ISRCTN18238549 https://doi.org/10.1186/ISRCTN18238549

A study to determine the feasibility of undertaking a large scale study comparing the clinical and patient-reported outcomes of oncoplastic breast conservation as an alternative to mastectomy with or without immediate breast reconstruction

Submission date	**Recruitment status**	[X] Prospectively registered
04/08/2020	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
26/08/2020	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
17/01/2025	Cancer	

Plain English summary of protocol

Background and study aims

Breast-conserving surgery (BCS) is the preferred treatment for many women with breast cancer. However, standard techniques frequently result in poor cosmetic outcomes and mastectomy (removal of the breast) with or without immediate breast reconstruction is often recommended. Currently, 40% of the 55,000 women diagnosed with breast cancer each year undergo a mastectomy but of these only 1 in 4 receive reconstruction. Oncoplastic breast conservation surgery (OPBCS) describes a range of volume replacement (e.g. local perforator flap [LPF]) and volume displacement techniques (e.g. therapeutic mammaplasty (TM)) that may extend the boundaries of standard BCS and allow some women to avoid mastectomy and potentially improve their quality of life.

There is a need for high-quality research to determine whether OPBCS offers a safe and effective alternative to mastectomy but preliminary work is needed to ensure a future large-scale study is feasible, well-designed and addresses questions important to patients and the NHS. The overall aim of this study is to assess the feasibility of undertaking a large-scale multicentre prospective cohort study to compare the clinical and cost-effectiveness of OPBCS as a safe and effective alternative to mastectomy with and without immediate breast reconstruction (IBR), and to determine the most appropriate outcome measures for use in the main study.

The feasibility study will have four parts:

1. A national survey (a nested service evaluation) to understand the current national practice of OPBCS
2. A pilot study to explore how many women are suitable for OPBCS as an alternative to mastectomy, choose to undergo the procedure, and whether existing patient-reported outcome questionnaires measure outcomes important to patients undergoing different types of surgery

accurately and can reliably be used in a future large study
3. Interviews with patients to explore their views of different surgical options and the adequacy of questionnaires used to assess key patient-reported outcomes
4. Design of the future study
This study will be the first-step providing high-quality evidence to support the use of OPBCS as an alternative to mastectomy. It will promote choice, improving outcomes for patients, many of whom will be long-term breast cancer survivors.

Who can participate?
Female patients over 18 years of age with invasive breast cancer or ductal carcinoma in situ (DCIS) not considered suitable for standard BCS or simple level 1 techniques who are assessed by the breast cancer (and oncoplastic, if applicable) multidisciplinary team (MDT) and the operating surgeon as being suitable candidates for either OPBCS (therapeutic mammaplasty or local perforator flaps) as an alternative to a mastectomy OR mastectomy with or without an immediate breast reconstruction (using any technique) and offered both OPBCS and mastectomy options. No restrictions will be placed on the size of the tumour as decisions on the suitability of a patient for simple BCS will be based on assessments of the size of the tumour relative to the overall size of the breast and its position within the breast rather than on explicit size criteria.

What does the study involve?
If a woman is considered suitable for OPBRS or mastectomy +/- IBR by her surgeon it will be discussed with her and she will be given time to consider her options. At this point the study will be introduced. If the potential participant chooses to undergo OPBRS or mastectomy +/- IBR, she will be offered the opportunity to join the study. If she consents, demographic details will be recorded and she will be asked to complete questionnaires before surgery and again at 3 and 12 months after surgery. Questionnaires can be completed online or on paper as per patient preference. After the patient has completed the questionnaires she will attend the hospital for surgery shortly after. On the day of surgery, data will be collected including technical details about what was done in the operating theatre and her hospital stay. The clinical team will be responsible for collecting this information, with support from the local clinical research network. Participants will be asked to complete further questionnaires at 3 and 12 months following surgery. It is anticipated that the majority of women will leave the hospital within the first week after surgery, therefore any participant with a device and internet access can consent to be contacted directly by email and prompted to answer the questionnaires directly onto the secure online database. If they do not want electronic questionnaires or do not have internet access via a suitable device (e.g. iPhone or another handheld device/phone), copies will be sent by post. Patients will be asked at the beginning of the study (when signing their consent form) whether they would like to complete questionnaires online or paper. Reminders will be sent by the research team to complete questionnaires if there has been no response from the patient after 1 month. Data regarding additional cancer treatments each patient undergoes (including chemotherapy, radiotherapy or hormone tablets) will also be recorded. Decisions regarding this treatment are usually made within a few weeks of surgery. This data will be collected at 3 months by clinical or case note review depending on local practice.
Patients will be asked if they are willing to be contacted to participate in the interview study at the time of signing the consent form. A sample of patients will be contacted by email or letter and invited to participate in the interview study. They will be sent an interview study patient information sheet and a consent form. Patients agreeing to participate in the interview study will be asked to return their consent form either by post or email in a prepaid envelope provided and to provide contact details to allow an interview to be arranged. The research team will contact consenting participants to arrange a telephone interview at a date and time that is convenient for them. Interviews are anticipated to last about 60 minutes.

What are the possible benefits and risks of participating?
This is an observational study, recording data about operations which are already happening and would go ahead regardless of inclusion in the study. Patients will not be randomly allocated to treatments. There are no additional clinical risks to study participants other than the intrinsic risk of surgery, which they would accept whether they were included in the study or not. Patient participants will be asked to complete validated questionnaires before their surgery and then at 3 and 12 months following surgery. Participants will be asked to give consent for data about them to be recorded including baseline demographic data, technical details of their surgery and length of hospital stay, any complications they experience and any additional ("adjuvant") cancer treatments they undergo. The study has been designed to minimise the burden of participation on patients and clinical teams. Where possible, study data will be entered directly onto a secure online database. Answers to the questionnaires can be entered directly by participants who have internet access and consent to give the email address to the study team. This will minimise additional hospital visits or telephone calls for participants. Those patients who do not have internet access or a suitable tablet or device to upload their own data will be sent questionnaires by post so they do not need to attend the hospital to record their responses.
There is a small risk of causing additional distress at the time the patient is approached about the study. However, breast surgeons are well accustomed to having challenging discussions with patients when they are newly diagnosed with breast cancer. Recruiting surgeons will be instructed to make a judgement on a case-by-case basis about the appropriateness of approaching individual patients about the study based on whether they suspect it would lead to any additional anxiety. The organisation of services will vary between units, but most UK surgical centres have at least two discussions between the breast team and the patient before a final decision about breast surgery is made to give patients time to consider their options. Therefore, it is anticipated that most surgeons recruiting to the study will briefly introduce the study at the end of an initial consultation, and offer potential participants a copy of the patient information leaflet to take away and consider. They will then be followed up by the surgical or research team with another appointment to make firm surgical plans, when study participation could be re-discussed and decided upon. There is a great deal of support available for patients with a new diagnosis of breast cancer starting with their breast care nurse who can signpost to further support as required.

Where is the study run from ?
University of Bristol within the Bristol Centre for Surgical Research, Bristol Medical School (UK)

When is the study starting and how long is it expected to run for?
September 2020 to March 2024

Who is funding the study?
The Above and Beyond Bristol-based charity and the Association of Breast Surgery (ABS) (UK)

Who is the main contact?
1. Miss Shelley Potter
Shelley.Potter@bristol.ac.uk
2. Dr Charlotte Davies
Charlotte.Davies@bristol.ac.uk

Contact information

Type(s)
Public

Contact name
Dr Charlotte Davies

ORCID ID
https://orcid.org/0000-0002-3468-4258

Contact details
Room 2.05
University of Bristol
Bristol Medical School
Canygne Hall
Whatley Road
Bristol
United Kingdom
BS8 2PS
+44 (0)117 9287209
Charlotte.Davies@bristol.ac.uk

Type(s)
Scientific

Contact name
Miss Shelley Potter

Contact details
University of Bristol
Bristol Medical School
Canynge Hall
Whatley Road
Bristol
United Kingdom
BS8 2PS
+44 (0)117 9287218
Shelley.Potter@bristol.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
281086

Study information

Scientific Title
Is A Novel THErapeutic mammaplasty procedure a safe and effective alternative to Mastectomy for treatment of breast cancer (ANTHEM Feasibility Study) - a multicentre prospective cohort study to evaluate the safety and effectiveness of oncoplastic breast conservation as an alternative to mastectomy with or without immediate breast reconstruction

Acronym
ANTHEM

Study objectives
The overall aim of the ANTHEM feasibility study is to assess the feasibility of undertaking a large-scale multicentre prospective cohort study to compare the clinical and cost-effectiveness of oncoplastic breast-conserving surgery (OPBCS) as a safe and effective alternative to mastectomy with and without (+/-) immediate breast reconstruction (IBR) and to determine the most appropriate outcome measures for use in the main study. In addition to explore women's decision making for different surgical procedures, rationale for choice and perceptions of outcome.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/08/2020, Wales REC 6 (c/o Public Health Wales, Building 1, Jobswell Road, St David' s Park, SA31 3HB, UK; +44 (0)7920 565 664, +44 (0)1874 615950; sue.byng@wales.nhs.uk), REC ref: 20/WA/0225

Primary study design
Observational

Study design
Multi-centre observational prospective cohort study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Breast reconstruction after breast cancer diagnosis

Interventions
Eligible patients will be identified from the breast cancer and if applicable oncoplastic multidisciplinary team (MDT) meetings as being potentially eligible for either OPBCS or mastectomy. Patient's suitability for both OPBCS and mastectomy +/- IBR will be assessed by their surgeon in clinic as per standard practice. If the operating surgeon considers the patient to be suitable for either OPBCS or mastectomy +/- IBR, they will be offered a choice of procedures. They will be invited to participate in the study and given a patient information leaflet (PIL). If patients elect to participate in the study, they will have a discussion with a member of the research or surgical team and sign a consent form. Patients will also be asked to consent to be contacted about taking part in an interview (Part 3 Interview study). If they are happy to be contacted about taking part in an interview they can provide their contact details (postal address, telephone or email) and a separate interview PIL and consent form will be sent to the patient.

If a woman is considered suitable for OPBRS or mastectomy +/- IBR by her surgeon it will be discussed with her and she will be given time to consider her options. At this point the study will be introduced. If the potential participant chooses to undergo OPBRS or mastectomy +/- IBR, she will be offered the opportunity to join the study. If she consents, demographic details will be

recorded and she will be asked to complete a baseline questionnaire before surgery (the BREAST-Q, EQ-5D-5L and ICECAP-A) and again at 3 and 12 months post-surgery. Questionnaires can be completed online or on paper as per patient preference.

Data collection for prospective cohort study:
After the patient has completed the baseline questionnaires she will attend the hospital for surgery shortly after. On the day of surgery, data will be collected including technical details about what was done in the operating theatre and her post-operative hospital stay. The clinical team will be responsible for collecting this information, with support from the local clinical research network (NIHR LCRN); The ANTHEM study is eligible to be added to the LCRN research portfolio. Participants will be asked to complete further questionnaires (BREAST Q, EQ-5D-5L, ICECAP-A) at 3 and 12 months following surgery. It is anticipated that the majority of women will leave hospital within the first week postoperatively, therefore any participant with a device and internet access can consent to be contacted directly by email and prompted to answer the questionnaires directly onto the secure online database, REDCap. If they do not want electronic questionnaires, or do not have internet access via a suitable device (e.g iPhone or other handheld device/phone, copies will be sent by post. Patients will be asked at the beginning of the study (when signing their consent form) whether they would like to complete questionnaires online or paper. Reminders will be sent by the research team to complete questionnaires if there has been no response from the patient after 1 month. Data regarding additional cancer treatments each patient undergoes (so-called “adjuvant” treatments including: chemotherapy, radiotherapy or hormone tablets will also be recorded. Decisions regarding this treatment are usually made within a few weeks of surgery. This data will be collected at 3 months by clinical or case note review depending on local practice.

Data collection for interview study:
Patients in the cohort study will be asked if they are willing to be contacted to participate in the interview study at the time of signing the consent form. A sample of patients will be contacted by e-mail or letter and invited to participate in the interview study. They will be sent an interview study PIL and a consent form. Patients agreeing to participate in the interview study will be asked to return their consent form either by post or e-mail in a prepaid envelope provided and to provide contact details to allow an interview to be arranged. The research team will contact consenting participants to arrange a telephone interview at a date and time that is convenient for them. Interviews are anticipated to last approximately 60 minutes.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Outcomes relate to the feasibility of identifying and recruiting patients offered different approaches to Oncoplastic Breast Conservation Surgery (OPBCS) to avoid mastectomy and to explore the utility of the BREAST Q as an outcome measure for the main study.

1. Centres and surgeons:
1.1. The provision of OPBCS in breast and plastic surgical units across the UK and the numbers of surgeons currently offering patients OPBCS (volume displacement (therapeutic mammaplasty [TM]) and replacement (local perforator flaps, [LPF] techniques) as an alternative to mastectomy measured using data from the ANTHEM national practice questionnaire (NPQ), collected at the beginning of the study.
1.2. The approximate numbers of OPBCS (TM and LPF) procedures offered to patients who would otherwise require a mastectomy at local centres across the UK (to inform the feasibility of

a future large-scale study) measured using data from the ANTHEM screening and enrolment logs at the screening and recruitment stage of the study.
1.3. The variations in the indications and contraindications for different approaches to OPBCS (TM and LPF) and immediate breast reconstruction (implant-based; pedicled and free-flaps) across the UK in particular what patient (e.g. age, body mass index, smoking), tumour (e.g. size; multifocality) and treatment (neoadjuvant therapy; need for post-mastectomy radiotherapy) factors influence decision making (to estimate the potential magnitude of benefit of OPBCS in the mastectomy population i.e. portion of patients eligible for OPBCS who would not be suitable for immediate breast reconstruction), measured using data collected from study case report forms at baseline, 3 months and 12 months post-surgery.
1.4. The coding of OPBCS procedures to inform the feasibility of undertaking data linkage in the future study, measured from process mapping and data collected from study care report forms at the beginning of the study.

2. Participants and pathways:
1.1. The proportion of patients offered OPBCS as an alternative to mastectomy at participating sites and types of OPBCS offered, measured using study case report forms at baseline
1.2. The proportion of patients suitable for OPBCS that elect to undergo the procedure and what proportion choose to undergo mastectomy +/- IBR and the reasons for this, measured using clinical case report forms at baseline
1.3. The proportion of patients undergoing OPBCS in whom mastectomy is avoided and outcomes for patients in whom it is not, measured using clinical case report forms at baseline, 3 months and 12 months post-surgery
1.4. Patients' views of OPBCS and mastectomy +/- IBR to understand decision-making for surgery and potential barriers to informed choice, measured using patient qualitative interviews at 3-12 months post-surgery
1.5. The variations in the patient pathway (e.g. use of neoadjuvant treatment; day-case vs inpatient procedures; simultaneous vs delayed contralateral symmetrisation) to inform optimal timing of outcome assessments in the main study, measured using data from study case report forms at baseline, 3 months and 12 months post-surgery

3. Outcome and measures:
3.1. Validity of existing tools (breast cancer core domains of the BREAST-Q) in the OPBCS population and whether these subscales are directly comparable across patient groups, measured using patient interviews at 3-12 months post-surgery
3.2. Whether subscales of the BREAST-Q measure key outcome domains using triangulation with established measures of normality (ICECAP-A) and quality of life (EQ-5D-5L) measured at baseline and 3 months and 12 months post-surgery
3.3. Whether the BREAST-Q subscales reflect key core outcome domains (satisfaction with breasts; emotional well-being and physical well-being), are adequate and whether the individual items are acceptable to patients, measured using patient qualitative interviews at 3 -12 months post-surgery
3.4. Comparative clinical and patient-reported outcome data to inform sample size calculations for the main study, measured using clinical case report forms and patient questionnaires BREASTQ, EQ-5D-5L and ICECAP-A at baseline and 3 months and 12 month post-surgery
3.5. The feasibility of collecting electronic PROMs in the main study, measured using BREAST Q, EQ-5D-5L and ICECAP-A at baseline, 3 months and 12 months post-surgery
3.6. The feasibility of using a novel 'targeted micro-costing' approach based on patient pathway mapping to collect resource use data on different procedures at multiple sites in the main trial, measured using data gathered from electronic notes, medical records and routine data throughout the study

Key secondary outcome(s)
Clinical and patient-reported outcomes measures (PROMs) measured at baseline, 3 months and 12 months post-surgery:
1. Satisfaction with breasts measured using BREAST Q
2. Psychosocial well-being measured using BREAST Q
3. Chest physical well-being measured using BREAST Q
4. Sexual well-being measured using BREAST Q
5. Quality of life measured using EQ-5D-5L
6. Normality measured using ICECAP-A

Completion date
31/03/2024

Eligibility

Key inclusion criteria
1. Female patients over 18 years of age
2. Invasive breast cancer or ductal carcinoma in situ (DCIS) not considered suitable for standard BCS or simple level 1 techniques
3. Assessed by the breast cancer (and oncoplastic, if applicable) multidisciplinary team (MDT) and the operating surgeon as being suitable candidates for either OPBCS (either TM or LPF) as an alternative to a mastectomy OR mastectomy with or without an immediate breast reconstruction (using any technique) and offered both OPBCS and mastectomy options
4. No restrictions will be placed on the size of the tumour as decisions on the suitability of a patient for simple BCS will be based on assessments of the size of the tumour relative to the overall size of the breast and its position within the breast rather than on explicit size criteria

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Female

Total final enrolment
361

Key exclusion criteria
1. Women offered OPBCS for reasons other than to avoid mastectomy (e.g. quality of life if large breasted)
2. Women offered standard BCS or level 1 procedures only
3. Women not able or willing to give informed consent

Date of first enrolment
01/12/2020

Date of final enrolment
31/12/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
North Bristol NHS Trust
Southmead Hospital
Westbury-on-Trym
Bristol
United Kingdom
BS10 5NB

Study participating centre
Royal Liverpool and Broadgreen University Hospitals NHS Trust
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Nottingham University Hospitals NHS Trust
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
University Hospitals Coventry and Warwickshire NHS Trust
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Sponsor information

Organisation
University of Bristol

ROR
https://ror.org/0524sp257

Funder(s)

Funder type
Charity

Funder Name
Above & Beyond

Funder Name
Association of Breast Surgery

Alternative Name(s)
British Association of Surgical Oncology, ABS, BASO

Funding Body Type
Government organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		24/12/2024	17/01/2025	Yes	No
Protocol article		16/04/2021	19/04/2021	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Qualitative results	12/06/2024	17/06/2024	Yes	No