ISRCTN36585784 https://doi.org/10.1186/ISRCTN36585784

ATNEC - Axillary management in T1-3N1M0 breast cancer patients with needle biopsy-proven nodal metastases at presentation after neoadjuvant chemotherapy

Submission date
26/10/2020

Recruitment status
Recruiting

Registration date
02/12/2020

Overall study status
Ongoing

Last Edited
06/06/2025

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-further-treatment-to-the-armpit-after-surgery-to-remove-breast-cancer-atnec

Background and study aims
Early-stage breast cancer patients with abnormal-looking armpit lymph glands on an ultrasound scan will have a sample (needle biopsy) of this lymph gland taken. If the sample shows cancer cells are present, patients are often given chemotherapy before surgery (called neoadjuvant chemotherapy) to shrink these cancer cells before their operation. Currently after chemotherapy, all patients undergo breast surgery (lumpectomy or mastectomy) and treatment to their armpit (either removal of all armpit lymph glands or radiotherapy to the armpit). Neoadjuvant chemotherapy results in complete disappearance of cancer in the lymph glands in around 40-70% of patients. For these patients there may be no extra benefit from more treatment to their armpit. Any extra armpit treatment may damage lymphatic drainage from the arm, which could lead to arm swelling (lymphoedema), restricted shoulder movement, pain, numbness and other sensory problems. These side effects make some daily activities difficult for patients, they are distressing and affect their quality of life. They are costly to the NHS in terms of treatments such as physiotherapy and attendance at lymphoedema clinics.
The aim of this study is to find out whether stopping further armpit treatment for patients with no cancer in the lymph glands after chemotherapy is safe, in terms of risk of cancer coming back and fewer lymphoedema cases at 5 years. After neoadjuvant chemotherapy and at the time of breast surgery, patients will undergo removal of at least three lymph glands from the armpit. If there is no cancer in the removed glands, patients will be randomly allocated to receive standard armpit treatment or no further treatment to the armpit.
Results of this study could benefit patients by avoiding unnecessary treatment to the armpit and thus reducing future problems with the arm and shoulder, and possibly improved quality of life and reduced healthcare costs.

Who can participate?
Patients aged 18 or older with early-stage breast cancer that has spread to the lymph gland in their armpit, who will receive (or has received) standard neoadjuvant chemotherapy

What does the study involve?
Eligibility for the randomised portion of the trial will be assessed following completion of neoadjuvant chemotherapy and surgery. The patient's clinician will assess how well their cancer has responded to treatment. If following these assessments, there is no remaining sign of cancer in the patient's armpit lymph glands, then they will be deemed eligible to take part in the randomised stage of the study. Patients eligible for the study will receive either:
1. No further treatment to your armpit, following neoadjuvant chemotherapy and breast surgery, or
2. Further treatment to your armpit, following neoadjuvant chemotherapy and breast surgery
Which treatment patients receive (option 1 or option 2) is decided by a process called randomisation. Neither patients nor their doctor will be able to choose which group is assigned; treatment allocation will be decided randomly by a computer.
If a patient is allocated further treatment to their armpit (option 2), they, together with their doctor, can choose either surgery to remove all remaining lymph glands in the armpit or radiotherapy to the armpit area.
All participants, regardless of which group they are allocated to, will still receive other standard treatment for their breast cancer, such as radiotherapy to the breast and chest wall, and hormone therapy. This treatment will be given as indicated, upon the advice of the clinical team.
Patients who are eligible for the study will also be asked to complete a short questionnaire booklet; there will be five further questionnaire booklets to complete over the course of the study. The researchers will use the responses to assess how patients are feeling with respect to their treatment. Each questionnaire should take approximately 20 minutes to complete.

What are the possible benefits and risks of participating?
The researchers cannot promise that this study will help participants, but it may help patients in the future. Findings from this study will also help inform the future care of patients with early breast cancer that has spread to the armpit. The researchers do not know whether removing further armpit treatment, if there are no signs of cancer left in patients' lymph glands, will have an impact on the risk of their cancer returning – that is why they are doing the study. All participants will be closely monitored by their clinical care team, and if there is any sign of cancer recurrence, their doctor will discuss the best course of action.
X-rays, nuclear medicine imaging and radiotherapy, where appropriate, are part of patients' routine care. If patients take part in this study, they will not undergo any additional imaging or radiotherapy. These procedures use ionising radiation to form images of the body and/or provide treatment and/or provide doctors with other clinical information. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. Patients' doctors will discuss other possible side-effects of radiotherapy with them. The chances of these things happening to patients are the same whether they take part in this study or not.
Participants will be asked to complete questionnaires which will take some of their time (about 20 minutes per questionnaire). As the questionnaires form a key part of our data collection for the study, it is important for participants to consider whether they will have the time to complete these fully. Participants will be issued with one questionnaire booklet at trial entry and then five further questionnaires at the following time points: 1 year, 2 years, 3 years, 4 years and 5 years.

Where is the study run from?
University Hospitals of Derby and Burton NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
March 2020 to March 2030

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
ATNEC Trial Management team
ATNEC@warwick.ac.uk

Study website
https://sites.google.com/nihr.ac.uk/atnec

Contact information

Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
280105

ClinicalTrials.gov number
NCT04109079

Secondary identifying numbers
CPMS 46520, IRAS 280105

Study information

Scientific Title
ATNEC - Axillary management in T1-3N1M0 breast cancer patients with needle biopsy-proven nodal metastases at presentation after neoadjuvant chemotherapy

Acronym
ATNEC

Study objectives
Omitting further axillary treatment (ALND and ART) for patients with early-stage breast cancer and axillary nodal metastases on needle biopsy, who after NACT have no residual cancer in the lymph nodes on sentinel node biopsy, will be non-inferior to axillary treatment in terms of disease-free survival (DFS) and will result in a reduced risk of lymphoedema at 5 years.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 22/10/2020, Yorkshire & The Humber – Bradford Leeds Research Ethics Committee (Newcastle Blood Donor Centre, Holland Drive, HRA Newcastle, Newcastle, NE2 4NQ, United Kingdom; +44 (0)207 104 8083, +44 (0)207 104 8088, +44 (0)207 104 8018; bradfordleeds.rec@hra.nhs.uk), ref: 20/YH/0232

Study design
Randomized; Both; Design type: Treatment, Process of Care, Surgery, Other, Health Economic

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)

Treatment

Participant information sheet
Not available in web format, please use the contact details or speak to the local hospital care team to request a participant information sheet

Health condition(s) or problem(s) studied
Breast cancer

Interventions
Current interventions as of 19/07/2023:

ATNEC is a multi-centre, randomised clinical trial with a non-inferiority endpoint and a pragmatic design. ATNEC will be conducted in patients with early-stage, node-positive breast cancer, whose usual treatment pathway would be neoadjuvant chemotherapy followed by breast surgery and further treatment to the armpit (lymph node clearance or radiotherapy to the armpit). Patients who have no residual cancer in the lymph glands after chemotherapy will be randomised to either have standard armpit treatment or no further treatment to the armpit.

An integrated feasibility study, with embedded qualitative research, will assess the willingness of clinicians and patients to participate in the ATNEC trial.

Pre-Randomisation:
To be eligible, a patient must be diagnosed with early-stage, confirmed node-positive breast cancer on needle biopsy, and planned to receive chemotherapy first (neoadjuvant chemotherapy) prior to surgery. The patient's primary tumour must have been evaluated for receptor status. Patients can be either female or male, and must be aged 18 years or older.

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 informed consent will be obtained.

Once a patient has consented to participate, the site team will be able to register them to the study via the ATNEC online registration portal. The patient will be assigned a unique trial number, which will be used to identify them throughout the study.

It is recommended that the patient's clinical team will mark the abnormal armpit lymph gland – this could be done either by using a clip, carbon dye or by inserting a magnetic seed as per local practice. Patients will then continue to receive neo-adjuvant chemotherapy, as per standard practice.

Following the completion of their chemotherapy, patients will undergo imaging assessment of the lymph glands to check for abnormal-looking lymph glands. If the armpit lymph glands are found to still contain residual cancer cells, the patient will not be eligible for randomisation and will continue with treatment for their cancer, per standard practice. If the ultrasound shows no confirmed evidence of residual cancer, then the patient will proceed to breast surgery (either lumpectomy to remove the lump, or mastectomy to remove the breast). During their operation, a procedure called a sentinel lymph node biopsy will also be performed; this will involve the removal of at least three lymph glands (including the original marked gland). The removed glands will be tested to provide definitive confirmation that the patient has no remaining cancer in their armpit glands. At this point, the patient will be deemed eligible for randomisation.

Patients who are deemed eligible, but have not previously been registered, can also enter the trial at this point. Patients who are willing to participate will be consented after their surgery, registration and randomisation will take place as one process.

Randomisation/Baseline:
Prior to randomisation, patients will be issued with a baseline questionnaire booklet containing the following questionnaires: the lymphoedema and breast cancer questionnaire (LBCQ), a shortened version of the Disability of the Arm, Shoulder and Hand (QuickDASH) questionnaire, a health utilisation questionnaire, and the EQ-5D-5L questionnaire which captures information about a patient's overall health state.

Eligible patients, with continuing consent, will be randomised to the study via the online ATNEC randomisation portal. Patients will be randomised to receive either standard treatment to the armpit (lymph node clearance or radiotherapy to the armpit) or no further armpit treatment.

Follow-Up:
Patients are required to complete five further questionnaire booklets: at 1 year, 2 years, 3 years, 4 years and 5 years post-randomisation. These questionnaire booklets will be posted directly to patients by Warwick Clinical Trials Unit, to complete at home. Posted questionnaires will include a pre-paid return envelope, so completed questionnaires can be returned to the Warwick Clinical Trials Unit.

Beyond the first year, sites will be asked to follow-up patients annually for at least 5 years. Follow-up can be by capturing information from hospital records or by telephone if the treating site has discharged the patient from clinical follow-up. After 5 years, follow-up information will be sought from NHS Digital health records, so long as the patient has given their consent for this.

Radiotherapy Quality Assurance Component:
The ATNEC trial will have an embedded radiotherapy quality assurance programme, coordinated by the National Radiotherapy Quality Assurance (RTTQA) group. Sites will be required to adhere to the specific radiotherapy planning and delivery guidelines, developed by the RTTQA team.

Qualitative Sub-Study:
Qualitative research has been embedded within the recruitment phase to identify and investigate recruitment issues and develop effective and realistic strategies to ensure the success of the trial. Participation in any aspect of the qualitative sub-study is optional.

Patients who appear eligible for ATNEC will be asked for their permission to audio-record their conversations with their doctor up until the point that they make their decision on whether or not to participate. Prior to any commencement of recording, patients will be given a brief patient information sheet explaining the qualitative sub-study. Patients will be given sufficient time to review this and ask any questions. If patients agree to be recorded, they will be asked to sign a consent form, providing permission for the audio-recordings of their consultations.

In addition, patients who were invited to take part in ATNEC (including those who declined to take part) may be invited for interview at a later date to discuss the reasons why they may, or may not, have chosen to take part in the trial. A separate patient information sheet will be provided for this purpose and, should the patient be happy to be interviewed, written informed consent will be obtained. Patients will be asked for their permission to have their interview audio-recorded. This permission is covered in the above-mentioned patient information sheet and informed consent form.

It will be made explicitly clear to patients, at the time of their consultation, or following the informed consent process for the trial, that their participation in the qualitative sub-study is completely optional. The decision of patients who decline to take part will be completely respected, and their medical care will not be affected in any way.

Researchers who are involved in the ATNEC trial consent process (i.e clinicians and research nurses) will also be invited for an interview. Research staff will also be provided with an information sheet and their informed consent will be required prior to any audio-recording of patient consultations and/or interviews.

An overall plan for the qualitative sub-study, including timelines for interviews, is attached to this application.

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Previous interventions:

ATNEC is a multi-centre, randomised clinical trial with a non-inferiority endpoint and a pragmatic design. ATNEC will be conducted in patients with early-stage, node-positive breast cancer, whose usual treatment pathway would be neoadjuvant chemotherapy followed by breast surgery and further treatment to the armpit (lymph node clearance or radiotherapy to the armpit). Patients who have no residual cancer in the lymph glands after chemotherapy will be randomised to either have standard armpit treatment or no further treatment to the armpit.

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the breast). During their operation, a procedure called a sentinel lymph node biopsy will also be performed; this will involve the removal of at least three lymph glands (including the original marked gland). The removed glands will be tested to provide definitive confirmation that the patient has no remaining cancer in their armpit glands. At this point, the patient will be deemed eligible for randomisation.

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may not, have chosen to take part in the trial. A separate patient information sheet will be provided for this purpose and, should the patient be happy to be interviewed, written informed consent will be obtained. Patients will be asked for their permission to have their interview audio-recorded. This permission is covered in the above-mentioned patient information sheet and informed consent form.

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An overall plan for the qualitative sub-study, including timelines for interviews, is attached to this application.

Intervention Type
Mixed

Primary outcome measure
Co-primary outcomes, collected annually for 5 years:
1. Disease-Free Survival (DFS); defined and calculated as the time from randomisation until the date of the first event of either a loco-regional invasive breast cancer relapse, distant relapse, ipsilateral or contralateral new invasive primary breast cancer or death by any cause or the censor date
2. Lymphoedema: self-reported based on two items from the validated Lymphoedema and Breast Cancer Questionnaire (LBCQ) (arm “swelling now” and arm “heaviness in the past year”). Lymphoedema will be defined as ‘yes’ to both questions at 5 years.

Secondary outcome measures
Collected annually for 5 years:
1. Arm function assessed using the shortened version of the Disability of the Arm, Shoulder and Hand (DASH), the 11-item QuickDASH questionnaire, over 5 years
2. Pain intensity and characteristics measured using questions from the Douleur Neuropathique (DN4) and Pain Numeric Rating Scale (NRS) and will relate to the areas affected by surgery and cancer treatment, over 5 years
3. Axillary recurrence-free interval, calculated from the date of randomisation to the date of axillary recurrence or the censor date. Axillary recurrence is defined as pathologically (cytology or biopsy) and/or radiologically confirmed recurrence in lymph nodes draining the primary tumour site. The date of axillary recurrence is the date on which imaging or pathology report (whichever comes first) confirms axillary recurrence. Axillary recurrence will be compared between the two allocated groups over 5 years
4. Overall survival; calculated as the time from randomisation until the date of death by any cause or the censor date. Overall survival will be compared between the two allocated groups over 5 years
5. Local (breast or chest wall) recurrence is defined as pathologically (cytology or biopsy) and/or radiologically confirmed recurrence after mastectomy in the skin or soft tissue of the chest wall within the anatomical area bounded by the mid-sternal line, the clavicle, the posterior axillary

line and the costal margin or any type of breast carcinoma in the breast after conservation therapy. The date of local recurrence is the date on which the imaging or pathology report (whichever comes first) confirms local recurrence. Local recurrence will be compared between the two allocated groups over 5 years
6. Regional (nodal) recurrence is defined as pathologically (cytology or biopsy) and/or radiologically confirmed recurrent tumour in the lymph nodes in the ipsilateral axilla, infraclavicular, supraclavicular fossa, interpectoral area or ipsilateral internal mammary chain. The date of regional recurrence is the date on which the imaging or pathology report (whichever comes first) confirms local recurrence. Regional (nodal) recurrence will be compared between the two allocated groups over 5 years
7. Distant metastasis is defined as confirmed metastasis (positive pathology and/or definitive evidence on imaging) in all other sites of recurrence and may include those classified as: soft-tissue category, visceral category, central nervous system and skeletal spread. The date of distant metastasis is the date on which the imaging or pathology report (whichever comes first) confirms metastasis. Distant metastases will be compared between the two allocated groups over 5 years.
8. Contralateral breast cancer is defined as a new primary malignancy in the opposite breast unless obviously contiguous with recurrent chest wall disease or proven on cytology/biopsy to be of metastatic origin. Contralateral breast cancers will be compared between the two allocated groups over 5 years.
9. Non-breast cancer is defined as any new non-breast primary malignancy, except for basal or squamous cell cancer of the skin, in situ carcinoma of the cervix, or in situ or stage 1 melanoma. New breast cancers will be compared between the two allocated groups over 5 years.
10. Economic evaluation (data to be collected annually, over 5 years, through annual follow-up and patient questionnaires):
10.1. Costs to the NHS and participants will be compared between the two allocated groups over 5 years
10.2. Quality-adjusted life years (QALYs) will be compared between the two groups over 5 years. QALYs based on responses to the EQ-5D-5L administered at baseline, 12, 24, 36, 48, and 60 months post-randomisation
10.3. Incremental cost per disease-free interval over 5 years
10.4. Incremental cost per lymphoedema avoided over 5 years
10.5. Incremental cost per QALY gained over 5 years
10.6. Incremental cost per QALY over the estimated lifetime of a participant with early-stage breast cancer

Overall study start date
01/03/2020

Completion date
01/03/2030

Eligibility

Key inclusion criteria
Current inclusion criteria as of 05/02/2024:

1. Age ≥18 years
2. Male or female
3. cT1-3N1M0 breast cancer at diagnosis (prior to NACT) as per AJCC 8th edition
3.2 Patients with occult primary invasive breast cancer (no identifiable invasive cancer in the

breast) with FNA or core biopsy provide nodal metastases are also eligible for the study.
4. FNA or core biopsy confirmed axillary nodal metastases at presentation
5. Oestrogen receptor and HER2 status evaluated on primary tumour
6. Received standard NACT as per local guidelines (Patients undergoing neoadjuvant endocrine therapy as part of another clinical trial are eligible)
7. Imaging of the axilla, as required, to assess response to NACT (per local guidelines)
8. Undergo a dual tracer sentinel node biopsy (SNB) after NACT with at least 3 nodes removed in total (sentinel nodes and marked node).
8.1 If a single tracer SNB is performed: the patient is eligible only if the involved node is marked before or during NACT, and at least 3 nodes (including the marked node) are removed during sentinel node biopsy.
8.2 If the node is not marked, or marked node is not removed: the patient is eligible only if the histology report shows evidence of downstaging with complete pathological response e.g. fibrosis or scarring in at least one node and at least 3 nodes removed.
8.3 If fewer than 3 nodes are found on histology: the patient is eligible only if BOTH points a) and b), below, are met:
a) involved node was marked and removed during SNB; and
b) removed marked node shows evidence of downstaging on histology e.g. fibrosis or scarring.
8.4 If the sentinel node(s) cannot be localised on SNB: axillary node sampling should be performed, the patient will be eligible if at least 3 nodes are removed (including the marked node).
9. No evidence of nodal metastases post NACT (isolated tumour cells, micro or macrometastasis)

Previous inclusion criteria as of 19/07/2023 to 05/02/2024:

1. Age ≥18 years
2. Male or female
3. cT1-3N1M0 breast cancer at diagnosis (prior to NACT) as per AJCC 8th edition
4. FNA or core biopsy confirmed axillary nodal metastases at presentation
5. Oestrogen receptor, progesterone receptor and HER2 status evaluated on primary tumour
6. Received standard NACT as per local guidelines (Patients undergoing neoadjuvant endocrine therapy as part of another clinical trial are eligible)
7. Imaging of the axilla to assess response to NACT (as per local guidelines)
8. Undergo dual tracer sentinel node biopsy after NACT and at least 3 nodes removed (sentinel nodes and marked node).
8.1 If a single tracer is used, the patient will be eligible if the involved node is marked before or during NACT, and the marked node and at least 3 nodes (including the marked node) are removed during sentinel node biopsy.
8.2 If axillary node sampling is performed following failed localisation of sentinel nodes, patient will be eligible if at least three nodes removed (including the marked node).
8.3 If node is not marked, or marked node is not removed, the patient will be eligible if the histology report shows evidence of downstaging with complete pathological response e.g. fibrosis or scarring in at least one node and at least 3 nodes removed.
8.4 If fewer than 3 nodes are found on histology, the patient is eligible if: a) involved node was marked and removed during SNB; and b) removed marked node shows evidence of downstaging on histology e.g. fibrosis or scarring.
9. No evidence of nodal metastases post NACT (isolated tumour cells, micro or macrometastasis)

Previous inclusion criteria:

1. Age ≥18 years
2. Male or female
3. T1-3N1M0 breast cancer at diagnosis (prior to NACT)
4. FNA or core biopsy confirmed axillary nodal metastases at presentation
5. Oestrogen receptor, progesterone receptor and HER2 status evaluated on primary tumour
6. Received standard NACT as per local guidelines (Patients undergoing neoadjuvant endocrine therapy as part of another clinical trial are eligible)
7. Ultrasound of the axilla at completion of NACT
8. Undergo dual tracer sentinel node biopsy after NACT and at least 3 nodes removed (sentinel nodes and marked node). If axillary node sampling is performed following failed localisation of sentinel nodes, patient will be eligible if at least three nodes removed (including the marked node)
9. No evidence of nodal metastases post NACT (isolated tumour cells, micro or macrometastasis)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 1900; UK Sample Size: 1900

Key exclusion criteria
Current exclusion criteria as of 19/07/2023:

1. Bilateral synchronous invasive breast cancer
2. Sentinel node biopsy prior to NACT
3. Previous axillary surgery on the same body side as the scheduled targeted sampling
4. Any previous cancer within 5 years or concomitant malignancy except:
4.1. Basal or squamous cell carcinoma of the skin
4.2. In situ carcinoma of the cervix
4.3. In situ melanoma
4.4. Contra- or ipsilateral in situ breast cancer

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Previous exclusion criteria:

1. Bilateral invasive breast cancer
2. Sentinel node biopsy prior to NACT
3. Marked node not removed except where the node/s removed show evidence of down-staging with complete pathological response e.g. fibrosis or scarring

4. Previous axillary surgery on the same body side as the scheduled targeted sampling
5. Any previous cancer within 5 years or concomitant malignancy except:
5.1. Basal or squamous cell carcinoma of the skin
5.2. In situ carcinoma of the cervix
5.3. In situ melanoma
5.4. Contra- or ipsilateral in situ breast cancer

Date of first enrolment
21/12/2020

Date of final enrolment
01/03/2026

Locations

Countries of recruitment
England

Isle of Man

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
NHS Grampian
Summerfield House
2 Eday Road
ABERDEEN
United Kingdom
AB15 6RE

Study participating centre
CAMBRIDGE UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
ADDENBROOKES HOSPITAL
HILLS ROAD
CAMBRIDGE
United Kingdom
CB2 0QQ

Study participating centre

FRIMLEY HEALTH NHS FOUNDATION TRUST
PORTSMOUTH ROAD
FRIMLEY
CAMBERLEY
United Kingdom
GU16 7UJ

Study participating centre
NHS Greater Glasgow and Clyde
J B Russell House
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
United Kingdom
G12 0XH

Study participating centre
NHS Forth Valley
33 Spittal Street
Stirling
United Kingdom
FK8 1DX

Study participating centre
NHS Ayrshire and Arran
PO Box 13, Boswell House
10 Arthur Street
AYR
United Kingdom
KA7 1QJ

Study participating centre
Belfast Health & Social Care Trust
Trust Headquarters
A Floor - Belfast City Hospital
Lisburn Road
Belfast
United Kingdom
BT9 7AB

Study participating centre

NHS Borders
Newstead
MELROSE
United Kingdom
TD6 9DB

Study participating centre
NORTH BRISTOL NHS TRUST
SOUTHMEAD HOSPITAL
SOUTHMEAD ROAD
WESTBURY-ON-TRYM
BRISTOL
United Kingdom
BS10 5NB

Study participating centre
CHELSEA AND WESTMINSTER HOSPITAL NHS FOUNDATION TRUST
CHELSEA & WESTMINSTER HOSPITAL
369 FULHAM ROAD
LONDON
United Kingdom
SW10 9NH

Study participating centre
WYE VALLEY NHS TRUST
COUNTY HOSPITAL
UNION WALK
HEREFORD
United Kingdom
HR1 2ER

Study participating centre
OXFORD UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
JOHN RADCLIFFE HOSPITAL
HEADLEY WAY
HEADINGTON
OXFORD
United Kingdom
OX3 9DU

Study participating centre

Liverpool University Hospitals NHS Foundation Trust
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
ST HELENS AND KNOWSLEY TEACHING HOSPITALS NHS TRUST
WHISTON HOSPITAL
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United Kingdom
L35 5DR

Study participating centre
University Hospitals Plymouth NHS Trust
Derriford Hospital
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PLYMOUTH
United Kingdom
PL6 8DH

Study participating centre
THE NEWCASTLE UPON TYNE HOSPITALS NHS FOUNDATION TRUST
FREEMAN HOSPITAL
FREEMAN ROAD
HIGH HEATON
NEWCASTLE-UPON-TYNE
United Kingdom
NE7 7DN

Study participating centre
NORTH TEES AND HARTLEPOOL NHS FOUNDATION TRUST
UNIVERSITY HOSPITAL OF HARTLEPOOL
HOLDFORTH ROAD
HARTLEPOOL
CLEVELAND
United Kingdom
TS24 9AH

Study participating centre
UNIVERSITY HOSPITALS OF LEICESTER NHS TRUST
LEICESTER ROYAL INFIRMARY
INFIRMARY SQUARE
LEICESTER
United Kingdom
LE1 5WW

Study participating centre
UNITED LINCOLNSHIRE HOSPITALS NHS TRUST
LINCOLN COUNTY HOSPITAL
GREETWELL ROAD
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United Kingdom
LN2 5QY

Study participating centre
WEST HERTFORDSHIRE HOSPITALS NHS TRUST
TRUST OFFICES
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VICARAGE ROAD
WATFORD
United Kingdom
WD18 0HB

Study participating centre
Somerset NHS Foundation Trust
Trust Management
Lydeard House
Musgrove Park Hospital
Taunton
United Kingdom
TA1 5DA

Study participating centre
NHS Highland
Reay House
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INVERNESS
United Kingdom
IV2 3HG

Study participating centre
ROYAL CORNWALL HOSPITALS NHS TRUST
ROYAL CORNWALL HOSPITAL
TRELISKE
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United Kingdom
TR1 3LJ

Study participating centre
UNIVERSITY HOSPITALS OF DERBY AND BURTON NHS FOUNDATION TRUST
ROYAL DERBY HOSPITAL
UTTOXETER ROAD
DERBY
United Kingdom
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Study participating centre
ROYAL FREE LONDON NHS FOUNDATION TRUST
ROYAL FREE HOSPITAL
POND STREET
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United Kingdom
NW3 2QG

Study participating centre
Mid and South Essex NHS Foundation Trust
Prittlewell Chase
Westcliff-on-sea
United Kingdom
SS0 0RY

Study participating centre
UNIVERSITY HOSPITALS OF MORECAMBE BAY NHS FOUNDATION TRUST
WESTMORLAND GENERAL HOSPITAL
BURTON ROAD
KENDAL
United Kingdom
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Study participating centre

UNIVERSITY HOSPITALS OF NORTH MIDLANDS NHS TRUST
NEWCASTLE ROAD
STOKE-ON-TRENT
United Kingdom
ST4 6QG

Study participating centre
BRIGHTON AND SUSSEX UNIVERSITY HOSPITALS NHS TRUST
ROYAL SUSSEX COUNTY HOSPITAL
EASTERN ROAD
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United Kingdom
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Study participating centre
Hywel Dda NHS Trust
Hafan Derwen
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Carmarthen
United Kingdom
SA31 3BB

Study participating centre
ASHFORD AND ST PETER'S HOSPITALS NHS FOUNDATION TRUST
ST PETERS HOSPITAL
GUILDFORD ROAD
CHERTSEY
United Kingdom
KT16 0PZ

Study participating centre
Airedale NHS Foundation Trust
Airedale General Hospital
Skipton Road
Steeton
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United Kingdom
BD20 6TD

Study participating centre

MID YORKSHIRE HOSPITALS NHS TRUST
PINDERFIELDS HOSPITAL
ABERFORD ROAD
WAKEFIELD
United Kingdom
WF1 4DG

Study participating centre
CALDERDALE AND HUDDERSFIELD NHS FOUNDATION TRUST
ROYAL INFIRMARY
ACRE STREET
HUDDERSFIELD
United Kingdom
HD3 3EA

Study participating centre
WRIGHTINGTON, WIGAN AND LEIGH NHS FOUNDATION TRUST
THE ELMS
ROYAL ALBERT EDWARD INFIRMARY
WIGAN LANE
WIGAN
United Kingdom
WN1 2NN

Study participating centre
BOLTON NHS FOUNDATION TRUST
THE ROYAL BOLTON HOSPITAL
MINERVA ROAD
FARNWORTH
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United Kingdom
BL4 0JR

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EAST CHESHIRE NHS TRUST
MACCLESFIELD
DISTRICT GEN HOSPITAL
VICTORIA ROAD
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United Kingdom
SK10 3BL

Study participating centre
MANCHESTER UNIVERSITY NHS FOUNDATION TRUST
COBBETT HOUSE
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NHS Lanarkshire
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Waverley Gate
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Study participating centre

THE ROTHERHAM NHS FOUNDATION TRUST
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Study participating centre
DONCASTER AND BASSETLAW TEACHING HOSPITALS NHS FOUNDATION TRUST
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ARMTHORPE ROAD
DONCASTER
United Kingdom
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Study participating centre
SHEFFIELD TEACHING HOSPITALS NHS FOUNDATION TRUST
NORTHERN GENERAL HOSPITAL
HERRIES ROAD
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United Kingdom
S5 7AU

Study participating centre
ROYAL BERKSHIRE NHS FOUNDATION TRUST
ROYAL BERKSHIRE HOSPITAL
LONDON ROAD
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United Kingdom
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MINDELSOHN WAY
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BIRMINGHAM
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LUTON AND DUNSTABLE UNIVERSITY HOSPITAL NHS FOUNDATION TRUST
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United Kingdom
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ROYAL DEVON & EXETER
HOSPITAL
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EXETER
United Kingdom
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SANDWELL AND WEST BIRMINGHAM HOSPITALS NHS TRUST
CITY HOSPITAL
DUDLEY ROAD
BIRMINGHAM
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B18 7QH

Study participating centre
THE ROYAL MARSDEN NHS FOUNDATION TRUST
FULHAM ROAD
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SW3 6JJ

Study participating centre
NORTH MIDDLESEX UNIVERSITY HOSPITAL NHS TRUST
NORTH MIDDLESEX HOSPITAL
STERLING WAY
LONDON
United Kingdom
N18 1QX

Study participating centre
NORTH CUMBRIA INTEGRATED CARE NHS FOUNDATION TRUST
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PENRITH
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Haslingden Road
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Hull University Teaching Hospitals NHS Trust
Hull Royal Infirmary
Anlaby Road
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United Kingdom
HU3 2JZ

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
St Marys Hospital
South Wharf Road
London
United Kingdom
W2 1BL

Study participating centre
Wirral University Teaching Hospital NHS Foundation Trust
Arrowe Park Hospital
Arrowe Park Road
Upton
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United Kingdom
CH49 5PE

Study participating centre

Countess of Chester Hospital NHS Foundation Trust
Countess of Chester Health Park
Liverpool Road
Chester
United Kingdom
CH2 1UL

Study participating centre
County Durham and Darlington NHS Foundation Trust
Darlington Memorial Hospital
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Darlington
United Kingdom
DL3 6HX

Study participating centre
NHS Dumfries and Galloway
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Study participating centre
James Paget University Hospitals NHS Foundation Trust
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Study participating centre
King's College Hospital NHS Foundation Trust
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United Kingdom
SE5 9RS

Study participating centre

Mid Cheshire Hospitals NHS Foundation Trust
Leighton Hospital
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Crewe
United Kingdom
CW1 4QJ

Study participating centre
Milton Keynes University Hospital NHS Foundation Trust
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United Kingdom
MK6 5LD

Study participating centre
The Royal Wolverhampton NHS Trust
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Heath Town
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
Gateshead Health NHS Foundation Trust
Queen Elizabeth Hospital
Sheriff Hill
Gateshead
United Kingdom
NE9 6SX

Study participating centre
NHS Fife
Hayfield House
Hayfield Road
Kirkcaldy
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KY2 5AH

Study participating centre

The Shrewsbury and Telford Hospital NHS Trust
Mytton Oak Road
Shrewsbury
United Kingdom
SY3 8XQ

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Bradford Teaching Hospitals NHS Foundation Trust
Bradford Royal Infirmary
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Bradford
United Kingdom
BD9 6RJ

Study participating centre
Tameside and Glossop Integrated Care NHS Foundation Trust
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Fountain Street
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United Kingdom
OL6 9RW

Study participating centre
The Clatterbridge Cancer Centre NHS Foundation Trust
Clatterbridge Hospital
Clatterbridge Road
Bebington
Wirral
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CH63 4JY

Study participating centre

Buckinghamshire Healthcare NHS Trust
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Amersham
United Kingdom
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Study participating centre
York and Scarborough Teaching Hospitals NHS Foundation Trust
York Hospital
Wigginton Road
York
United Kingdom
YO31 8HE

Study participating centre
Victoria Hospital (blackpool)
Whinney Heys Road
Blackpool
United Kingdom
FY3 8NR

Study participating centre
Croydon University Hospital
London Road
Croydon
United Kingdom
CR7 7YE

Study participating centre
Lister Hospital
Coreys Mill Lane
Stevenage
United Kingdom
SG1 4AB

Study participating centre
Ipswich Hospital
Heath Road

Ipswich
United Kingdom
IP4 5PD

Study participating centre
King Edward VII Hospital (Parapet)
St. Leonards Road
Windsor
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SL4 3DP

Study participating centre
University Hospital Galway
Newcastle Road
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H91 YR71

Study participating centre
Cheltenham General Hospital
Sandford Road
Cheltenham
United Kingdom
GL53 7AN

Study participating centre
Harrogate District Hospital
Lancaster Park Road
Harrogate
United Kingdom
HG2 7SX

Study participating centre
Royal Preston Hospital
Sharoe Green Lane
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre
North Tyneside General Hospital
Rake Lane
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NE29 8NH

Study participating centre
Queen Alexandra Hospital
Southwick Hill Road
Cosham
Portsmouth
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PO6 3LY

Study participating centre
St Vincent's University Hospital
Elm Park
Dublin
Ireland
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Study participating centre
East Surrey Hospital
Canada Avenue
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RH1 5RH

Study participating centre
Singleton Hospital
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Sketty
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SA2 8QA

Study participating centre
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New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
Whittington Hospital
Magdala Avenue
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N19 5NF

Study participating centre
Worcestershire Royal Hospital
Charles Hastings Way
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WR5 1DD

Study participating centre
Yeovil District Hospital
Higher Kingston
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BA21 4AT

Sponsor information

Organisation
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Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research; Grant Codes: NIHR128311

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. The researchers intend to publish the protocol in an open-access journal.
2. Planned publication in a high-impact peer-reviewed journal. Publication of the results will be based on outcomes at least 5 years following the last recruited participant. No interim publication of results is planned at present.

Intention to publish date
01/03/2031

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request. Participant data is stored on a secure server at WCTU where each participant has been assigned a de-identified trial number. Any requests for access to the trial data should be sent to the CI who will inform the data custodians and agreement will be made through the data access committee which will comprise of the principal investigators from the trial management group. For each data sharing request, it is essential that a proforma is completed which will describe the purpose, scope, data items requested, analysis plan and acknowledgment of the trial management team. Requestors who are granted access to the data will be required to complete a data-sharing agreement which will be signed by the requester, sponsor and principal investigator(s). The researchers anticipate that data sharing will be possible after the publication of the primary endpoint of the trial.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No