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Comparing surgical treatments for people with early breast cancer that has spread to the armpit (axillary) lymph nodes: targeted armpit surgery (targeted axillary dissection) versus standard armpit surgery (axillary node clearance)

Submission date 06/06/2025	**Recruitment status** Recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [X] Record updated in last year
Registration date 18/07/2025	**Overall study status** Ongoing	
Last Edited 09/09/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

Breast cancer affects 55,000 patients each year in the UK, and in ~20% of cases, the cancer will have spread to the armpit (axillary) lymph nodes. The current standard treatment for these patients is to remove all the axillary lymph nodes (axillary node clearance), even if only one or two are affected. However, one in three patients will experience life-changing complications as a result of this treatment, including permanent swelling of the arm (lymphoedema), long-term pain, and problems with shoulder function. These complications dramatically affect quality of life and are costly to the NHS. Axillary node clearance (ANC) was believed to give patients the best chance of surviving their breast cancer, but there is no evidence to show that this is true if the spread to the axillary lymph nodes is limited. More targeted surgery to the armpit, called a targeted axillary dissection (TAD), in which just the lymph nodes containing cancer and the first draining (sentinel) lymph nodes are removed, may be just as safe and reduce the risk of life-changing complications. The TADPOLE study aims to determine whether targeted armpit surgery (TAD) reduces the risk of lymphoedema at 12 months after the operation without increasing the risk of the cancer returning, compared to ANC.

Who can participate?

Adults diagnosed with primary T1-2 breast cancer, with limited spread of the cancer to their armpit lymph nodes (i.e. 2 or fewer lymph nodes affected) being treated at any hospital participating in the TADPOLE study. Detailed clinical inclusion and exclusion criteria apply and will be assessed by a clinician/surgeon at the participating hospital.

What does the study involve?

Participants will undertake clinical assessments at baseline, including measurements of arm

circumference, and will be asked to complete health-related quality of life questionnaires. All participants will be followed up in person during a hospital visit for the 1-year follow-up. All other follow-ups will be done remotely by telephone at 1 month and then 2, 3, 4 and 5 years after surgery for a range of clinical, safety, and patient-reported outcomes. Participants are required to complete health-related quality of life questionnaires at 1, 2 and 5 years. Mammograms will also be performed yearly for 5 years, as per standard care. Participants will be randomised at a 2:1 ratio to TAD:ANC. Participants may also take part in an interview to discuss their experiences of the study if they wish to.

What are the possible benefits and risks of participating?
Please see the TADPOLE supplementary Participant Information Leaflet, available on the TADPOLE study website, for further information about the risks and benefits of participating

Where is the study run from?
The Bristol Trials Centre, a UK Clinical Research Collaboration registered Clinical Trials Unit, which is part of the University of Bristol's Medical School, is running the study

When is the study starting and how long is it expected to run for?
September 2023 to July 2033. Recruitment to the study is expected to start in September 2025 and will continue for 28 months. Following this, there will be 5 years of follow-up, so the study results will not be expected until 2033.

Who is funding the study?
The National Institute of Health and Social Care Research (NIHR) – Health Technology Assessment Programme (NIHR-HTA)

Who is the main contact?
Study coordinator (Lucy Dabner) Tadpole-trial@bristol.ac.uk

Cancer Research UK plain English summary link added to plain English summary field

Contact information

Type(s)
Public

Contact name
Ms Lucy Dabner

Contact details
Bristol Trials Centre, Bristol Medical School, University of Bristol, 1-5 Whiteladies Road, Clifton
Bristol
United Kingdom
BS8 1NU
+44 0117 45 51524
Tadpole-trial@bristol.ac.uk

Type(s)
Scientific, Principal investigator

Contact name

Prof Shelley Potter

Contact details
University of Bristol, Level 2, Learning and Research building
Bristol
United Kingdom
BS10 5NB
-
shelley.potter@bristol.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
333212

Central Portfolio Management System (CPMS)
58409

National Institute for Health and Care Research (NIHR)
158400

Study information

Scientific Title
Targeted axillary dissection versus axillary node clearance in patients with positive axillary lymph nodes in early breast cancer: a multicentre, pragmatic, phase III randomised controlled trial

Acronym
TADPOLE v1.0

Study objectives
The hypothesis is that targeted armpit surgery (targeted axillary dissection) reduces the risk of lymphoedema at 12 months after the operation without increasing the risk of the cancer returning, compared to standard armpit surgery (axillary node clearance).

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 12/06/2025, Wales Research Ethics Committee 3 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 02922 941107; Wales.REC3@wales.nhs.uk), ref: 25/WA/0139

Study design
Multi-centre parallel-group pragmatic phase III randomized controlled trial with a 9-month internal pilot phase and embedded qualitative research plus quality assurance and health economic analysis and Study Within A Trial (SWAT)

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Adults diagnosed with primary T1-2 breast cancer, with low nodal disease

Interventions
The TADPOLE trial is a multi-centre, parallel group, pragmatic phase 3 randomised controlled trial with a 9-month internal pilot phase, embedded qualitative research, surgical and radiotherapy quality assurance (QA), health economic analysis and Study Within A Trial (SWAT).

Patients with early breast cancer and low volume nodal disease (i.e. the cancer has spread to 2 or fewer lymph nodes) undergoing surgery as their first treatment will be randomised in a 2:1 ratio to receive either targeted axillary dissection (TAD) or axillary node clearance (ANC), respectively. The internal pilot will establish whether sufficient numbers of eligible patients can be identified, recruited and will adhere to their allocated treatment for the trial to robustly answer the trial questions. The internal pilot will last for 9 months. If the progression criteria are met, the main trial recruitment will continue for a further 19 months (total recruitment 28 months) at a minimum of 40 UK sites. If the main trial proceeds, patients from the internal pilot will be included in the final analysis. All participants will be followed up for 5 years post-surgery. Consent will be obtained for long-term (10-and 20-year) follow-up via linkage to routinely collected data, subject to funding.

Patients with breast cancer and low-volume nodal disease recommended for primary surgery by the local site's Multi-Disciplinary Team (MDT) meeting will be screened. Potentially eligible participants will be provided with information about the trial using a layered approach. They will initially be informed about the study at a clinic appointment with their surgeon, at which their breast cancer diagnosis and the initial treatment plan are discussed. This appointment will include a description of both the TAD and ANC procedures and the risks and benefits of both options. Patients will be supported by their clinical nurse specialist (breast care nurse) and will be allowed to ask questions.

Clinical/research teams at participating sites will then follow up with the patient to answer any questions. If the patient would like to participate, they will arrange a baseline visit, which will be timed to coincide with another hospital appointment (if possible). Once written informed consent has been provided, patients will be randomised by computer during (or shortly after) their baseline visit to receive either TAD or ANC alongside their primary breast surgery. Randomisation will take place before surgery to allow enough time for theatre list planning (TAD is a shorter procedure than ANC); patients to be effectively counselled about their allocated procedure, and for participants allocated to TAD to have an additional ultrasound procedure to mark the involved lymph node(s).

Patients will undertake clinical assessments at baseline, including measurements of their arm circumference, and will be asked to complete health-related quality of life questionnaires. All participants will be followed up in person during a hospital visit for the 1-year follow-up. All other follow-ups will be done remotely by telephone at 1 month and then 2, 3, 4 and 5 years after surgery for a range of clinical, safety and patient-reported outcomes. Participants can also choose to have all their follow-ups in person if they prefer, and the local site has capacity. Participants will be required to complete health-related quality of life questionnaires at 1, 2 and 5 years. Mammograms will also be performed yearly for 5 years, as per standard care.

Some patients will also be invited to take part in the embedded qualitative study and can optionally consent to the trial team audio-recording the interviews about their experience. Some patients who decline to participate in the study will also be approached to take part in qualitative interviews about their reasons for not taking part.

A Study Within A Trial is also embedded into TADPOLE, where an evaluation of language and interpretation services used in TADPOLE will take place to assess how these have facilitated the recruitment of low-level English-speaking participants from ethnic minority groups.

Intervention Type
Procedure/Surgery

Primary outcome(s)
The following co-primary outcome measures will be assessed:
1. Lymphoedema at 12 months post-surgery, defined as BOTH an objective increase in arm circumference of >2cm from baseline, and using two items from the validated Lymphoedema and Breast Cancer Questionnaire (LBCQ) for patients to self-report lymphoedema symptoms defined as a response of 'yes' to both: arm "swelling now" and arm "heaviness in the past year" from. A composite endpoint combining objective and patient-reported outcomes was considered important to minimise potential bias in the trial.
2. Locoregional recurrence (LRR) at 5 years, defined as pathologically and/or radiologically confirmed recurrent tumour in the ipsilateral breast after breast conserving surgery or the skin or soft tissues of the chest wall within the anatomical boundaries of the breast after mastectomy; ipsilateral axilla, infraclavicular, supraclavicular fossa, interpectoral area or ipsilateral internal mammary chain. The date of locoregional recurrence will be the date on the imaging or pathology report, whichever comes first.

Key secondary outcome(s))
The following secondary outcome measures will be collected (all timepoints are measured from post-last axillary surgery):
1. Surgical complications measured using data collected from the electronic case report form (eCRF) at 1-month post-surgery
2. Surgical and oncological outcomes measured using data collected from patient medical records at 1-month post-surgery
3. Patient-reported lymphoedema assessed using two questions from the LBCQ questionnaire (as per primary outcome) at 12, 24 and 60 months
4. Objective assessment of lymphoedema using measurement of arm circumference at 12 months
5. Arm and shoulder morbidity measured using the QuickDASH questionnaire at 12, 24 and 60 months
6. Pain measured using the Numerical Pain Rating Scale (NPRS) at 1 and 12 months
7. Overall and disease-free survival measured using data collected from patient medical records at 60 months
8. Health-related quality of life measured using the EQ-5D-5L, FACT-B+4 and LYMPH-Q at 12, 24, and 60 months
9. Resource use to estimate costs measured using the ModRUM questionnaire and data collected from the patient's medical records at 12, 24, 60 months and modelled beyond the end of the trial

Completion date
31/07/2033

Eligibility

Key inclusion criteria
ALL of the following must apply:
1. Adults (> = 18 years of age)
2. Primary T1-2 breast cancer of any grade (multifocal/multicentric disease is permitted)
3. Low volume N1 axillary nodal disease confirmed on core biopsy or fine needle aspiration cytology, defined as:
3.1. Clinically normal (cN0)
3.2. Radiologically detected nodal involvement
3.3. With < = 2 involved nodes on USS
4. Able and willing to provide written informed consent
5. Willing, fit and able to undergo primary surgical treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Participants may not enter the study if ANY of the following apply:
1. > = 3 suspicious nodes on USS or clinically abnormal nodes (cN1)
2. T3 or T4 disease by clinical or radiological assessment
3. Pure invasive lobular carcinoma
4. Bilateral breast cancer
5. Previous ipsilateral breast cancer or ductal carcinoma in situ
6. Received neoadjuvant systemic anticancer therapy (neoSACT)
7. Received neoadjuvant endocrine therapy (defined as > 4 weeks of treatment)
8. Previous axillary surgery (sentinel node biopsy, axillary node clearance or axillary sample)
9. Other invasive cancers unless:
9.1. Disease-free for 5 years or
9.2. Previous basal cell carcinoma, cervical carcinoma in situ, non-muscle invasive urothelial carcinoma
10. High-risk group for developing breast cancer as defined by NICE guidance
11. Pregnant or breastfeeding
12. Any serious and/or unstable pre-existing medical, psychiatric or other condition that would prevent compliance with the trial or consent process
13. Prisoners

Date of first enrolment

01/10/2025

Date of final enrolment
31/01/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
North Bristol NHS Trust

ROR
https://ror.org/036x6gt55

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

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

Individual participant data (IPD) sharing plan
After the study ends, the data will be deposited at the University of Bristol Research Data Repository (data.bris.ac.uk/data), where, once published, they will be assigned a DOI. A metadata record will be published openly by the repository, and this record will clearly state how data can be accessed by bona fide researchers. Access requests will be directed to the Research Data team at the University of Bristol, who will assess the motives of potential data re-users before granting access to the data. Only anonymised data will be shared, and only participants who consented to this will be included in the dataset.

IPD sharing plan summary
Stored in non-publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes