS/HSC Site
○ Non-NHS/HSC Site

		Forename	Claire
		Middle name	
		Family name	Murphy
		Email	
Organisation name	AIREDALE NHS FOUNDATION TRUST	Qualification (MD...)	Consultant surgeon
Address	AIREDALE GENERAL HOSPITAL SKIPTON ROAD STEETON KEIGHLEY	Country	United Kingdom
Post Code	BD20 6TD		
Country	ENGLAND		

IN7

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	BETSI CADWALADR UNIVERSITY LHB
Address	EXECUTIVE OFFICES, YSBYTY GWYNEDD PENRHOSGARNEDD BANGOR GWYNEDD
Post Code	LL57 2PW
Country	WALES

Forename	Julie
Middle name	
Family name	Jones
Email	
Qualification (MD...)	Associate specialist Medical oncology
Country	United Kingdom

IN8

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	THE PRINCESS ALEXANDRA HOSPITAL NHS TRUST
Address	HAMSTEL ROAD HARLOW
Post Code	CM20 1QX
Country	ENGLAND

Forename	Dr A
Middle name	
Family name	Konstantis
Email	
Qualification (MD...)	Oncologist
Country	

IN9

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	ISLE OF WIGHT NHS TRUST
Address	ST MARYS HOSPITAL PARKHURST ROAD NEWPORT
Post Code	PO30 5TG
Country	ENGLAND

Forename	Dr Akash
Middle name	
Family name	Maniam
Email	
Qualification (MD...)	Medical Oncologist
Country	

IN10

◉ NHS/HSC Site
○ Non-NHS/HSC Site

		Forename	Rose
		Middle name	
		Family name	Oliver
		Email	
Organisation name	BETSI CADWALADR UNIVERSITY LHB	Qualification (MD...)	Oncology ANP
Address	EXECUTIVE OFFICES, YSBYTY GWYNEDD PENRHOSGARNEDD BANGOR GWYNEDD	Country	
Post Code	LL57 2PW		
Country	WALES		

IN11

◉ NHS/HSC Site
○ Non-NHS/HSC Site

		Forename	Emma
		Middle name	
		Family name	Dangerfield
		Email	
Organisation name	SWANSEA BAY UNIVERSITY LOCAL HEALTH BOARD	Qualification (MD...)	RN
Address	ONE TALBOT GATEWAY, SEAWAY DRIVE SEAWAY PARADE INDUSTRIAL ESTATE BAGLAN PORT TALBOT WEST GLAMORGAN	Country	United Kingdom
Post Code	SA12 7BR		
Country	WALES		

IN12

◉ NHS/HSC Site
○ Non-NHS/HSC Site

		Forename	Joanne
		Middle name	
		Family name	Fields
		Email	
Organisation name	HAMPSHIRE HOSPITALS NHS FOUNDATION TRUST	Qualification (MD...)	ANP
Address	BASINGSTOKE AND NORTH HAMPSHIRE HOS ALDERMASTON ROAD BASINGSTOKE HAMPSHIRE	Country	United Kingdom
Post Code	RG24 9NA		
Country	ENGLAND		

IN13

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

Forename	Emma
Middle name	
Family name	Thompson
Email	
Organisation name	SOUTH TEES HOSPITALS NHS FOUNDATION TRUST
Address	JAMES COOK UNIVERSITY HOSPITAL MARTON ROAD MIDDLESBROUGH
Post Code	TS4 3BW
Country	ENGLAND
Qualification (MD...)	Consultant breast radiographer
Country	United Kingdom

IN14

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

Forename	Elin
Middle name	
Family name	Jones
Email	
Organisation name	HYWEL DDA UNIVERSITY LHB
Address	CORPORATE OFFICES, YSTWYTH BUILDING HAFAN DERWEN ST DAVIDS PARK, JOBSWELL ROAD CARMARTHEN DYFED
Post Code	SA31 3BB
Country	WALES
Qualification (MD...)	Consultant oncologist
Country	

IN15

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

Forename	Prof Hany
Middle name	
Family name	Eldeep
Email	
Organisation name	MILTON KEYNES UNIVERSITY HOSPITAL NHS FOUNDATION TRUST
Address	STANDING WAY EAGLESTONE MILTON KEYNES
Post Code	MK6 5LD
Country	ENGLAND
Qualification (MD...)	Clinical oncologist
Country	United Kingdom

IN16

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

Forename	Samantha
Middle name	
Family name	Weller
Email	
Qualification (MD...)	Research nurse
Country	United Kingdom

Organisation name	SURREY AND SUSSEX HEALTHCARE NHS TRUST
Address	TRUST HEADQUARTERS EAST SURREY HOSPITAL CANADA AVENUE REDHILL SURREY
Post Code	RH1 5RH
Country	ENGLAND

IN17

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

Forename	Michelle
Middle name	
Family name	Donlon
Email	
Qualification (MD...)	Breast surgeon
Country	United Kingdom

Organisation name	COUNTY DURHAM AND DARLINGTON NHS FOUNDATION TRUST
Address	DARLINGTON MEMORIAL HOSPITAL HOLLYHURST ROAD DARLINGTON
Post Code	DL3 6HX
Country	ENGLAND

IN18

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

Forename	Matthew Philip
Middle name	
Family name	Rowland
Email	
Qualification (MD...)	Surgeon
Country	United Kingdom

Organisation name	LIVERPOOL UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
Address	ROYAL LIVERPOOL UNIVERSITY HOSPITAL PRESCOT STREET LIVERPOOL
Post Code	L7 8XP
Country	ENGLAND

IN19

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

Forename	Iain
Middle name	

			Family name	Macpherson
			Email	
	Organisation name	GREATER GLASGOW AND CLYDE	Qualification (MD...)	Oncologist
	Address	GARTNAVEL ROYAL HOSPITAL 1055 GREAT WESTERN ROAD GLASGOW	Country	United Kingdom
	Post Code	G12 0XH		
	Country	SCOTLAND		

IN20

◉ NHS/HSC Site
○ Non-NHS/HSC Site

		Forename	Rachel
		Middle name	
		Family name	Stocking
		Email	
Organisation name	WEST SUFFOLK NHS FOUNDATION TRUST	Qualification (MD...)	Oncology research nurse
Address	WEST SUFFOLK HOSPITAL HARDWICK LANE BURY ST. EDMUNDS	Country	United Kingdom
Post Code	IP33 2QZ		
Country	ENGLAND		

IN21

◉ NHS/HSC Site
○ Non-NHS/HSC Site

		Forename	Annabel
		Middle name	
		Family name	Tomlinson
		Email	
Organisation name	MID CHESHIRE HOSPITALS NHS FOUNDATION TRUST	Qualification (MD...)	Surgery & Cancer Lead Research Nurse
Address	LEIGHTON HOSPITAL LEIGHTON CREWE	Country	United Kingdom
Post Code	CW1 4QJ		
Country	ENGLAND		

IN22

◉ NHS/HSC Site
○ Non-NHS/HSC Site

		Forename	Chiara
		Middle name	
		Family name	Intrivici
		Email	
Organisation name	UNITED LINCOLNSHIRE HOSPITALS NHS TRUST	Qualification (MD...)	Consultant oncoloigst

	Address	LINCOLN COUNTY HOSPITAL GREETWELL ROAD LINCOLN	Country	United Kingdom
	Post Code	LN2 5QY		
	Country	ENGLAND		

IN23

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

		Forename	Lucy
		Middle name	
		Family name	McAvan
		Email	
Organisation name	UNIVERSITY HOSPITALS COVENTRY AND WARWICKSHIRE NHS TRUST	Qualification (MD...)	Consultant oncologist
Address	WALSGRAVE GENERAL HOSPITAL CLIFFORD BRIDGE ROAD COVENTRY	Country	
Post Code	CV2 2DX		
Country	ENGLAND		

IN24

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

		Forename	Emma
		Middle name	
		Family name	Thompson
		Email	
Organisation name	NORTH TEES AND HARTLEPOOL NHS FOUNDATION TRUST	Qualification (MD...)	
Address	UNIVERSITY HOSPITAL OF HARTLEPOOL HOLDFORTH ROAD HARTLEPOOL	Country	United Kingdom
Post Code	TS24 9AH		
Country	ENGLAND		

IN25

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

		Forename	Peter
		Middle name	
		Family name	Hall
		Email	
Organisation name	LOTHIAN	Qualification (MD...)	consultant oncologist
Address	WAVERLEYGATE 2-4 WATERLOO PLACE EDINBURGH CITY OF EDINBURGH	Country	United Kingdom

Post Code	EH1 3EG
Country	SCOTLAND

IN26

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Forename	Judith
Middle name	
Family name	Fraser
Email	
Qualification (MD...)	consultant oncologist
Country	United Kingdom

Organisation name	FORTH VALLEY
Address	CARSEVIEW HOUSE THE CASTLE BUSINESS PARK STIRLING
Post Code	FK9 4SW
Country	SCOTLAND

IN27

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Forename	Angie
Middle name	
Family name	Bowie
Email	
Qualification (MD...)	Research nurse
Country	

Organisation name	EAST SUSSEX HEALTHCARE NHS TRUST
Address	ST ANNES HOUSE 729 THE RIDGE ST. LEONARDS-ON-SEA
Post Code	TN37 7PT
Country	ENGLAND

IN28

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Forename	Stephanie
Middle name	
Family name	Sutherland
Email	
Qualification (MD...)	Oncologist
Country	United Kingdom

Organisation name	EAST AND NORTH HERTFORDSHIRE NHS TRUST
Address	LISTER HOSPITAL COREYS MILL LANE STEVENAGE HERTFORDSHIRE
Post Code	SG1 4AB
Country	ENGLAND

IN29

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	GEORGE ELIOT HOSPITAL NHS TRUST
Address	LEWES HOUSE COLLEGE STREET NUNEATON
Post Code	CV10 7DJ
Country	ENGLAND

Forename	Michaela
Middle name	
Family name	Hill
Email	
Qualification (MD...)	
Country	United Kingdom

IN30

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	THE NEWCASTLE UPON TYNE HOSPITALS NHS FOUNDATION TRUST
Address	FREEMAN HOSPITAL FREEMAN ROAD HIGH HEATON NEWCASTLE UPON TYNE
Post Code	NE7 7DN
Country	ENGLAND

Forename	Henry
Middle name	
Family name	Cain
Email	
Qualification (MD...)	
Country	United Kingdom

IN31

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	IMPERIAL COLLEGE HEALTHCARE NHS TRUST
Address	THE BAYS ST MARYS HOSPITAL SOUTH WHARF ROAD LONDON
Post Code	W2 1BL
Country	ENGLAND

Forename	Farah
Middle name	
Family name	Rehman
Email	
Qualification (MD...)	
Country	

IN32

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Forename	Nicky
Middle name	
Family name	Levitt
Email	
Qualification (MD...)	
Country	

Organisation name	OXFORD UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
Address	JOHN RADCLIFFE HOSPITAL HEADLEY WAY HEADINGTON OXFORD
Post Code	OX3 9DU
Country	ENGLAND

IN33

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Forename	Anne
Middle name	
Family name	Kendall
Email	
Qualification (MD...)	
Country	

Organisation name	GREAT WESTERN HOSPITALS NHS FOUNDATION TRUST
Address	GREAT WESTERN HOSPITAL MARLBOROUGH ROAD SWINDON
Post Code	SN3 6BB
Country	ENGLAND

IN34

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Forename	Robert
Middle name	
Family name	Milligan
Email	
Qualification (MD...)	
Country	United Kingdom

Organisation name	GATESHEAD HEALTH NHS FOUNDATION TRUST
Address	QUEEN ELIZABETH HOSPITAL SHERIFF HILL GATESHEAD
Post Code	NE9 6SX
Country	ENGLAND

PART D: Declarations

D1. Declaration by Chief Investigator

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.

2. I undertake to fulfil the responsibilities of the chief investigator for this study as set out in the UK Policy Framework for Health and Social Care Research.

3. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.

4. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.

5. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.

6. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.

7. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.

8. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.

9. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 2018.

10. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:

    - Will be held by the REC (where applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
    - May be disclosed to the operational managers of review bodies, or the appointing authority for the REC (where applicable), in order to check that the application has been processed correctly or to investigate any complaint.
    - May be seen by auditors appointed to undertake accreditation of RECs (where applicable).
    - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
    - May be sent by email to REC members.

11. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 2018.

12. I understand that the main REC or its operational managers may share information in this application or supporting documentation with the Medicines and Healthcare products Regulatory Agency (MHRA) where it is relevant to the Agency's statutory responsibilities.

13. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the Health Research Authority (HRA) together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after the issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication*(Not applicable for R&D Forms)*

HRA would like to include a contact point with the published summary of the study for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

- ◯ Chief Investigator
- ◯ Sponsor
- ◯ Study co-ordinator
- ◯ Student
- ◯ Other – please give details
- ◯ None

Access to application for training purposes *(Not applicable for R&D Forms)*

Optional – please tick as appropriate:

☐ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

This section was signed electronically by Professor Linda Sharp on 30/06/2023 15:36.

Job Title/Post:	Professor of Cancer Epidemiology
Organisation:	Newcastle University
Email:	linda.sharp@ncl.ac.uk

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co−sponsors by a representative of the lead sponsor named at A64-1.

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.

2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.

3. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.

4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.

5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.

6. The responsibilities of sponsors set out in the UK Policy Framework for Health and Social Care Research will be fulfilled in relation to this research.

   Please note: *The declarations below do not form part of the application for approval above. They will not be considered by the Research Ethics Committee.*

7. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

8. Specifically, for submissions to the Research Ethics Committees (RECs) I declare that any and all clinical trials approved by the HRA since 30th September 2013 (as defined on IRAS categories as clinical trials of medicines, devices, combination of medicines and devices or other clinical trials) have been registered on a publically accessible register in compliance with the HRA registration requirements for the UK, or that any deferral granted by the HRA still applies.

This section was signed electronically by Miss Laura Frisby on 30/06/2023 14:17.

Job Title/Post:	Regulatory Compliance Officer
Organisation:	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Email:	laura.frisby2@nhs.net