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Therapeutic mammaplasty is a safe and effective alternative to mastectomy with or without immediate breast reconstruction

Shelley Potter[1,2], Adam Trickey[1], Tim Rattay[3], Rachel L O'Connell[4], Rajiv Dave[5], Elizabeth Baker[6], Lisa Whisker[7], Joanna Skillman[8], Matthew D. Gardiner[9,10], R Douglas Macmillan[7], Chris Holcombe[11] on behalf of the TeaM and iBRA-2 Steering Groups[§], the Breast Reconstruction Research Collaborative[§] and the Mammary Fold Academic and Research Collaborative[§]

[1]Population Health Sciences, Bristol Medical School, 39 Whatley Road, Clifton, Bristol, BS8 2PS, UK, [2]Bristol Breast Care Centre, North Bristol NHS Trust, Southmead Road, BS10 5NB, UK, [3]Cancer Research Centre, University of Leicester, Clinical Sciences Building, Leicester Royal Infirmary, Leicester LE2 7LX, UK, [4]The Royal Marsden NHS Foundation Trust, Downs Road, Sutton, Surrey, SM2 5PT, UK, [5]Nightingale Breast Unit, Manchester University NHS Foundation Trust, Southmoor Road, Manchester, M23 9LT, UK, [6]Department of Breast Surgery, Airedale General Hospital, Skipton Road, Keighley, West Yorkshire, BD20 6TD, UK, [7]Nottingham Breast Institute, Nottingham University Hospitals NHS Trust, Hucknall Road, Nottingham NG5 1PB, UK, [8]Department of Plastic Surgery, University Hospitals Coventry and Warwickshire NHS Trust, Clifford Bridge Road, Coventry, CV2 2DX, UK, [9]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Nuffield Orthopaedic Centre, Windmill Road, Headington, Oxford, OX3 7HE, UK; [10]Department of Plastic Surgery, Frimley Health NHS Foundation Trust, Slough SL2 4HL, UK;[11]Linda McCartney Centre, Royal Liverpool and Broadgreen University Hospital, Prescot Street, Liverpool, L7 8XP, UK

[§]Members of the iBRA-2 and TeaM Steering Groups, the Breast Reconstruction Research Collaborative and Mammary Fold Academic and Research Collaborative are PUBMED citable collaborators and are listed at the end of this manuscript.

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Corresponding author: Shelley Potter - Bristol Centre for Surgical Research, Population Health Sciences, Bristol Medical School. 2.14 Canynge Hall, Whatley Road, Clifton, Bristol, BS8 2PS.
E-mail Shelley.Potter@bristol.ac.uk, Tel: (+44) 0117 287218

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Abstract

Introduction: Therapeutic mammaplasty (TM) may be an alternative to mastectomy but few well-designed studies have evaluated the success of this approach or compared the short-term outcomes of TM with mastectomy with or without (+/-) immediate breast reconstruction (IBR). Data from the national iBRA-2 and TeaM studies were combined to compare the safety and short-term outcomes of TM and mastectomy +/- IBR

Method: The subgroup of patients in the TeaM study who underwent TM to avoid mastectomy were identified and demographic, complication, oncology, and adjuvant treatment data compared to patients undergoing mastectomy +/- IBR in the iBRA-2 study. The primary outcome was the percentage of successful breast conserving surgery (BCS) in the TM group. Secondary outcomes included post-operative complications and time to adjuvant therapy.

Results: 2,916 patients; (TM n=376; mastectomy n=1532; IBR n=1008; [implant-based n=675; pedicled-flap n=105; free-flap n=228]) were included in the analysis. Patients undergoing TM were more likely to be obese and to have undergone bilateral surgery than those undergoing IBR. However, patients undergoing mastectomy +/- IBR were more likely to experience complications than the TM group (TM n=79, 21.0%; mastectomy n=570, 37.2%; mastectomy and IBR n=359, 35.6%; $p<0.001$). Breast conservation was possible in 87% of TM patients. TM did not delay adjuvant treatment.

Conclusion: TM may allow high-risk patients who would not be candidates for IBR to safely avoid mastectomy. Further work is needed to explore the comparative patient-reported and cosmetic outcomes of the different approaches and to establish long-term oncological safety.

Key words: Therapeutic mammaplasty; breast cancer; mastectomy; breast reconstruction; cohort study; collaborative

Introduction

Breast conserving surgery (BCS) and adjuvant radiotherapy is the preferred option for many women with breast cancer[1]. However, standard BCS often results in poor cosmetic outcomes which can adversely impact women's quality of life[2-6]. Volume of tissue resected, in particular, is a predictor of poor outcome[7 8]. Mastectomy is therefore often recommended for patients with large or multiple tumours and currently 40%[9] of the 55,000 women[10] diagnosed with breast cancer every year undergo this form of treatment in the UK. Although national guidelines[11] recommend that immediate breast reconstruction (IBR) should be routinely offered in this group, only a quarter of women undergoing mastectomy currently receive immediate reconstruction[12 13]. Many thousands of women therefore have a simple mastectomy which can dramatically impact their psychological well-being[14 15].

Therapeutic mammaplasty (TM) is a procedure that combines a wide local excision to remove the cancer with breast reduction and mastopexy techniques to reshape the remaining tissue[16 17]. These techniques can extend the boundaries of BCS by allowing adequate resection of large or multifocal cancers in patients with medium/large or ptotic breasts without compromising oncological outcomes[18-20]. This may offer women a safe and effective alternative to mastectomy, with or without reconstruction.

There is however, limited high-quality comparative evidence to support the benefits of TM as an alternative to mastectomy with or without IBR. Single-centre case-series suggest that overall, patients undergoing TM may report better quality of life than those undergoing mastectomy and IBR[21 22] and there is emerging evidence to suggest that TM may be a cost-effective alternative to mastectomy and immediate implant-based[23] and free-flap reconstruction[24] in a North American setting.

While these results are promising, there remains a need for high-quality research to establish the benefits of TM as a safe and effective alternative to mastectomy with or without IBR[25]. Randomised controlled trials (RCTs) are ideally needed but RCTs in this context are not feasible due to patient and surgeon preference[26-28]. A large-scale multicentre prospective cohort study is therefore required to compare the clinical and patient-reported outcomes of TM and mastectomy and to establish the cost-effectiveness of the approach. Before such a study can be planned, however, preliminary work is needed to explore what proportion of patients could potentially avoid mastectomy by undergoing a TM procedure and the relative safety of this approach. Two large trainee-led prospective cohort studies

have evaluated the short-term outcomes of TM[29] and mastectomy with and without IBR[30] separately. In the current study, we undertook a pooled analysis to evaluate the potential for TM to successfully avoid mastectomy and compare the short-term outcomes of the different techniques.

Methods

The methods for the iBRA-2[30 31] and TeaM[29 32] prospective cohort studies have been reported previously. Both studies collected identical data items during an overlapping time period and 37 centres participated in both studies supporting the validity of a pooled analysis.

In brief, all breast and plastic surgical units performing mastectomy with and without IBR and TM were invited to participate in the iBRA-2 and TeaM studies respectively via the professional associations (Association of Breast Surgery [ABS] and British Association of Plastic Reconstructive and Aesthetic Surgeons [BAPRAS] and the breast and plastic surgery collaborative research networks (Reconstructive Surgery Trials Network [RSTN] and the Mammary Fold Academic and Research Collaborative [MFAC]).

Consecutive patients undergoing mastectomy with or without IBR for invasive or pre-invasive breast cancer between July and December 2016 at participating centres were recruited prospectively to the iBRA-2 study.

Patients undergoing TM defined as 'the oncoplastic application of breast reduction or mastopexy techniques including removal of skin to reduce the skin envelope to treat invasive or pre-invasive (ductal carcinoma in situ; DCIS) breast cancer using breast conserving surgery'[32] between 1st September 2016 and 30th June 2017 at participating centres were recruited to the TeaM study. Surgeon-reported indication for offering TM was recorded prospectively and only the subgroup of patients offered TM 'to avoid mastectomy' were included in the current study.

Patients in both studies were identified from multidisciplinary team (MDT) meetings; operating diaries and clinics. Demographic and operative data were collected prospectively and oncological data including adequacy of resection for TM patients and recommended adjuvant treatments were obtained from post-operative MDT meetings. Date of first adjuvant treatment was obtained by review of appropriate clinical information systems. Complications, readmissions and re-operations were

collected prospectively by clinical or case-note review depending on whether the patient needed to attend for follow up. REDCap[33] data capture software was used for data collection in both studies.

Both studies were classified as service evaluations according to the NHS Health Research Authority online decision tool http://www.hra-decisiontools.org.uk/research/ so ethical approval was not required. Each participating centre was required to register the study locally and obtain local governance approvals prior to entering patients in the studies.

Primary and secondary outcomes

Primary and secondary outcomes in iBRA-2 and TeaM were selected based on current best practice[34] and the National Institute of Health and Care Excellence (NICE) guidelines[11]. Standardised definitions were used across both studies allowing for meaningful pooling of the data[29 30].

The primary outcome for this study was the percentage of patients successfully avoiding mastectomy in the TM group. Secondary outcomes were major and minor complications and time to adjuvant therapy. Major complications were defined as complications requiring readmission or re-operation and minor complications were those that were managed conservatively. Time to adjuvant treatment was defined as time from last cancer surgery to first dose of chemotherapy or first fraction of radiotherapy. Adequate margins were defined in the TeaM study according to local policy[29 32].

Quality assurance

For quality assurance purposes, the lead investigator at each site was asked to identify an individual not previously involved in data collection to independently validate 5-10% of the data. Similar procedures were used in both studies and are consistent with those used in other collaborative projects[35].

Statistical analysis

Data from patients undergoing mastectomy with and without IBR in the iBRA-2 study and the subgroup of patients undergoing TM to avoid mastectomy in the TeaM study were combined to compare the short-term clinical and oncological outcomes of the different procedure types.

Descriptive summary statistics were calculated for each variable for the pooled cohort overall and split by procedure type (therapeutic mammaplasty; mastectomy only; mastectomy and immediate breast

reconstruction). Categorical data were summarised by counts and percentages and continuous data by median, interquartile range (IQR), and range. Procedure groups were compared using Chi-squared and Kruskall-Wallis tests. Complications and oncological data were summarised by patient and procedure.

Univariable and multivariable logistic regression were used to explore clinicopathological variables hypothesised to be associated with complications based on the literature and expert opinion. These included patient and procedure-related factors namely age, body mass index (BMI), smoking status, American Society of Anaesthesiologists' (ASA) grade; diabetes, ischaemic heart disease (IHD); other comorbidities, neoadjuvant chemotherapy (NAC), unilateral vs bilateral surgery to the breast, axillary surgery (none; sentinel node biopsy [SNB]; axillary node clearance [ANC]), and procedure type (therapeutic mammaplasty; mastectomy only; mastectomy and immediate breast reconstruction).

Time to adjuvant treatment was calculated for all patients and by procedure type with adjuvant therapy as the event. Kaplan-Meier analyses, univariable and multivariable Cox survival models with time to adjuvant therapy split by procedure type were created including patient age; BMI, diabetes, IHD, other co-morbidities, smoking status (non-smoker; ex-smoker and current smoker); neoadjuvant chemotherapy, ASA grade and unilateral vs. bilateral surgery and presence of post-operative complications (none, minor and major) as the variables of interest, clustered by centre. The Kaplan Meier curves were curtailed at 150 days when only 14 patients remained in the analysis.

STATA 15 (STATA Inc, Texas) was used for all analyses.

Results

The TeaM study[29] recruited 376 patients undergoing 385 TM procedures to avoid mastectomy from 50 centres in the UK and Europe between 1st September 2016 and 30th June 2017.

The iBRA-2 study[30] recruited 2,540 patients undergoing mastectomy with (n=1008) and without (n=1564) IBR from 76 centres between 1st July and 31st December 2016. Of the 1008 patients receiving IBR, 675 patients underwent 773 implant-based reconstructions; 105 patients received 106 pedicled-flaps and 228 patients underwent 247 free-flap reconstructions. Data from these cohorts were pooled and 2,916 patients were included in the combined analysis.

Patient demographics

Table 1 summarises patient demographics by procedure type. Patients undergoing TM were older than patients undergoing IBR. They also had higher BMIs and were more likely to have undergone simultaneous bilateral surgery than patients in the other groups (table 1). Participant demographics by type of reconstruction performed are summarised in supplementary table 1.

Post-operative complications

Post-operative complications by procedure type are summarised in table 2 with details of complications by type of IBR and per breast summarised in supplementary tables 2 and 3 respectively. Complications following TM were significantly lower than those observed following mastectomy with or without immediate reconstruction. Only 1 in 5 (n=79, 21.0%) patients undergoing TM experienced a complication compared with approximately a third of patients undergoing mastectomy with (n=359, 35.6%) or without (n=570, 37.2%) IBR (table 2). Univariable regression identified age, BMI, diabetes, IHD, having other co-morbidities, being an ex-smoker, ASA grade, and undergoing an ANC as risk factors associated with developing a complication. Compared to undergoing a simple mastectomy without reconstruction, TM was associated with a reduced risk of complications (odds ratio [OR] 0.44, 95% confidence interval [CI] 0.31-0.63) but immediate reconstruction did not increase the risk (table 3). Age, BMI, other co-morbidities being an ex-smoker and undergoing an ANC remained strongly associated with complications in the multivariable model and current smoking and bilateral surgery were also identified as independent risk factors. Undergoing a TM remained strongly associated with a lower risk of complications (adjusted odd ratio [aOR] 0.46, 95% CI 0.30-0.71) in the multivariable model (table 3).

Major complications following TM were uncommon with just 2% (n=8) of patients requiring readmission or reoperation for a complication of their surgery. This compares with 5% (n=76) of patients undergoing mastectomy only and 14% (n=145) of patients receiving immediate reconstruction (table 2). Age, undergoing immediate reconstruction and bilateral surgery were associated with major complications in the univariable analysis (table 3). All of these variables, except age, remained strongly associated with major complications in the multivariable model and smoking, diabetes, having other co-morbidities and BMI were also identified as independent risk factors in this model. Immediate breast reconstruction (aOR 4.02, 95% CI 2.23-7.25) was the strongest predictor of major

complications in the multivariable model with undergoing TM associated with a lower risk of experiencing a major complication in both univariable (OR 0.41, 95% CI 0.20-0.84) and multivariable models (aOR 0.36, 95% CI 0.15-0.85) (table 3). Univariable and multivariable analysis of risk factors for any and major complications by type of reconstruction performed are summarised in supplementary table 4.

Oncological outcomes

Table 4 summarises post-operative histology by the procedure performed. TM was performed less frequently for pure DCIS than mastectomy with immediate reconstruction. Approximately a third of all patients (n=956, 32.0%) had multifocal disease, including those who had TM (n=120, 31.2%). The median invasive and whole tumour size (WTS) were similar in in the TM and immediate reconstruction groups. Patients undergoing IBR were more likely to be node negative than patients in the other groups (table 4).

The 376 patients in the TeaM study underwent 385 TM procedures for cancer. Of these, 305 (79.2%) had clear margins according to local guidelines at the first operation; 71 (18.4%) had involved or close margins and the margin status was unknown in 9 (2.3%) cases. In the group for whom margins were not adequate, 30/71 (42.3%) had a successful re-excision; 33 (46.5%) underwent completion mastectomy. The outcome of the remaining 8 (11.3%) cases was unknown. Overall, 335/385 (87.0%) TM procedures resulted in successful breast conservation. Notably, of the 33/71 (46.5%) who required a completion mastectomy, only 11 (32.3%) had an IBR within the study period (figure 1).

Time to adjuvant therapy

Adjuvant therapy was recommended in the majority of patients in the TM group (n=343, 91.2%) compared with less than half (n=431, 42.8%) in those undergoing immediate reconstruction (table 5). There was no significant difference in the median time to adjuvant treatment across the treatment groups (table 5). Longer time to adjuvant treatment was associated with the development of complications (minor complications, aHR 0.85, 95% CI 0.74-0.97; major complications aHR 0.63, 95% CI 0.51-0.78) and obesity (aHR 0.75, 95% CI 0.64-0.88) in this analysis (table 6). Further details of time to adjuvant treatment and risk factors for delays to adjuvant treatment by type of IBR are summarised in supplementary tables 5 and 6 respectively.

Discussion

This large prospective study suggests that TM may allow the majority of women considered suitable for the procedure to successfully avoid mastectomy and that overall, TM is associated with fewer complications than mastectomy and immediate reconstruction. TM may particularly improve outcomes for patients considered high-risk (current smokers, high BMI) who may not be offered immediate reconstruction because of their risk profile. Reducing risk of complications with breast cancer surgery is an important consideration as complications have been shown to result in delays to adjuvant therapy[30] which could adversely impact on long-term oncological outcomes and compromise survival.

The rate of successful breast conservation in this subset of patients offered TM to avoid mastectomy was higher than may be expected based on previous systematic reviews that demonstrate higher completion mastectomy rates in patients with smaller (T1) tumours[36-38]. The patients in the current study had larger tumours, validating the inclusion criteria that the TM group were offered this option as an alternative to mastectomy. Despite this, the completion mastectomy rate in the current study was less than 10%. This is consistent with previous findings[39] and suggests that TM is a viable option for allowing women to avoid mastectomy. Recent retrospective data from a large population-based study suggests that oncoplastic breast conservation may occupy a niche between standard BCS and mastectomy[40]. Our study suggests that it should possibly be promoted as an alternative to mastectomy and reconstruction.

Currently, the recommendation for mastectomy is clearly defined for those with extensive disease. Likewise, the role of breast conservation is clear for those with relatively small disease foci who can be anticipated to achieve an acceptable cosmetic outcome. There is, however, a widening middle ground in which the extended role of breast conservation offered by oncoplastic surgery can provide an alternative to mastectomy. Patients suitable for TM will have breast ptosis and be accepting of being smaller breasted and, usually, undergoing bilateral surgery. The extended role of breast conservation has been fuelled by neoadjuvant therapy, better understanding of tumour biology, and increasingly widespread oncoplastic surgical training with the result that surgeons with an understanding of reduction and mastopexy techniques are more likely to routinely consider and offer these options[41].

Good cosmetic outcomes are reported[42] and there is emerging data to suggest that avoiding mastectomy and IBR may be associated with improvements in quality of life[21].

At the limits of the spectrum the term 'extreme oncoplasty'[21] has even emerged to describe resections of large tumours (T3), multifocal or multicentric disease that would traditionally have been recommended mastectomy[43]. Single-centre series are generally small but mostly show promising results with low rates of conversion to mastectomy although long-term oncological outcomes are lacking[42-44].

The rate of IBR in patients requiring completion mastectomy following unsuccessful TM in the current study is low. This may be because they were considered high-risk and therefore not good candidates for IBR but may also reflect the anticipated need for post-mastectomy radiotherapy. Evidence suggesting oncological benefits of postmastectomy radiotherapy in patients with one to three positive lymph nodes[45] means that many more patients are now offered treatment. Radiotherapy has been shown to adversely impact both clinical and patient-reported outcomes of immediate breast reconstruction[46], particularly with implants[47] and despite recent updated national guidance[48], many surgeons would not offer immediate reconstruction if postmastectomy radiotherapy is likely to be required[13]. Avoiding mastectomy may therefore have particular benefits in this group but work is needed to explore this further.

This study adds to the evidence-base to support the benefits of TM compared to mastectomy but has limitations. Firstly, this is a pooled analysis of two separate studies, and it is not clear to what extent these groups are directly comparable. In particular, although the overall post-operative tumour size and proportion of patients with multifocality in both groups was similar, we did not assess how many patients in the iBRA-2 cohort would be technically suitable for TM for morphological (e.g. small, non-ptotic breasts) or tumour related (e.g. multicentric disease) reasons or the proportion who would elect to undergo TM to avoid mastectomy. A future prospective study in patients offered all surgical options will therefore be needed to directly compare the outcomes of different operative procedure types and explore patient decision-making. Only short-term outcomes of TM such as complications and time to adjuvant therapy have been considered in this study. While these data are promising, further long-term studies will be needed to prospectively assess the oncological safety, particularly of more extreme oncoplastic resections as well as the patient-reported and cosmetic outcomes and cost-

effectiveness of as TM compared to mastectomy with and without immediate reconstruction in directly comparable patient groups.

A future study directly comparing TM as an alternative to mastectomy with and without IBR in patients with large, multifocal and/or multicentre tumours is the next step in generating the evidence needed to change practice and improve outcomes for patients. Recent experience with the MIAMI feasibility study[49] (ISRCTN17987569) has demonstrated that an RCT in this context is unlikely to be feasible. A well-designed multicentre prospective study including validated patient-reported outcomes and a cost-effectiveness analysis is needed but preliminary work will be required to determine whether it is possible to identify and recruit patients to all treatment groups if fully informed choice is offered and to establish the optimal study design. A key issue is the selection of an appropriate patient-reported outcome assessment tool. The BREAST-Q[50] includes core breast cancer modules with four subscales (satisfaction with breasts, psychosocial well-being; physical well-being and sexual well-being) for use in patients with breast cancer having BCS and mastectomy with and without immediate reconstruction. These scales are comparable but to date, only one study has used the BCS 'satisfaction with breasts' scale in patients undergoing TM procedures[51]. Work is therefore needed to determine whether it is valid in this group. Qualitative work is also needed to explore patients' decision making for, and experiences of, different types of surgery and factors influencing their choice. This will provide important information to help inform shared decision-making consultations in the main study and allow patients to make the choice that is right for them.

This study shows that oncoplastic breast conservation is likely to offer better outcomes than mastectomy with or without breast reconstruction for many women, and together with emerging evidence to support the long-term oncological safety[18 20 52] of oncoplastic breast conservation adds further support to the use of therapeutic mammaplasty as an alternative to mastectomy. Further work is now needed determine whether TM improves patient-reported outcomes and is cost-effective compared to mastectomy with and without immediate breast reconstruction before definitive recommendations for best practice can be made.

Conflict of interest

The authors have no conflicts of interest to declare

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Authors' contributions

SP, RDM, LW and CH conceived the study design (pooled analysis); SP contributed to the design, conduct, analysis of the data, interpretation of the results and wrote the first draft of the paper. AT performed the analysis, contributed to data interpretation and drafted the manuscript. RLOC, TR, EB, RVD contributed to the study design and data collection for iBRA-2 and TeaM; MDG and JS contributed to study design and interpretation of the data. All authors read and approved the final manuscript.

Members of the iBRA-2 steering group are (in alphabetical order) Nicola LP Barnes, Jane Blazeby, Elizabeth Conroy, Rajiv V Dave, Matthew D Gardiner, Adrian Harnett, Chris Holcombe, Ciara O'Brien, Rachel L O'Connell, Shelley Potter, Tim Rattay, Joanna Skillman, and Paula Williamson.

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Local iBRA-2 investigators (alphabetically by centre) and members of the Breast Reconstruction Research Collaborative are PUBMED citable collaborators in this study and were: **Aberdeen Royal Infirmary, NHS Grampian**; Alain Curnier, Amir Tadros, Ivan Depasquale, Yazan A Masannat Elizabeth Smyth, Mairi Fuller, Roger Bourne, Steven Heys, Ishrak Hamo. **Addenbrookes Hospital, Cambridge Universities NHS Foundation Trust**; Fatima Aloraifi, Laura Fopp, Radhika Bali, Sarah Bache, Sarah L Benyon, Michael S Irwin, Amit Agrawal, Charles M Malata. **Airedale NHS Foundation Trust**; Claire Murphy. **Basildon and Thurrock Hospitals NHS Foundation Trust**; Adam Misky, Dennis Wayne Chicken. **Beaumont Hospital and the RCSI**; Nassreen Abdullah, Arnold D K Hill. **Belfast City**

Hospital, Belfast Health and Social Care Trust; Carolyn Cullinane, Gareth Irwin, Stuart A McIntosh, Sigi Refsum, Samantha Sloan, Peter Mallon. **Betsi Cadwaladr University Health Board**; Chiara Sirianni, Ilyas Khattak, Chiara Sirianni. **Blackpool Teaching Hospitals NHS Foundation Trust**; Geerthan Nagachandra, Pasupathy Kiruparan, Debasish Debanth. **Breast Care Centre, North Bristol NHS Trust, Southmead Hospital, Bristol**; Simon Davey, Terry-Ann Curran, Matilda Svenning, Sasirekha Govindarajulu, Zenon Rayter, Rachel Ainsworth, Simon Cawthorn, Ajay Sahu, Sherif Wilson, Elena Prousskaia. **Breast Unit Department. University of Naples "Federico II", Naples, Italy**; Antonello Accurso, Nicola Rocco, Rosa Di Micco, Antonello Accurso, Gennaro Limite. **Breast Unit Department S. Maria delle Grazie ASL Na 2 Pozzuoli**; Raffaele Ceccarino, Raffaele Liccardo, Guido Coco. **Broomfield Hospital, Mid Essex Hospital Services NHS Trust**; Metin Nizamoglu, Mary Morgan, Venkat Ramakrishnan. **Cannizzaro Hospital, Catania**; Giuseppe Catanuto. **Castle Hill Hospital, Hull and East Yorkshire Hospitals NHS Trust**; Alex Wilkins, Penelope McManus, Peter Kneeshaw, Kartikae Grover, Tapan Mahapatra, Brendan Wooler, Bilal Elahi, Naila Ihsan. **Charing Cross Hospital, Imperial College Healthcare NHS Trust**; Alexandra Bucknor, Dimitris Reissis, Judith Hunter, Simon Wood, Navid Jallali, Francis P Henry, Liaquat S Verjee, Jason Lee. **Chesterfield Royal Hospital NHS Foundation Trust**; Shazia M Khan, Iman Azmy, Julia Massey, Ciaran Hollywood, Michael Oluwajana. **Countess of Chester Hospital NHS Foundation Trust**; Sonia Bathla, Joanna Seward, Claudia Harding-MacKean. **Darent Valley Hospital, Dartford and Gravesham NHS Trust**; Risha Lane, Kothandaraman Murali, Bashishta Biswas, Pawel Trapszo, Seema Seetharam. **Dorset County Hospital NHS Foundation Trust**; Katy Kennedy, Louise Alder, Tomasz Graja. **East Cheshire NHS Trust**; Khalid Amin, Jalal Kokan, Chandeena Roshanlall. **Edinburgh Breast Unit, Western General Hospital, NHS Lothian**; Emma Gill, Dhananjay Kulkarni, JM Dixon, Oliver Young, Talha Saleem. **Glasgow Royal Infirmary, NHS Greater Glasgow and Clyde**; M Biddle, Marie Kearns, Eva Weiler-Mithoff, Ben Chew, Andy Malyon, John Scott, David McGill, Iain Mackay. **Glenfield Hospital, University Hospitals of Leicester**; Salena Bains, Sara Barrows, Tim Rattay, Simon Pilgrim, Sheila Shokuhi, Kelly Lambert, Frances Kenny, Kalliope Valassiadou, Monika Kaushik, Jaroslaw Krupa, Dimitris Dragoumis. **Good Hope Hospital, Heart of England NHS Foundation Trust**; Quratul ain, Pavlos Lampropoulos, Sarah Moss, Haitham Khalil, Anwar Haq, Balapathiran Balasubramanian. **Guy's and St Thomas' NHS Foundation Trust**; Petros Charalampoudis, Hisham Hamed, Ashutosh Kothari, Tibor Kovacs, Michael Douek. **Harrogate and District NHS Foundation Trust**; Iftikhar Mehmood,

Biswajit Ray, Matthew Adelekan. **Homerton University Hospital NHS Foundation Trust**; Laura Humphreys, Salim Tayeh, Christina Choy, Laila Parvanta. **Istituto Oncologico Veneto, Padova, Italy**; Silvia Michieletto, Tania Saibene. **James Paget University Hospitals NHS Foundation Trust**; James O'Brien, Sue Down, Sarah Downey, Jerome Pereira. **Lincoln County Hospital, United Lincolnshire Hospitals NHS Trust**; A S Sami, Anzors Gvaramadze, Jibril A Jibril, Dinesh Thekkinkattil. **Llanelli Peony Breast Unit**; S Udayasankar, Saira Khawaja, Yousef Shariaha, Simon Holt. **Luton and Dunstable University Hospital**; Ruth James, Hirah Rizki, Katharine Kirkpatrick, Duraisamy Ravichandran, Deepak Shrestha. **Maidstone and Tunbridge Wells NHS Trust**; Ellora Barua, Deepika Akolekar. **Mid Cheshire Hospitals NHS Foundation Trust**; Ahmed Hamad, Eleftheria Kleidi, Susan Hignett, Vanessa Pope, Salma Naseem. **Milton Keynes University Hospital NHS Foundation Trust**; Jennifer Isherwood, Rachel Soulsby, Amanda Taylor, Kian Chin. **Morriston Hospital, Abertawe Bro Morgannwg University Health Board**; Dai Nguyen. **Musgrove Park Hospital, Taunton and Somerset NHS Foundation Trust**; Francesca Guest, Amanda Thorne. **Nevill Hall Hospital, Aneurin Bevan University Health Board**; Valentina Lefemine. **Norfolk and Norwich University Hospitals NHS Foundation Trust**; Chris Kirchhoff, Declan C Murphy, Michelle Lo, Ruth Harcourt, Simon J Pain, Maged I Hussien, Katalin Zechmeister, E.M. Sassoon, Andrea Figus, Richard M Haywood, Rozina Ali, Susanna Alexander, Adrian Harnett, Konstantinos Geropantas, Daniel Epurescu. **North Middlesex University Hospital**; Rebecca Lewis, Oladapo Fafemi, Jasdeep Gahir, Tasha Gandamihardja. **Nottingham Breast Institute, Nottingham University Hospitals NHS Trust**; Jennett Kelsall, Nazli Muhibullah, Charlene Otieno, Fayyaz Mazari, Marta Dauria, Lisa Whisker, Douglas Macmillan, Eleanor Gutteridge, Tuabin Rasheed, Hazem Khout, Kristjan Asgeirsson, Stephen McCulley. **Ospedale Santa Chiara, University of Pisa, Italy**; Maria Donatella Mariniello, Manuela Roncella, Matteo Ghilli, Livio Colizzi, Elena Rossetti, Lo Russo Marzia, Loredana Fustaino, Alessandro Quattrini Li. **Oxford University Hospitals NHS Foundation Trust**; Kate L Harvey, Rebecca Windle, Dionysios Dennis Remoundos, Pankaj Roy, Gael MacLean, Asha Adwani. **Peterborough City Hospital, North West Anglia NHS Foundation Trust**; Elena Popa, Steven Goh, Geeta Shetty. **Poole Hospital NHS Foundation Trust**; Sarah Clark. **Portsmouth Hospitals NHS Trust**; Lorenzo Bernaudo, Avi Agrawal, Lucy Mansfield. **Princess Alexandra Hospital NHS Trust**; Sally Tebbal, Ashraf Patel, Veronica Grassi. **Queen Elizabeth Hospital Birmingham, University Hospitals Birmingham NHS Foundation Trust**; Ojas Pujji, Kathryn Hamnett, Naren Basu. **Royal Bolton Hospital, Bolton NHS Foundation Trust**;

Emily Granger, Michael Durbar, Panagiotis Pikoulas, Clare Garnsey, Philip Walker, Angela J Vollermere, Ioannis Michalakis. **Royal Devon and Exeter NHS Foundation Trust**; Robin Jones, Mina Youssef, Charlotte Ives, Mohammad Masood, Julie Dunn, Sisse Olsen, Douglas Ferguson, Rachel Tillett. **Royal Free London NHS Foundation Trust**; Anna Allan, Alex Woollard, Rebecca Canny, Alexander Woollard, Afshin Mosahebi, Stephen Hamilton, Shadi Ghali,Daniel Marsh, Jagdeep Chana, Nilesh Sojitra, Ibby Younis. **Royal Hampshire County Hospital, Hampshire Hospitals NHS Foundation** Trust; Dick Rainsbury, Natalie Chand, Vasileios Kalles, Anne Stebbing, Kevin Harris, Siobhan Laws. **Royal Liverpool and Broadgreen University Hospitals NHS Trust**; Chris Holcombe, Anne Tansley, Geraldine Mitchell, Emma de Sousa, Julia Henderson, Mysore Chandrashekar. **Royal Marsden NHS Foundation Trust**; Bernadette Pereira, Chloe Constantinou, Dalia Elfadl, Foivos Irakleidis, Izaro Hernan, Miriam Byrne, Natalie To, Rachel O'Connell, Jennifer Rusby, Peter Barry, Katerine Krupa, William Allum, Fiona MacNeill, Nicola Roche, Gerald Gui, Kelvin Ramsey, Paul Harris, Stuart James, Kieran Power. Royal United Hospitals Bath NHS Foundation Trust; Shelley Potter, Richard Sutton, Jamie McIntosh, Nicola Laurence. **Royal Victoria Infirmary, Newcastle Upon Tyne Hospitals NHS Foundation Trust**; Louise MacLennan, Robert Milligan, Henry Cain, Adam Critchley, Joe O'Donoghue, Loraine Kalra, Nick Collis. **Salisbury NHS Foundation Trust**; Gina Weston-Petrides, Roanne Fiddes, Victoria Brown, Anna Aertssen, Diana Slade-Sharman, Mansoor Khan, Caroline McGuiness. **Sant'Andrea Hospital of Rome**; Vittoria Amorosi, Santanelli di Pompeo Fabio. **St Bartholomew's Hospital, Barts Health NHS Trust**; Georgios Exarchos, Natasha Jiwa, Jennifer Hu, Serena Ledwidge, Laura Johnson, Anthony Peel, Naseem Dhooma. **St Vincent's University Hospital, Dublin**; Eric Farrell, Liam Devane, Ruth Tevlin, Enda McDermott, Ruth Prichard, Denis Evoy, Jane Rothwell, James Geraghty, Colin Morrison, Catriona Lawlor. **St. James University Hospital, The Leeds Teaching Hospitals NHS Trust**; Fiona Langlands, Lauren Taylor, Philip Turton, Raj Achuthan, Kieran Horgan, Shireen Mckenzie, Brian Hogan, Mark Lansdown, Channegowda Navin. **The Ipswich Hospital NHS Trust**; Liz Sherwin, Caroline Mortimer, Neeraj Garg. **The Mid Yorkshire Hospitals NHS Trust**; Rahma Adam, Tahera Arif, Zbigniew Kryjak, Deedar Ali, Ravi Sowdi. **The Royal Wolverhampton NHS Trust**; Elena Fage, Senthurun Mylvaganam, Pilar Matey, Raghavan Vidya, Tapan Sircar. **University Hospital of North Tees**; Oubida Asaad, Pud Bhaskar, Matei Dordea. **University Hospital of South Manchester**; Ada Chrysafi, Damian McCartan, Rajiv Dave, Rachel Foster, Rebecca Wilson, Sylvia Okwemba, Yousef Majeed, Ciara O'Brien, Vinod Mathen, John Murphy,

Nicola Barnes, Ashu Gandhi, James Harvey, Cliona C Kirwan, Richard Johnson. **University Hospitals Coventry & Warwickshire**; Krupali Patel, Maria Dalmau Ribas, Natali Vigneswaran, Tom Challoner, Joanna Skillman, Alan Park, Maged Rizkalla, Abigail Tomlins, Kat McEvoy. **University Hospitals of North Midlands NHS Trust**; Sadaf Jafferbhoy, Soni Soumian, Sankaran Narayanan, Robert Kirby. **West Hertfordshire Hospitals NHS Trust**; Sladana Bajrusevic, Joseph Maalo, Michalis Charalambous, Lee Min Lai, Kelvin Chong , Simon Thomson, Sherif Monib. **Whiston Hospital, St Helens and Knowsley Teaching Hospitals NHS Trust**; Leena Chagla, Riccardo Audisio, Rieka Taghizadeh, Azhar Iqbal. **Wirral University Teaching Hospital NHS Foundation Trust**; Karen James, Maria Callaghan, Shabbir Poonawala, Jonathan Lund, Raman Vinayagam. **Worcestershire Acute Hospitals NHS Trust**; Sadaf Jafferbhoy, Steven Thrush, Rachel Bright Thomas, Michelle Mullan, Jevan Taylor. **York Teaching Hospital NHS Foundation Trust**; Ryo Yoshimura, Tom Mathew, Ben Mancey Jones, Kailas Munot, Rana Nasr, Jenny Piper, Deena El-Sharief. **Zagazig University Hospital, Egypt**; Mohammed Mustafa.

Local TeaM investigators (alphabetically by centre) and members of the Mammary Fold Academic and Research Collaborative were: **Aberdeen Royal Infirmary, NHS Grampian**: Caitlin MacLeod, Elizabeth Smyth, Ivan Depasquale, Mairi Fuller, Nina Saeed, Yazan Masannat. **Addenbrookes Hospital, Cambridge Universities NHS Foundation Trust:** Amir Tan Mohd-Amin, Amit Agrawal. **Belfast City Hospital, Belfast Health and Social Care Trust:** Gareth Irwin, Sam Sloan, Sigi Refsum, Stuart McIntosh. **Breast Care Centre, North Bristol NHS Trust, Southmead Hospital, Bristol:** Abdulla Ibrahim, Ajay Sahu, Sasirekha Govindarajulu, Simon Cawthorn. **Breast Unit Department. University of Naples "Federico II", Naples, Italy:** Antonello Accurso. **Brighton and Sussex University Hospitals NHS Trust:** Rathi Rathinaezhil. **Castle Hill Hospital, Hull and East Yorkshire Hospitals NHS Trust:** Alex Wilkins, Eiman Khalifa, Kartikae Grover, Penny McManus, Peter Kneeshaw, Tapan Mahapatra. **Chesterfield Royal Hospital NHS Foundation Trust:** Iman Azmy, Julia Massey. **Darent Valley Hospital, Dartford and Gravesham NHS Trust**: Pawel Trapszo, Risha Lane, Seema Seetharam. **Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy:** Nicola Rocco. **East Cheshire NHS Trust:** Chandeena Roshanlall, Jalal Kokan, Khalid Amin. **Edinburgh Breast Unit, Western General Hospital, NHS Lothian:** Alexander Leeper, Dhananjay Kulkarni, JM Dixon, Oliver Young, Talha Saleem. **Forth Valley Royal Hospital, NHS Forth Valley:** Jennifer McIlhenny. **Gartnavel General Hospital, NHS Greater Glasgow and Clyde:** Andy

Malyon, James Mansell, Keith Ogsto, Laszlo Romics. **Glenfield Hospital, University Hospitals of Leicester**: Dimitris Dragoumis, Jaroslaw Krupa, Kalliope Valassiadou, Kelly Lambert, Monika Kaushik, Shelia Shokuhi, Simon Pilgrim, Xiang Wei Jonathan Lee. **Gloucestershire Hospital NHS Foundation Trust:** Asmaa Al-Allak, Clare Fowler, Eleanore Massey, Fiona Court, Richard Hunt, Sarah Vestey. **Good Hope Hospital, Heart of England NHS Foundation Trust:** Haitham Khalil. **Heatherwood and Wexham Park Hospital, Frimley Health NHS Foundation Trust:** Mohsen Elgammal. **Homerton University Hospital NHS Foundation Trust:** Laila Parvanta. **Lincoln County Hospital, United Lincolnshire Hospitals NHS Trust:** A S Sami, Anzors Gvaramadze, Dinesh Thekkinkattil. **Luton and Dunstable University Hospital:** Katharine Kirkpatrick, Ruth James. **Mid Yorkshire Hospitals NHS Trust:** Arish Noshirwani, Tehera Arif, Zbigniew Kryjak. **Milton Keynes University Hospital NHS Foundation Trust:** Amanda Taylor, Farah H Syed, Gazalla Safdar, Kian Chin, Rachel Soulsby. **Musgrove Park Hospital, Taunton and Somerset NHS Foundation Trust:** Amanda Thorne, Francesca Guest, Mohammed El-Abbar. **Ninewells Hopsital, NHS Tayside:** D.Alex Munnoch, E.Jane Macaskill, Fiona Hogg, Pauline McGee, Vassilis Pitsinis. **Northern Lincolnshire and Goole NHS Foundation Trust:** Jenny Smith, Sundus Makkiyah, Syed Mustafa. **Nottingham Breast Institute, Nottingham University Hospitals NHS Trust:** Charlene Otieno, Dana Photiou, Douglas Macmillan, Ellie Gutteridge, Fayyaz Mazari, Georgette Oni, Hazem Khout, Jennett Kelsall, Kelly Hallam, Kristjan Asgeirron, Lisa Whisker, Marta D'Auria, Samim Al-zubaidi, Stephen McCulley, Tuabin Rasheed, James Bailey, Lisa Brock, Nazli Muhibullah. **Oxford University Hospitals NHS Foundation Trust:** Alexandra Tenovici, Dionysios-Dennis Remoundos, Nikos Chaidos, Oana Predescu, Pankaj Roy, Rebecca Windle. **Peterborough City Hospital, North West Anglia NHS Foundation Trust:** Elena Popa, Geeta Shetty, Jan Rezulski, Steven Goh, Tholkifl Abdullah. **Pilgrim Hospital Boston, United Lincolnshire Hospitals NHS Trust:** Dinesh Thekkinkattil. **Prince Philip Hospital, Hywel Dda University Health Board:** Saira Khawaja, Sujatha Udayasankar. **Princess Alexandra Hospital NHS Trust:** Sally Tebbal, Veronica Grassi. **Queen Elizabeth Hospital Birmingham, University Hospitals Birmingham NHS Foundation Trust:** Adam Talbot, Naren Basu, Jagdeep Singh. **Royal Bolton Hospital, Bolton NHS Foundation Trust:** Amy Smith, Angela Volleamere, Clare Garnsey, Panagiotis Pikoulas. **Royal Devon and Exeter NHS Foundation Trust:** Charlotte Ives, Douglas Ferguson, Rachel Tillett, Sarah Dean, Sisse Olsen. **Royal Hampshire County Hospital, Hampshire Hospitals NHS Foundation Trust:** Dick Rainsbury, Lashan Peiris, Olivia Sjokvist, Siobhan Laws. **Royal Liverpool and Broadgreen University**

Hospitals NHS Trust: Anne Tansley, Emma De Sousa, Geraldine Mitchell, Julia Henderson, Mysore Chandrashekar, Shelley Potter. **Royal Marsden NHS Foundation Trust:** Aikaterini Micha, Amy Godden, Bernadette Pereira, Chloe Constantinou, Jennifer Rusby, Katherine Krupa, Natalie To, Peter Barry. **Royal Victoria Infirmary, Newcastle Upon Tyne Hospitals NHS Foundation Trust:** Adam Critchley, Baek Kim, Henry Cain, Joe O'Donoghue, John Henton, Loraine Kalra, Louise MacLennan, Ruth Bennett, Stewart Nicholson. **Sant'Andrea Hospital of Rome:** Guido Paolini, Luca Francesco Renzi, Santanelli Di Pompeo, Vitto Ria. **St Bartholomew's Hospital, Barts Health NHS Trust:** Jennifer Hu, Laura Johnson, Rebecca S Lewis, Sirwan Hadad, Souganthy Sundaramoorthy. **St George's University Hospitals NHS Foundation Trust:** Anup Sharma, Delia Toomey, Dibyesh Banerjee, Sarah Shuk Kay Tang. **St. James University Hospital, The Leeds Teaching Hospitals NHS Trust:** Lauren Taylor, Philip Turton, Raj Achuthan, Shireen McKenzie, Tanvir Ahmad. **The Pennine Acute Hospitals NHS Trust:** Kate Williams, Mohammed Absar, Nabila Nasir. **The Ulster Hospital, South Eastern Health and Social Care Trust:** Igor Jerzy Rychlik, Lynn Darragh, Ruth Johnston, Stephen Kirk. **Torbay and South Devon NHS Foundation Trust:** Jacqueline Rees-Lee, Michael Green. **West Hertfordshire Hospitals NHS Trust:** Abhishek Sharma, Kelvin Chong, Lee Min Lai. **Whipps Cross University Hospital, Barts Health NHS Trust:** Jia Choong, Shweta Aggarwal, Zaker Ullah. **Whiston Hospital, St Helens and Knowsley Teaching Hospitals NHS Trust:** Leena Chagla, Ommen Koshy, Sonia Bathla, Tamara Kiernan, Ajay Ashok Bhojwani. **Wirral University Teaching Hospital NHS Foundation Trust:** Jonathan Lund, Karen James, Maria Callaghan, Raman Vinayagam, Shabbir Poonawala. **Worcestershire Acute Hospitals NHS Trust:** Jevan Taylor, Michelle Mullan, Rachel Bright-Thomas. **Wythenshawe Hospital, Manchester University NHS Foundation Trust:** Ashu Gandhi, Ged Byrne, Ibrahim Ibrahim, James Harvey, John Murphy, Lyndsey Highton, Ada Chrysafi, Richard Hawley-Jones Nicola Barnes, Owen Morris, Sumohan Chatterjee, Vinod Mathen, Yousef Majeed, Cliona Kirwan. **York Teaching Hospital NHS Foundation Trust:** Ben Mancey-Jones, Denna El Sharief, Kailas Munot, Rana Nasr, Richard Frame

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Table 1: Demographics of participants by procedure type

	All patients (n=2916)	Therapeutic mammaplasty (n=376, 12.9%)	Mastectomy only (n=1532, 52.5%)	Mastectomy and immediate breast reconstruction (n=1008, 34.6%)	P value
Age in years, median (IQR) (range)	57 (48-68) (21-96)	56 (49-65) (29-85)	65 (54-75) (26-96)	50 (44-57) (21-82)	<0.001[k]
<35	100 (3.4%)	11 (2.9%)	34 (2.2%)	55 (5.5%)	<0.001[x]
35-44	370 (12.7%)	33 (8.8%)	115 (7.5%)	222 (22.0%)	
45-54	769 (26.4%)	114 (30.3%)	257 (16.8%)	398 (39.5%)	
55-64	659 (22.6%)	122 (32.5%)	320 (20.9%)	217 (21.5%)	
65-75	580 (19.9%)	71 (18.9%)	406 (26.5%)	103 (10.2%)	
>75	425 (14.6%)	23 (6.1%)	392 (25.6%)	10 (1.0%)	
Not reported	13 (0.5%)	2 (0.5%)	8 (0.5%)	3 (0.3%)	
BMI, median (IQR) (range)	26.7 (23.4-31) (13.4-80.7)	28.8 (25-33) (18.3-56)	27.3 (23.7-32.2) (13.4-80.7)	25.3 (22.4-28.8) (15.6-61.4)	<0.001[k]
Underweight	56 (1.9%)	1 (0.3%)	33 (2.2%)	22 (2.2%)	<0.001[x]
Normal	967 (33.2%)	87 (23.1%)	445 (29.0%)	435 (43.2%)	
Overweight	883 (30.3%)	114 (30.3%)	457 (29.8%)	312 (31.0%)	
Obese	477 (16.4%)	97 (25.8%)	252 (16.4%)	128 (12.7%)	
Severely obese	346 (11.9%)	69 (18.4%)	221 (14.4%)	56 (5.6%)	
Not reported	187 (6.4%)	8 (2.1%)	124 (8.1%)	55 (5.5%)	
Smoking status					
Non-smoker	2097 (71.9%)	278 (73.9%)	1082 (70.6%)	737 (73.1%)	
Current smoker	316 (10.8%)	40 (10.6%)	180 (11.7%)	96 (9.5%)	0.516[x]
Ex-smoker	452 (15.5%)	51 (13.6%)	241 (15.7%)	160 (15.9%)	
Missing	51 (1.8%)	7 (1.9%)	29 (1.9%)	15 (1.5%)	
Co-morbidities					
Diabetes	248 (8.5%)	16 (4.3%)	189 (12.3%)	43 (4.3%)	<0.001[x]
Ischaemic heart disease	151 (5.2%)	11 (2.9%)	133 (8.7%)	7 (0.7%)	<0.001[x]
Other co-morbidity	1329 (45.6%)	143 (38.0%)	848 (55.3%)	338 (33.5%)	<0.001[x]
Previous oncological therapy					
Neoadjuvant chemotherapy	478 (16.4%)	56 (14.9%)	230 (15.0%)	192 (19.1%)	0.034[x]
Neoadjuvant endocrine therapy	210 (7.2%)	24 (6.4%)	136 (8.9%)	50 (5.0%)	<0.001[x]
ASA grade					
Grade 1	840 (28.8%)	135 (35.9%)	333 (21.7%)	372 (36.9%)	
Grade 2	1729 (59.3%)	223 (59.3%)	906 (59.1%)	600 (59.5%)	<0.001[x]
Grade 3	329 (11.3%)	16 (4.3%)	279 (18.2%)	34 (3.4%)	
Grade 4	6 (0.2%)	0 (0.0%)	6 (0.4%)	0 (0.0%)	
Missing	12 (0.4%)	2 (0.5%)	8 (0.5%)	2 (0.2%)	
Laterality of surgery					
Unilateral TM/Mx+/-IBR	2476 (84.9%)	241 (64.1%)	1427 (93.2%)	808 (80.2%)	
Bilateral TM/Mx+/-IBR	197 (6.8%)	8 (2.1%)	71 (4.6%)	118 (11.7%)	
Unilateral TM/Mx+/-IBR+ contralateral symmetrisation	217 (7.4%)	126 (33.5%)	19 (1.2%)	72 (7.1%)	<0.001[x]
Unilateral TM/Mx+/-IBR + contralateral oncological procedure	36 (0.9%)	1 (0.3%)	15 (1.0%)	10 (1.0%)	
Axillary surgery*					
None	192 (6.6%)	65 (17.3%)	49 (3.2%)	78 (7.7%)	
Sentinel node biopsy/Axillary sample	1674 (57.4%)	251 (66.8%)	871 (56.9%)	552 (54.8%)	<0.001[x]
Axillary clearance	759 (26.0%)	60 (16.0%)	506 (33.0%)	193 (19.2%)	
Missing	291 (10.0%)	0 (0.0%)	106 (6.9%)	185 (18.4%)	

[k]Kruskal-Wallis test across procedure groups, [x]Chi-squared test across procedure groups; ASA – American Society of Anaesthesiologists; BMI – body mass index; IBR – immediate breast reconstruction; IQR – interquartile range; Mx – mastectomy; SNB – sentinel node biopsy; TM – therapeutic mammoplasty *axillary surgery performed at the time of therapeutic mammaplasty/mastectomy +/- IBR based on pre-operative assessment of disease (e.g. axillary surgery not routinely performed for patients having breast conserving surgery for ductal carcinoma in situ)

Table 2: Post-operative complications by patient

	All patients (n=2916)	Therapeutic mammaplasty (n=376)	Mastectomy only (n=1532)	Mastectomy and immediate breast reconstruction (n=1008)	p value
At least one breast or donor site complication	1008 (34.6%)	79 (21.0%)	570 (37.2%)	359 (35.6%)	<0.001[a]
Any major complication	229 (7.9%)	8 (2.1%)	76 (5.0%)	145 (14.4%)	<0.001[a]
Unplanned readmission following surgery	188 (6.5%)	4 (1.1%)	60 (3.9%)	124 (12.3%)	<0.001[a]
Re-operation for complications of surgery	133 (4.6%)	8 (2.1%)	29 (1.9%)	96 (9.5%)	<0.001[a]

[a]Chi squared test across the procedure groups

Table 3: Univariable and multivariable logistic regression for (i) any post-operative complication and (ii) major complications

	Any complication					Major complications				
	Univariable			Multivariable (n=2313)		Univariable			Multivariable (n=2289)	
	N (events, %)	Odds ratio (95% Confidence intervals)	p value	Odds ratio (95% confidence intervals)	p value	N (events, %)	Odds ratio (95% Confidence intervals)	p value	Odds ratio (95% confidence intervals)	p value
Procedure type	2893 (1008, 34.8%)					2868 (229, 8.0%)				
Therapeutic mammaplasty	376 (79, 21.0%)	0.44 (0.31, 0.63)	<0.001	0.46 (0.30, 0.71)	<0.001	376 (8, 2.1%)	0.41 (0.20, 0.84)	0.014	0.36 (0.15, 0.85)	0.019
Mastectomy only	1517 (570, 37.6%)	Reference		Reference		1499 (76, 5.1%)	Reference		Reference	
Mastectomy and immediate breast reconstruction	1000 (359, 35.9%)	0.93 (0.74, 1.17)	0.535	1.28 (0.95, 1.72)	0.109	993 (145, 14.6%)	3.20 (2.20, 4.65)	<0.001	4.02 (2.23, 7.25)	<0.001
Age	2880 (1005, 34.9%)	1.01 (1.01, 1.02)	<0.001	1.01 (1.01, 1.02)	0.002	2855 (229, 8.0%)	0.99 (0.98, 1.00)	0.022	1.01 (0.99, 1.03)	0.172
BMI	2707 (947, 35.0%)					2682 (216, 8.1%)				
Underweight	55 (16, 29.1%)	1.04 (0.56, 1.93)	0.911	0.85 (0.53, 1.37)	0.497	53 (4, 7.6%)	0.95 (0.27, 3.41)	0.939	1.55 (0.57, 4.25)	0.395
Normal weight	959 (272, 28.4%)	Reference		Reference		949 (75, 7.9%)	Reference		Reference	
Overweight	874 (315, 36.0%)	1.42 (1.15, 1.77)	0.001	1.27 (0.98, 1.65)	0.076	869 (58, 6.7%)	0.83 (0.58, 1.19)	0.315	0.95 (0.64, 1.41)	0.794
Obese	476 (199, 41.8%)	1.81 (1.44, 2.29)	<0.001	1.77 (1.33, 2.34)	<0.001	470 (48, 10.2%)	1.33 (0.92, 1.90)	0.125	1.65 (1.05, 2.59)	0.030
Severely obese	343 (145, 42.3%)	1.85 (1.37, 2.50)	<0.001	1.74 (1.17, 2.58)	0.006	341 (31, 9.1%)	1.17 (0.75, 1.82)	0.501	1.67 (0.92, 3.03)	0.093
Co-morbidities										
Ischaemic heart disease	2868 (1001, 34.9%)					2844 (228, 8.0%)				
No	2719 (937, 34.5%)	Reference		Reference		2695 (220, 8.2%)	Reference		Reference	
Yes	149 (64, 43.0%)	1.43 (1.00, 2.04)	0.048	1.06 (0.70, 1.61)	0.785	149 (8, 5.4%)	0.64 (0.34, 1.20)	0.163	0.69 (0.27, 1.72)	0.424
Diabetes	2829 (986, 34.9%)					2804 (224, 8.0%)				
No	2583 (874, 33.8%)	Reference		Reference		2558 (198, 7.7%)	Reference		Reference	
Yes	246 (112, 45.5%)	1.63 (1.27, 2.11)	<0.001	1.09 (0.79, 1.50)	0.598	246 (26, 10.6%)	1.41 (0.91, 2.17)	0.120	1.66 (1.04, 2.64)	0.035
Other	2874 (1003, 34.9%)					2849 (228, 8.0%)				
No	1550 (468, 30.2%)	Reference		Reference		1540 (111, 7.2%)	Reference		Reference	
Yes	1324 (535, 40.4%)	1.57 (1.29, 1.90)	<0.001	1.32 (1.04, 1.66)	0.022	1309 (117, 8.9%)	1.26 (0.97, 1.65)	0.082	1.43 (1.03, 2.00)	0.035
Smoking status	2843 (993, 34.9%)					2818 (228, 8.1%)				
Non-smoker	2078 (689, 33.2%)	Reference		Reference		2060 (154, 7.5%)	Reference		Reference	
Ex-smoker	450 (184, 40.9%)	1.39 (1.13, 1.72)	0.002	1.29 (1.02, 1.63)	0.031	446 (41, 9.2%)	1.25 (0.86, 1.82)	0.236	1.16 (0.77, 1.74)	0.482
Current smoker	315 (120, 38.1%)	1.24 (0.99, 1.56)	0.066	1.43 (1.11, 1.83)	0.005	312 (33, 10.6%)	1.46 (0.96, 2.24)	0.079	1.84 (1.17, 2.89)	0.008
Neoadjuvant chemotherapy	2872 (1002, 34.9%)					2848 (228, 8.0%)				
No	475 (153, 32.2%)	Reference		Reference		470 (42, 8.9%)	Reference		Reference	
Yes	2397 (849, 35.4%)	0.87 (0.68, 1.11)	0.254	0.82 (0.61, 1.10)	0.179	2378 (186, 7.8%)	1.16 (0.75, 1.78)	0.510	1.24 (0.76, 2.02)	0.399
ASA grade	2881 (1005, 34.9%)					2856 (228, 8.0%)				
1	837 (238, 28.4%)	Reference		Reference		835 (63, 7.5%)	Reference		Reference	
2	1710 (624, 36.5%)	1.45 (1.20, 1.74)	<0.001	1.07 (0.83, 1.37)	0.600	1687 (141, 8.4%)	1.12 (0.83, 1.50)	0.463	0.87 (0.61, 1.23)	0.428
3	328 (140, 42.7%)	1.87 (1.44, 2.45)	<0.001	1.03 (0.70, 1.54)	0.867	328 (24, 7.3%)	0.97 (0.59, 1.59)	0.896	0.88 (0.47, 1.65)	0.689
4	6 (3, 50.0%)	2.52 (0.50, 12.72)	0.264	0.96 (0.16, 5.80)	0.962	6 (0, 0.0%)	NA	NA	NA	NA
Bilateral surgery	2893 (1008, 34.8%)					2868 (229, 8.0%)				
No	2455 (843, 34.3%)	Reference		Reference		2433 (181, 7.4%)	Reference		Reference	
Yes	438 (165, 37.7%)	1.16 (0.88, 1.52)	0.301	1.54 (1.18, 2.01)	0.001	435 (48, 11.0%)	1.54 (1.07, 2.23)	0.021	1.71 (1.14, 2.57)	0.010
Axillary surgery	2604 (909, 34.9%)					2582 (196, 7.6%)				
None	192 (26.6%)	Reference		Reference		188 (11, 5.9%)	Reference		Reference	
Sentinel node biopsy/Axillary sample	1661 (548, 33.0%)	1.36 (0.91, 2.03)	0.130	1.13 (0.74, 1.71)	0.480	1650 (134, 8.1%)	1.42 (0.83, 2.44)	0.201	1.33 (0.77, 2.27)	0.304
Axillary clearance	751 (310, 41.3%)	1.94 (1.26, 3.01)	0.003	1.69 (1.04, 2.74)	0.033	744 (51, 6.9%)	1.18 (0.65, 2.15)	0.578	1.08 (0.59, 1.97)	0.801

ASA – American Society of Anaesthesiologists, BMI – body mass index, NA – Not applicable

Table 4: Postoperative histology in procedures performed for malignancy

	All procedures performed for cancer (n=2992)	Therapeutic Mammaplasty (n=385)	Mastectomy only (n=1564)	Mastectomy and immediate breast reconstruction (n=1043)	p
Invasive status					
DCIS	406 (13.6%)	18 (4.7%)	141 (9.0%)	247 (23.7%)	<0.001[x]
Invasive disease	2547 (85.1%)	361 (93.8%)	1413 (90.4%)	773 (74.1%)	
Not reported	39 (1.3%)	6 (1.6%)	10 (0.6%)	23 (2.2%)	
Focality					
Unifocal disease	1998 (66.8%)	258 (67.0%)	1091 (69.8%)	649 (62.2%)	0.002[x]
Multifocal disease	956 (32.0%)	120 (31.2%)	455 (29.1%)	381 (36.5%)	
Not reported	38 (1.3%)	7 (1.8%)	18 (1.2%)	13 (1.3%)	
Invasive disease Grade	(n=2547)	(n=361)	(n=1413)	(n=773)	
Grade 1	223 (8.8%)	44 (12.2%)	98 (6.9%)	81 (10.5%)	<0.001[x]
Grade 2	1327 (52.1%)	140 (38.8%)	759 (53.7%)	428 (55.4%)	
Grade 3	920 (36.1%)	120 (33.2%)	543 (38.4%)	257 (33.3%)	
Not reported	77 (3.0%)	57 (15.8%)	13 (0.9%)	7 (0.9%)	
Histological type					
Ductal	1783 (70.0%)	243 (67.3%)	986 (69.8%)	554 (71.7%)	0.078[x]
Lobular	426 (16.7%)	53 (14.7%)	246 (17.4%)	127 (16.4%)	
Mixed/Other	326 (12.8%)	64 (17.7%)	175 (12.4%)	87 (11.3%)	
Not reported	12 (0.5%)	1 (0.3%)	6 (0.4%)	5 (0.7%)	
Invasive tumour size (mm) median (IQR) (range)	23 (13-36) (0-250)	20 (11-32) (0-155)	25 (15-40) (0-200)	20 (11-30) (0-250)	<0.001[k]
Whole tumour size (mm) median (IQR) (range)	30 (20-50) (0-450)	29 (18-45) (0-145)	32 (20-50) (0-450)	30 (17-50) (0-250)	0.003[k]
Receptor status*					
ER					
Positive	2017 (79.2%)	279 (77.3%)	1106 (78.3%)	632 (81.8%)	<0.001[x]
Negative	484 (19.0%)	51 (14.1%)	298 (21.1%)	135 (17.5%)	
Unknown	46 (1.8%)	31 (8.6%)	9 (0.6%)	6 (0.8%)	
HER-2					
Positive	478 (18.8%)	56 (15.5%)	273 (19.3%)	149 (19.3%)	<0.001[x]
Negative	1947 (76.4%)	261 (72.3%)	1087 (76.9%)	599 (77.5%)	
Unknown	122 (4.8%)	44 (12.2%)	53 (3.8%)	25 (3.2%)	
Nodal status					
Number of lymph nodes involved (macromets only) median (IQR) (range)	0 (0-1) (0-31)	0 (0-1) (0-18)	0 (0-2) (0-30)	0 (0-1) (0-31)	<0.001[k]
N0	1888 (63.1%)	225 (58.4%)	905 (57.9%)	758 (72.7%)	<0.001[x]
N1	984 (32.9%)	87 (22.6%)	642 (41.1%)	255 (24.5%)	
Not reported	120 (4.0%)	73 (19.0%)	17 (1.1%)	30 (2.9%)	
DCIS	(n=406)	(n=18)	(n=141)	(n=247)	
Low grade	27 (6.7%)	13 (72.2%)	7 (5.0%)	20 (8.1%)	0.613[x]
Intermediate grade	95 (23.4%)	5 (27.8%)	38 (27.0%)	52 (21.1%)	
High grade	282 (69.5%)	0 (0.0%)	95 (67.4%)	174 (70.5%)	
Not reported	2 (0.5%)	0 (0.0%)	1 (0.7%)	1 (0.4%)	

*Invasive disease only; [k]Kruskal-Wallis test across procedure groups, [x]Chi-squared test across procedure groups

DCIS – ductal carcinoma in situ IQR – interquartile range, NAC – neoadjuvant chemotherapy

Table 5: Multidisciplinary team decision-making and time to adjuvant therapy by procedure type

	All patients (n=2916)	Therapeutic Mammaplasty (n=376)	Mastectomy only (n=1532)	Mastectomy and immediate breast reconstruction (n=1008)	P value
Patient accepts adjuvant treatment (either chemotherapy or radiotherapy or both)	1578 (54.1%)	343 (91.2%)	804 (52.8%)	431 (42.8%)	<0.001[x]
Time from last oncological procedure to first adjuvant treatment (days) median (IQR) (n=1432)	53 (42-65)	55 (43-67)	52 (41-66)	54 (41-65)	0.085[k]
Chemotherapy as 1st adjuvant treatment	719 (50.2%)	92 (30.6%)	409 (55.4%)	218 (55.5%)	<0.001[x]
Time from last oncological procedure to chemotherapy (days) median (IQR) (n=719)	47 (37-59)	49 (41-60)	47 (37-59)	47 (37-60)	0.592[k]
Radiotherapy as 1st adjuvant treatment	713 (49.8%)	209 (69.4%)	329 (44.6%)	175 (44.5%)	<0.001[x]
Time from last oncological procedure to radiotherapy (days) median (IQR) (n=713)	59 (48-72)	57 (48-70)	59 (48-73)	61 (47-73)	0.632[k]

IQR – interquartile range; MDT – multidisciplinary team;

[k]Kruskal-Wallis test across procedure groups, [x]Chi-squared test across procedure groups

Table 6: Cox univariable and multivariable survival analyses for adjuvant treatment

		Univariable		Multivariable (N=1301)	
	N (%)	**Hazard Ratio (95% Confidence Intervals)**	**p-value**	**Hazard Ratio (95% Confidence Intervals)**	**p-value**
Procedure type	1432				
Therapeutic Mammaplasty	301 (21.0%)	0.89 (0.77, 1.02)	0.102	1.06 (0.87, 1.29)	0.548
Mastectomy only	738 (51.5%)	Reference		Reference	
Mastectomy and immediate breast reconstruction	393 (27.4%)	0.97 (0.85, 1.10)	0.600	0.96 (0.82, 1.12)	0.571
Post-operative complications	1432				
None	861 (60.1%)	Reference		Reference	
Minor complications	478 (33.4%)	0.83 (0.74, 0.93)	0.002	0.85 (0.74, 0.97)	0.017
Major complications	93 (6.5%)	0.71 (0.58, 0.87)	0.001	0.63 (0.51, 0.78)	<0.001
Chemotherapy as first adjuvant treatment	719 (50.2%)	1.71 (1.50, 1.94)	<0.001	2.11 (1.84, 2.41)	<0.001
Age	1428	1.00 (0.99, 1.00)	0.202	1.01 (1.00, 1.01)	0.043
BMI	1373				
Underweight	29 (2.1%)	0.83 (0.64, 1.07)	0.152	0.88 (0.63, 1.22)	0.429
Normal weight	453 (33.0%)	Reference		Reference	
Overweight	447 (32.6%)	0.97 (0.85, 1.12)	0.701	0.97 (0.84, 1.13)	0.726
Obese	266 (19.4%)	0.73 (0.64, 0.83)	<0.001	0.75 (0.64, 0.88)	<0.001
Severely obese	178 (13.0%)	0.73 (0.62, 0.86)	<0.001	0.79 (0.65, 0.95)	0.015
Co-morbidities					
Ischaemic heart disease	1428				
No	1372 (96.1%)	Reference		Reference	
Yes	56 (3.9%)	0.69 (0.55, 0.86)	<0.001	0.78 (0.59, 1.05)	0.100
Diabetes	1403				
No	1290 (92.0%)	Reference		Reference	
Yes	113 (8.1%)	0.82 (0.72, 0.94)	0.005	0.97 (0.82, 1.14)	0.718
Other comorbidity	1422				
No	824 (58.0%)	Reference		Reference	
Yes	598 (42.1%)	0.91 (0.80, 1.03)	0.151	0.90 (0.75, 1.09)	0.285
Smoking status	1409				
Non-smoker	1031 (73.2%)	Reference		Reference	
Ex-smoker	204 (14.5%)	1.14 (0.98, 1.33)	0.089	1.18 (1.00, 1.40)	0.038
Current smoker	174 (12.4%)	0.93 (0.81, 1.07)	0.315	0.92 (0.79, 1.08)	0.326
Neoadjuvant chemotherapy	1421				
No	1083 (76.2%)	Reference		Reference	
Yes	338 (23.8%)	1.03 (0.92, 1.15)	0.603	1.56 (1.33, 1.82)	<0.001
ASA grade	1425				
1	474 (33.3%)	Reference		Reference	
2	823 (57.8%)	0.92 (0.81, 1.03)	0.133	1.04 (0.88, 1.21)	0.657
3	126 (8.8%)	0.86 (0.70, 1.05)	0.144	1.05 (0.78, 1.43)	0.731
4	2 (0.1%)	0.75 (0.63, 0.89)	0.001	1.29 (0.94, 1.78)	0.119
Bilateral surgery (vs none)	232 (16.2%)	1.01 (0.86, 1.17)	0.927	1.03 (0.84, 1.26)	0.797

ASA – American Society of Anaesthesiologists, BMI – body mass index

Supplementary table 1: Demographics of participants by procedure type

	All patients (n=2916)	Therapeutic mammaplasty (n=376, 12.9%)	Mastectomy only (n=1532, 52.5%)	Mastectomy and immediate breast reconstruction (n=1008, 34.6%)			P value
				Implant (n=675, 23.2%)	Pedicled flap (n=105, 3.6%)	Free-flap (n=228, 7.8%)	
Age in years, median (IQR) (range)	57 (48-68) (21-96)	56 (49-65) (29-85)	65 (54-75) (26-96)	50 (43-57) (23-82)	52 (47-60) (25-74)	50 (44.5-56) (21-72)	<0.001[k]
<35	100 (3.4%)	11 (2.9%)	34 (2.2%)	42 (6.2%)	4 (3.8%)	9 (4.0%)	<0.001[x]
35-44	370 (12.7%)	33 (8.8%)	115 (7.5%)	160 (23.7%)	14 (13.3%)	48 (21.1%)	
45-54	769 (26.4%)	114 (30.3%)	257 (16.8%)	248 (36.7%)	50 (47.6%)	100 (43.9%)	
55-64	659 (22.6%)	122 (32.5%)	320 (20.9%)	141 (20.9%)	22 (21.0%)	54 (23.7%)	
65-75	580 (19.9%)	71 (18.9%)	406 (26.5%)	71 (10.5%)	15 (14.3%)	17 (7.5%)	
>75	425 (14.6%)	23 (6.1%)	392 (25.6%)	10 (1.5%)	0 (0.0%)	0 (0.0%)	
Not reported	13 (0.5%)	2 (0.5%)	8 (0.5%)	3 (0.4%)	0 (0.0%)	0 (0.0%)	
BMI, median (IQR) (range)	26.7 (23.4-31) (13.4-80.7)	28.8 (25-33) (18.3-56)	27.3 (23.7-32.2) (13.4-80.7)	24.4 (21.9-27.6) (16.0-61.4)	26.6 (23.3-30.6) (18.5-39.2)	27.4 (24.2-30.1) (15.6-31.1)	<0.001[k]
Underweight	56 (1.9%)	1 (0.3%)	33 (2.2%)	20 (3.0%)	0 (0.0%)	2 (0.9%)	<0.001[x]
Normal	967 (33.2%)	87 (23.1%)	445 (29.0%)	328 (48.6%)	37 (35.2%)	70 (30.7%)	
Overweight	883 (30.3%)	114 (30.3%)	457 (29.8%)	191 (28.3%)	35 (33.3%)	86 (37.7%)	
Obese	477 (16.4%)	97 (25.8%)	252 (16.4%)	65 (9.6%)	22 (21.0%)	41 (18. 0%)	
Severely obese	346 (11.9%)	69 (18.4%)	221 (14.4%)	35 (5.2%)	5 (4.8%)	16 (7.0%)	
Not reported	187 (6.4%)	8 (2.1%)	124 (8.1%)	36 (5.3%)	6 (5.7%)	13 (5.7%)	
Smoking status							
Non-smoker	2097 (71.9%)	278 (73.9%)	1082 (70.6%)	499 (73.9%)	75 (71.4%)	163 (71.5%)	
Current smoker	327 (11.2%)	51 (13.6%)	180 (11.7%)	73 (10.8%)	12 (11.4%)	11 (4.8%)	0.038[x]
Ex-smoker	441 (15.1%)	40 (10.6%)	241 (15.7%)	91 (13.5%)	18 (17.1%)	51 (22.4%)	
Missing	51 (1.8%)	7 (1.9%)	29 (1.9%)	12 (1.8%)	0 (0.0%)	3 (1.3%)	
Co-morbidities							
Diabetes	248 (8.5%)	16 (4.3%)	189 (12.3%)	25 (3.7%)	7 (6.7%)	11 (4.8%)	<0.001[x]
Ischaemic heart disease	151 (5.2%)	11 (2.9%)	133 (8.7%)	3 (0.4%)	2 (1.9%)	2 (0.9%)	<0.001[x]
Other co-morbidity	1329 (45.6%)	143 (38.0%)	848 (55.3%)	222 (32.9%)	36 (34.3%)	80 (35.1%)	<0.001[x]
Previous oncological therapy							
Neoadjuvant chemotherapy	478 (16.4%)	56 (14.9%)	230 (15.0%)	128 (19.0%)	21 (20.0%)	43 (18.9%)	0.002[x]
Neoadjuvant endocrine therapy	210 (7.2%)	24 (6.4%)	136 (8.9%)	28 (4.1%)	8 (7.6%)	14 (6.1%)	<0.001[x]
ASA grade							
Grade 1	840 (28.8%)	135 (35.9%)	333 (21.7%)	273 (40.4%)	40 (38.1%)	59 (25.9%)	
Grade 2	1729 (59.3%)	223 (59.3%)	906 (59.1%)	379 (56.2%)	61 (58.1%)	160 (70.2%)	<0.001[x]
Grade 3	329 (11.3%)	16 (4.3%)	279 (18.2%)	23 (3.4%)	3 (2.9%)	8 (3.5%)	
Grade 4	6 (0.2%)	0 (0.0%)	6 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Missing	12 (0.4%)	2 (0.5%)	8 (0.5%)	0 (0.0%)	1 (1.0%)	1 (0.4%)	
Laterality of surgery							
Unilateral TM/Mx+/-IBR	2476 (84.9%)	241 (64.1%)	1427 (93.2%)	528 (78.2%)	96 (91.4%)	184 (80.7%)	
Bilateral TM/Mx+/-IBR	197 (6.8%)	8 (2.1%)	71 (4.6%)	98 (14.5%)	1 (1.0%)	19 (8.3%)	
Unilateral TM/Mx+/-IBR+ contralateral symmetrisation	217 (7.4%)	126 (33.5%)	19 (1.2%)	43 (6.4%)	8 (7.6%)	21 (9.2%)	<0.001[x]
Unilateral TM/Mx+/-IBR + contralateral oncological procedure	36 (0.9%)	1 (0.3%)	15 (1.0%)	6 (0.9%)	0 (0.0%)	4 (1.8%)	
Axillary surgery							
None	192 (6.6%)	65 (17.3%)	49 (3.2%)	40 (5.9%)	12 (11.4%)	26 (11.4%)	
Sentinel node biopsy/Axillary sample	1674 (57.4%)	251 (66.8%)	871 (56.9%)	419 (62.1%)	38 (36.2%)	95 (41.7%)	<0.001[x]
Axillary clearance	759 (26.0%)	60 (16.0%)	506 (33.0%)	119 (17.6%)	26 (24.8%)	48 (21.1%)	
Missing	291 (10.0%)	0 (0.0%)	106 (6.9%)	97 (14.4%)	29 (27.6%)	59 (25.9%)	

[k]Kruskal-Wallis test, [x]Chi-squared test; ASA – American Society of Anaesthesiologists; BMI – body mass index; IBR – immediate breast reconstruction; IQR – interquartile range; Mx – mastectomy; SNB – sentinel node biopsy; TM – therapeutic mammoplasty

Supplementary table 2: Post-operative complications by patient

	All patients (n=2916)	Therapeutic mammaplasty (n=376)	Mastectomy only (n=1532)	Implant (n=675)	Pedicled flap (n=105)	Free flap (n=228)	p value
At least one breast or donor site complication	1008 (34.6%)	79 (21.0%)	570 (37.2%)	223 (33.0%)	42 (40.0%)	94 (41.2%)	<0.001[a]
Any major complication	229 (7.9%)	8 (2.1%)	76 (5.0%)	100 (14.8%)	7 (6.7%)	38 (16.7%)	<0.001[a]
Unplanned readmission following surgery	188 (6.5%)	4 (1.1%)	60 (3.9%)	88 (13.0%)	5 (4.8%)	31 (13.6%)	<0.001[a]
Re-operation for complications of surgery	133 (4.6%)	8 (2.1%)	29 (1.9%)	69 (10.2%)	5 (4.8%)	22 (9.7%)	<0.001[a]

[a]Chi squared test

Supplementary Table 3: Details of complications per breast (n (%)) by procedure type

Complication	Per breast data, n (%)					
	Therapeutic mammaplasty (N=385)	Mastectomy only (N=1606)	Implant (N=773)	Pedicled flap (N=106)	Free flap (N=247)	p-value
Seroma requiring aspiration	15 (3.9)	434 (27.0)	77 (10.0)	7 (6.6)	10 (4.1)	<0.001
Haematoma	8 (2.1)	70 (4.4)	27 (3.5)	0 (0.0)	6 (2.4)	
Managed conservatively	6 (1.6)	21 (1.3)	8 (1.0)	0 (0.0)	1 (0.4)	0.060
Requiring surgical evacuation	2 (0.5)	49 (3.1)	19 (2.5)	0 (0.0)	5 (2.0)	
Infection	23 (6.0)	142 (8.8)	104 (13.5)	10 (9.4)	22 (8.9)	
Requiring oral antibiotics	17 (4.4)	110 (6.9)	45 (5.8)	7 (6.6)	8 (3.2)	<0.001
Requiring intravenous therapy antibiotics	4 (1.0)	23 (1.4)	25 (3.2)	0 (0.0)	11 (4.5)	
Requiring surgical debridement/drainage	2 (0.5)	9 (0.6)	34 (4.4)	3 (2.8)	3 (1.2)	
Skin necrosis, including T junction necrosis	28 (7.3)	20 (1.3)	55 (7.1)	10 (9.4)	22 (8.9)	
Minor – managed conservatively	27 (7.0)	17 (1.1)	24 (3.1)	8 (7.6)	14 (5.7)	<0.001
Major requiring surgical debridement	1 (0.3)	3 (0.2)	31 (4.0)	2 (1.9)	8 (3.2)	
Wound dehiscence	14 (3.6)	38 (2.4)	37 (4.8)	3 (2.8)	22 (8.9)	
Managed conservatively	13 (3.4)	35 (2.2)	16 (2.1)	2 (1.9)	19 (7.7)	<0.001
Requiring return to theatre	1 (0.3)	3 (0.02)	21 (2.7)	1 (0.9)	3 (1.2)	

[x]Chi-squared test across procedure groups

Supplementary table 4: Univariable and multivariable logistic regression for (i) any post-operative complication and (ii) major complications

	Any complication					Major complications				
	Univariable			Multivariable (n=2313)		Univariable			Multivariable (n=2289)	
	N (events, %)	Odds ratio (95% Confidence intervals)	p value	Odds ratio (95% confidence intervals)	p value	N (events, %)	Odds ratio (95% Confidence intervals)	p value	Odds ratio (95% confidence intervals)	p value
Procedure type	2893 (1008, 34.8%)					2868 (229, 8.0%)				
Therapeutic mammaplasty	376 (79, 21.0%)	0.44 (0.31, 0.63)	<0.001	0.46 (0.30, 0.71)	<0.001	376 (8, 2.1%)	0.41 (0.20, 0.84)	0.014	0.37 (0.16, 0.86)	0.021
Mastectomy only	1517 (570, 37.6%)	Reference		Reference		1499 (76, 5.1%)	Reference		Reference	
Implant-based	667 (223, 33.4%)	0.83 (0.64, 1.08)	0.170	1.15 (0.83, 1.59)	0.401	663 (100, 15.1%)	3.33 (2.17, 5.09)	<0.001	4.28 (2.28, 8.01)	<0.001
Pedicled flap	105 (42, 40.0%)	1.11 (0.61, 2.00)	0.735	1.55 (0.84, 2.87)	0.164	104 (7, 6.7%)	1.35 (0.66, 2.78)	0.414	1.43 (0.52, 3.95)	0.488
Free flap	228 (94, 41.2%)	1.17 (0.83, 1.64)	0.377	1.62 (0.99, 2.63)	0.053	226 (38, 16.8%)	3.78 (2.38, 6.01)	<0.001	4.92 (2.31, 10.48)	<0.001
Age	2880 (1005, 34.9%)	1.01 (1.01, 1.02)	<0.001	1.01 (1.01, 1.02)	0.002	2855 (229, 8.0%)	0.99 (0.98, 1.00)	0.022	1.01 (0.99, 1.03)	0.172
BMI	2707 (947, 35.0%)					2682 (216, 8.1%)				
Underweight	55 (16, 29.1%)	1.04 (0.56, 1.93)	0.911	0.84 (0.52, 1.36)	0.486	53 (4, 7.6%)	0.95 (0.27, 3.41)	0.939	1.53 (0.55, 4.21)	0.415
Normal weight	959 (272, 28.4%)	Reference		Reference		949 (75, 7.9%)	Reference		Reference	
Overweight	874 (315, 36.0%)	1.42 (1.15, 1.77)	0.001	1.24 (0.95, 1.62)	0.106	869 (58, 6.7%)	0.83 (0.58, 1.19)	0.315	0.95 (0.63, 1.42)	0.798
Obese	476 (199, 41.8%)	1.81 (1.44, 2.29)	<0.001	1.73 (1.30, 2.29)	<0.001	470 (48, 10.2%)	1.33 (0.92, 1.90)	0.125	1.71 (1.08, 2.70)	0.022
Severely obese	343 (145, 42.3%)	1.85 (1.37, 2.50)	<0.001	1.71 (1.15, 2.55)	0.009	341 (31, 9.1%)	1.17 (0.75, 1.82)	0.501	1.70 (0.94, 3.07)	0.079
Co-morbidities										
Ischaemic heart disease	2868 (1001, 34.9%)					2844 (228, 8.0%)				
No	2719 (937, 34.5%)	Reference		Reference		2695 (220, 8.2%)	Reference		Reference	
Yes	149 (64, 43.0%)	1.43 (1.00, 2.04)	0.048	1.05 (0.69, 1.60)	0.807	149 (8, 5.4%)	0.64 (0.34, 1.20)	0.163	0.68 (0.27, 1.71)	0.416
Diabetes	2829 (986, 34.9%)					2804 (224, 8.0%)				
No	2583 (874, 33.8%)	Reference		Reference		2558 (198, 7.7%)	Reference		Reference	
Yes	246 (112, 45.5%)	1.63 (1.27, 2.11)	<0.001	1.09 (0.79, 1.50)	0.593	246 (26, 10.6%)	1.41 (0.91, 2.17)	0.120	1.68 (1.05, 2.68)	0.031
Other	2874 (1003, 34.9%)					2849 (228, 8.0%)				
No	1550 (468, 30.2%)	Reference		Reference		1540 (111, 7.2%)	Reference		Reference	
Yes	1324 (535, 40.4%)	1.57 (1.29, 1.90)	<0.001	1.32 (1.04, 1.67)	0.023	1309 (117, 8.9%)	1.26 (0.97, 1.65)	0.082	1.43 (1.02, 2.01)	0.038
Smoking status	2843 (993, 34.9%)					2818 (228, 8.1%)				
Non-smoker	2078 (689, 33.2%)	Reference		Reference		2060 (154, 7.5%)	Reference		Reference	
Ex-smoker	450 (184, 40.9%)	1.39 (1.13, 1.72)	0.002	1.28 (1.01, 1.61)	0.039	446 (41, 9.2%)	1.25 (0.86, 1.82)	0.236	1.16 (0.78, 1.74)	0.467
Current smoker	315 (120, 38.1%)	1.24 (0.99, 1.56)	0.066	1.44 (1.13, 1.84)	0.004	312 (33, 10.6%)	1.46 (0.96, 2.24)	0.079	1.88 (1.19, 2.99)	0.007
Neoadjuvant chemotherapy	2872 (1002, 34.9%)					2848 (228, 8.0%)				
No	475 (153, 32.2%)	Reference		Reference		470 (42, 8.9%)	Reference		Reference	
Yes	2397 (849, 35.4%)	0.87 (0.68, 1.11)	0.254	0.82 (0.61, 1.10)	0.187	2378 (186, 7.8%)	1.16 (0.75, 1.78)	0.510	1.21 (0.74, 1.98)	0.445
ASA grade	2881 (1005, 34.9%)					2856 (228, 8.0%)				
1	837 (238, 28.4%)	Reference		Reference		835 (63, 7.5%)	Reference		Reference	
2	1710 (624, 36.5%)	1.45 (1.20, 1.74)	<0.001	1.06 (0.82, 1.36)	0.662	1687 (141, 8.4%)	1.12 (0.83, 1.50)	0.463	0.83 (0.58, 1.20)	0.327
3	328 (140, 42.7%)	1.87 (1.44, 2.45)	<0.001	1.03 (0.69, 1.53)	0.888	328 (24, 7.3%)	0.97 (0.59, 1.59)	0.896	0.84 (0.44, 1.58)	0.584
4	6 (3, 50.0%)	2.52 (0.50, 12.72)	0.264	0.96 (0.16, 5.80)	0.962	6 (0, 0.0%)	NA	NA	NA	NA
Bilateral surgery	2893 (1008, 34.8%)					2868 (229, 8.0%)				
No	2455 (843, 34.3%)	Reference		Reference		2433 (181, 7.4%)	Reference		Reference	
Yes	438 (165, 37.7%)	1.16 (0.88, 1.52)	0.301	1.56 (1.19, 2.03)	0.001	435 (48, 11.0%)	1.54 (1.07, 2.23)	0.021	1.65 (1.09, 2.51)	0.018
Axillary surgery	2604 (909, 34.9%)					2582 (196, 7.6%)				
None	192 (26.6%)	Reference		Reference		188 (11, 5.9%)	Reference		Reference	
Sentinel node biopsy/Axillary sample	1661 (548, 33.0%)	1.36 (0.91, 2.03)	0.130	1.17 (0.76, 1.79)	0.480	1650 (134, 8.1%)	1.42 (0.83, 2.44)	0.201	1.29 (0.75, 2.21)	0.357
Axillary clearance	751 (310, 41.3%)	1.94 (1.26, 3.01)	0.003	1.73 (1.05, 2.83)	0.030	744 (51, 6.9%)	1.18 (0.65, 2.15)	0.578	1.08 (0.58, 2.00)	0.817

ASA – American Society of Anaesthesiologists, BMI – body mass index, NA – Not applicable

Supplementary table 5: Postoperative histology in procedures performed for malignancy

	All procedures performed for cancer (n=3117)	Therapeutic Mammaplasty (n=385)	Mastectomy only (n=1564)	Implant (n=707)	Pedicled flap (n=105)	Free flap (n=231)	p
Invasive status							
DCIS	406 (13.6%)	18 (4.7%)	141 (9.0%)	163 (23.1%)	26 (24.8%)	58 (25.1%)	<0.001
Invasive disease	2547 (85.1%)	361 (93.8%)	1413 (90.4%)	533 (75.4%)	77 (73.3%)	163 (70.6%)	
Not reported	39 (1.3%)	6 (1.6%)	10 (0.6%)	11 (1.6%)	2 (1.9%)	10 (4.3%)	
Focality							
Unifocal disease	1998 (66.8%)	258 (67.0%)	1091 (69.8%)	446 (63.1%)	72 (68.6%)	131 (56.7%)	0.002
Multifocal disease	956 (32.0%)	120 (31.2%)	455 (29.1%)	251 (35.5%)	33 (31.4%)	97 (42.0%)	
Not reported	38 (1.3%)	7 (1.8%)	18 (1.2%)	10 (1.4%)	0 (0.0%)	3 (1.3%)	
Invasive disease	(n=2547)	(n=361)	(n=1413)	(n=533)	(n=77)	(n=163)	
Grade							
Grade 1	223 (8.8%)	44 (12.2%)	98 (6.9%)	58 (10.9%)	7 (9.1%)	16 (9.8%)	<0.001
Grade 2	1327 (52.1%)	140 (38.8%)	759 (53.7%)	285 (53.5%)	47 (61.0%)	96 (58.9%)	
Grade 3	920 (36.1%)	120 (33.2%)	543 (38.4%)	186 (24.1%)	21 (27.3%)	50 (30.7%)	
Not reported	77 (3.0%)	57 (15.8%)	13 (0.9%)	4 (0.8%)	2 (2.6%)	1 (0.6%)	
Histological type							
Ductal	1783 (70.0%)	243 (67.3%)	986 (69.8%)	382 (71.7%)	55 (71.4%)	117 (71.8%)	0.081
Lobular	426 (16.7%)	53 (14.7%)	246 (17.4%)	89 (16.7%)	10 (13.0%)	28 (17.2%)	
Mixed/Other	326 (12.8%)	64 (17.7%)	175 (12.4%)	60 (11.3%)	10 (13.0%)	17 (10.4%)	
Not reported	12 (0.5%)	1 (0.3%)	6 (0.4%)	2 (0.4%)	2 (2.6%)	1 (0.6%)	
Invasive tumour size (mm) median (IQR) (range)	23 (13-36) (0-250)	20 (11-32) (0-155)	25 (15-40) (0-200)	19 (10-30) (0-127)	20 (9-35.5) (0-250)	21 (13-32.5) (0-110)	<0.001
Whole tumour size (mm) median (IQR) (range)	30 (20-50) (0-450)	29 (18-45) (0-145)	32 (20-50) (0-450)	28 (16-50) (0-180)	32 (16-46.5) (0-250)	35 (21-58) (0-210)	<0.001
Receptor status*							
ER							
Positive	2017 (79.2%)	279 (77.3%)	1106 (78.3%)	445 (83.5%)	56 (72.7%)	131 (80.4%)	<0.001
Negative	484 (19.0%)	51 (14.1%)	298 (21.1%)	86 (16.1%)	18 (23.4%)	31 (19.0%)	
Unknown	46 (1.8%)	31 (8.6%)	9 (0.6%)	2 (0.4%)	3 (3.9%)	1 (0.6%)	
HER-2							
Positive	478 (18.8%)	56 (15.5%)	273 (19.3%)	109 (20.5%)	12 (15.6%)	28 (17.2%)	<0.001
Negative	1947 (76.4%)	261 (72.3%)	1087 (76.9%)	408 (76.6%)	61 (79.2%)	130 (79.8%)	
Unknown	122 (4.8%)	44 (12.2%)	53 (3.8%)	16 (3.0%)	4 (5.2%)	5 (3.1%)	
Nodal status							
Number of lymph nodes involved (macromets only) median (IQR) (range)	0 (0-1) (0-31)	0 (0-1) (0-18)	0 (0-2) (0-30)	0 (0-0) (0-17)	0 (0-1) (0-20)	0 (0-1) (0-31)	<0.001
N0	1888 (63.1%)	225 (58.4%)	905 (57.9%)	523 (74.0%)	71 (67.6%)	164 (71.0%)	<0.001
N1	984 (32.9%)	87 (22.6%)	642 (41.1%)	168 (23.8%)	28 (26.7%)	59 (25.5%)	
Not reported	120 (4.0%)	73 (19.0%)	17 (1.1%)	16 (2.3%)	6 (5.7%)	8 (3.5%)	
Preinvasive disease	(n=406)	(n=18)	(n=141)	(n=163)	(n=26)	(n=58)	
Low grade	27 (6.7%)	13 (72.2%)	7 (5.0%)	12 (7.4%)	1 (3.8%)	7 (12.1%)	
Intermediate grade	95 (23.4%)	5 (27.8%)	38 (27.0%)	38 (23.3%)	5 (19.2%)	9 (15.5%)	0.743
High grade	282 (69.5%)	0 (0.0%)	95 (67.4%)	112 (68.7%)	20 (76.9%)	42 (72.4%)	
Not reported	2 (0.5%)	0 (0.0%)	1 (0.7%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	

*Invasive disease only; IQR – interquartile range, NAC – neoadjuvant chemotherapy

Supplementary table 6: Multidisciplinary team decision-making and time to adjuvant therapy by procedure type

	All patients (n=2916)	Therapeutic Mammaplasty (n=376)	Mastectomy only (n=1532)	Implant (n=675)	Pedicled flap (n=105)	Free flap (n=228)	P value
Patient accepts adjuvant treatment (either chemotherapy or radiotherapy or both)	1578 (54.1%)	343 (91.2%)	804 (52.8%)	288 (42.7%)	50 (47.6%)	93 (40.8%)	<0.001
Time from last oncological procedure to first adjuvant treatment (days) median (IQR) (n=1432)	53 (42-65)	55 (43-67)	52 (41-66)	51 (41-63)	57 (42-73)	57 (46-72)	0.007
Chemotherapy as 1st adjuvant treatment	719 (50.2%)	92 (30.6%)	409 (55.4%)	147 (56.5%)	25 (52.1%)	46 (54.1%)	<0.001
Time from last oncological procedure to chemotherapy (days) median (IQR) (n=719)	47 (37-59)	49 (41-60)	47 (37-59)	46 (35-57)	46 (39-64)	57 (41-70)	0.087
Radiotherapy as 1st adjuvant treatment	713 (49.8%)	209 (69.4%)	329 (44.6%)	113 (43.5%)	23 (47.9%)	39 (45.9%)	<0.001
Time from last oncological procedure to radiotherapy (days) median (IQR) (n=713)	59 (48-72)	57 (48-70)	59 (48-73)	60 (45-68)	63 (53-85)	62 (50-76)	0.292

IQR – interquartile range; MDT – multidisciplinary team