**Short-term safety outcomes of immediate implant-based breast reconstruction with and without mesh: The iBRA multicentre prospective cohort study**

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**Abstract**

**Background**

Biological and/or synthetic mesh may improve outcomes of immediate implant-based breast reconstruction (IBBR); breast reconstruction performed using implants or expanders at the time of mastectomy, but there is a lack of high-quality evidence to support the safety or effectiveness of the technique. We undertook a national prospective multicentre cohort study to establish the short-term safety of IBBR performed with and without mesh, and to inform the feasibility of undertaking a future randomised clinical trial (RCT) comparing different techniques.

**Methods**

Consecutive women undergoing IBBR for malignancy or risk-reduction using any technique at participating breast and plastic surgical units between February 2014 and June 2016 were included. Patient demographics, operative, oncological and complication details were collected pre and post-surgery. Outcomes of interest were implant loss defined as removal of the expander or implant, infection requiring treatment with antibiotics and/or surgery, unplanned return to theatre and unplanned readmission to hospital for complications of reconstructive surgery up to 3 months post-reconstruction assessed by clinical review or patient self-report. Follow up is complete. The study was registered with the ISRCTN Registry, reference number ISRCTN37664281.

**Findings**

2,108 patients underwent 2,655 IBBR at 81 units across the UK. 1,638/2,108 (78%) patients had planned single-stage reconstructions and 1,376/2,108 (65%) underwent reconstruction using biological (n=1,133/2,108, 54%) or synthetic (n=243/2,108, 12%) mesh. 3 month outcome data was available for 2,081/2,108 (99%) patients. Of these, 9% (n=182/2,081) patients experienced implant loss; 18% (n=372/2,081) required readmission and 18% (n=370/2,081) required return to theatre for complications within three months of their initial surgery. One in four (n=522/2,081) women required treatment for an infection

**Interpretation**

Complications following IBBR are higher than recommended by national standards. An RCT is now needed to establish the optimal approach to IBBR.

**Funding**

National Institute for Health Research; Association of Breast Surgery and British Association of Plastic, Reconstructive and Aesthetic Surgeons.

**Keywords:** breast reconstruction; implant; acellular dermal matrix; mesh; complications; cohort study; trainee collaborative

**Research in context**

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| **Evidence before this study**At the initiation of this study (August 2013) we searched MEDLINE, EMBASE and the Cochrane database using the search terms for implant reconstruction [implant$; expander$; prosthe$] AND mesh [including ADM; acellular derma$; AlloDerm, SurgiMend, Strattice] to identify original papers and systematic reviews evaluating the outcomes of mesh-assisted implant reconstruction. We identified eight systematic reviews and 61 primary studies including one randomised clinical trial (RCT). All the systematic reviews were of low quality and at high risk of bias. The RCT compared two-stage expander-implant reconstruction with and without mesh. It was well-designed and at low risk of bias but was stopped prematurely due to problems with recruitment. The primary outcome was post-operative pain and pain during the expansion period but not the safety of using mesh. Interim analysis suggested that there was unlikely to be a difference in pain scores between the treatment groups. The remaining studies comprised 40 comparative studies and 20 case-series all of which were at high risk of bias. An updated PUBMED search in April 2018 identified one small randomised clinical trial comparing standard two-stage expander-implant reconstruction and mesh-assisted single-stage direct-to-implant breast reconstruction. The complication rate in the single-stage mesh-assisted direct to implant group was significantly higher than that in patients receiving two-stage expander implant reconstruction and the study was stopped prematurely. A further small RCT compared biological and synthetic mesh in single-stage direct-to-implant breast reconstruction. Although this study provided evidence that a trial may be possible, it was underpowered and insufficiently well designed to produce meaningful results. Several small explanatory trials have compared different types of biological mesh. These studies did not demonstrate any differences between products but were small and underpowered.  |
| **Added value of this study**This prospective cohort study of over 2000 patients undergoing immediate implant-based breast reconstruction in the UK has provided high-quality ‘real world’ data regarding the short-term safety outcomes of different implant-based techniques with and without mesh. Rates of key complications including implant loss, infection, readmission and re-operation for complications of reconstructive surgery are much higher than anticipated and although associated with smoking and increased body mass index, an association was not seen with the use or type of mesh in this non-randomised study. These findings support the need for a future pragmatic RCT to determine the most clinical and cost-effective technique of implant-based breast reconstruction. |
| **Implications of all available evidence**Complications following immediate implant-based reconstruction with and without mesh are high and patients should be carefully counselled regarding their surgical options. Surgeons should commit to robustly evaluating mesh-assisted implant-based breast reconstruction in the context of a well-designed RCT. Further work is needed to explore the most acceptable study design and test the feasibility of randomisation in a pilot RCT. Urgent work will also be necessary to determine how the unacceptably high complication rates demonstrated in this study may be reduced.  |

**INTRODUCTION**

Up to 40%1,2 of the 1.7 million3 women diagnosed with breast cancer each year will require a mastectomy as the surgical treatment for their disease. Mastectomy can profoundly impact body image and self-esteem and immediate breast reconstruction is offered to improve quality of life4.

Implant-based breast reconstruction (IBBR) is the most commonly-performed reconstructive procedure worldwide5,6. Traditionally a two-stage procedure is performed involving the initial placement of a tissue expander in the subpectoral pocket, sequential expansions with saline until the desired volume is achieved and replacement of the expander with a fixed-volume implant. The introduction of biological and synthetic meshes have revolutionised this technique. The mesh is sutured between the lower edge of the pectoralis muscle and the chest wall to create a larger subpectoral pocket which can accommodate a fixed-volume implant at the time of the initial surgery. This facilitates single-stage direct-to-implant (DTI) reconstruction without the need for a second procedure with significant associated benefits for patients and healthcare providers. The mesh may improve cosmetic outcomes by allowing better lower-pole projection and creating a more natural looking ptotic result. A range of biological (e.g. acellular dermal matrix, [ADM]) and synthetic (e.g. titanium-coated polypropylene) meshes are available. These differ significantly in price and in the absence of comparative evidence, product selection is largely dependent on surgeon preference.

Recently, the practice of IBBR has evolved further with the introduction of ‘muscle-sparing’ techniques7. These involve wrapping the implant in mesh and placing it on top, rather than under the pectoralis muscle. This prepectoral technique may further improve outcomes for patients by reducing post-operative pain and preventing implant ‘animation’, the upward movement of the implant seen when the pectoralis muscle contracts7.

Despite the widespread adoption of mesh-assisted techniques into practice, evidence to support the proposed benefits of mesh is lacking7-10. A recent multicentre Dutch randomised clinical trial (RCT) has demonstrated significantly increased complication rates in single-stage DTI reconstruction with mesh compared with standard two-stage expander-implant techniques11. The study was criticised as the participating surgeons had limited experience with the technique12, but further analysis failed to identify a learning curve effect13. Other large multicentre prospective studies, however have not demonstrated any significant difference in complication rates or patient-reported outcomes between single-stage DTI and two-stage techniques14 or between two-stage expander-implant reconstruction performed with and without ADM15. While these findings are supportive of the technique, there remains the need for high-quality randomised evidence to support practice. A recent small RCT comparing biological and synthetic mesh in single-stage DTI reconstruction was underpowered and insufficiently well-designed to generate meaningful results16.

There is therefore a need for high-quality research to establish the safety and effectiveness of mesh in IBBR; determine what mesh should be recommended and as practice evolves to determine if the implant should be placed on top of or underneath the pectoralis muscle7.

Randomised clinical trials are ideally needed, but RCTs in breast reconstruction are challenging due to patient and surgeon preference17 and previous trials have closed prematurely due to failure to recruit18,19. Careful pre-trial work is therefore needed to ensure that a future RCT is well-designed and addresses questions that are important to patients and the reconstructive community.

iBRA (implant Breast Reconstruction evAluation)20 is a four-phase study that aims to inform the feasibility, design and conduct of a future trial in IBBR. Phase 1 was previously reported21,22. Here we report the primary endpoint for phase 2, a prospective multicentre national study to determine the short-term clinical outcomes of different approaches to IBBR and inform the selection of comparators and sample size for a future RCT.

**METHODS**

**Study design and participants**

We undertook a prospective multicentre study to understand current practice and investigate the short-term safety outcomes of different approaches to IBBR to inform the feasibility of undertaking a future RCT comparing different techniques.

All breast or plastic surgical units performing immediate IBBR were invited to participate in the iBRA study through the UK Trainee Collaborative Research Network and the professional associations (Association of Breast Surgery [ABS] and the British Association of Plastic Reconstructive and Aesthetic Surgeons [BAPRAS]).

Consecutive women aged 16 or over undergoing mastectomy and IBBR using any technique for malignancy or risk-reduction at participating centres between 1st February 2014 and 30th June 2016 were recruited to the study. Excluded were patients undergoing reconstruction using an implant in combination with a tissue-flap (e.g. latissimus dorsi flap and implant), those undergoing delayed reconstruction and patients undergoing revisional surgery.

Ethical approval was not required as defined by the HRA decision tool (http://www.hra-decisiontools.org.uk/research/). The study involved collection of clinical and patient-reported outcome data as routinely recommended by ‘Oncoplastic Surgery: Guidelines for Good Practice’ and outcomes assessed against these quality standards23. Each participating centre was required to obtain local audit approvals and register the study prior to commencing study recruitment consistent with the methodology of previously-reported multicentre prospective trainee collaborative studies. Patient consent was not required for routine clinical data collection, but patients provided informed written consent to receive patient-reported outcome questionnaires in keeping with the methods employed in the UK National Mastectomy and Breast Reconstruction Audit24. All data were recorded in an anonymised format on a secure web-based database (REDCap)25 (http://www.projectredcap.org/).

**Procedures**

Patients were identified prospectively from clinics, multidisciplinary team (MDT) meetings and theatre lists. Simple demographic, co-morbidity and operative data were collected for each participant.

All patients underwent skin or nipple-sparing mastectomy followed by immediate implant-based breast reconstruction. Implants or tissue expanders could be placed under the pectoralis muscle (subpectoral) with or without biological or synthetic mesh or on top of the muscle (prepectoral) supported by mesh. As one aim of the study was to explore the current practice to inform a future trial, no restrictions were placed on the technique, but rather details of the procedures performed were recorded.

Participating surgeons performed the procedures according to their routine practice. Mesh choice (biological or synthetic and the specific product used); implant selection (definitive fixed-volume implant, adjustable implant or temporary tissue expander) and implant positioning (pre or subpectoral) were as per surgeon preference. Strategies to reduce infection (e.g. use of laminar flow, glove change prior to implant insertion, wound lavage) were as per local policy. Reconstructions were considered two-stage if a temporary expander was placed at the time of the initial mastectomy and a second procedure was planned to insert a definitive implant at a later date.

Precise details of the techniques used varied by surgeon, but broadly, for submuscular reconstructions, a tissue expander was inserted in a pocket created under the pectoralis muscle. Serratus fascia could be raised to provide complete expander coverage or the lateral aspect of the expander could be left subcutaneous as per surgeon preference.

Subpectoral reconstruction with mesh involved releasing the lower boarder of the pectoralis muscle from the chest wall and suturing the mesh to the free edge of the muscle. A definitive fixed volume implant, adjustable implant or tissue expander was then inserted according to surgeon preference and the mesh either sutured at the level of the inframammary fold or tucked under the implant depending on the product used. For dermal sling reconstruction, the pectoralis muscle was detached in a similar way and the lower mastectomy flap de-epithelialized and sutured to the free muscle edge to provide coverage of the lower pole of the implant.

Finally, for pre-pectoral reconstruction, the pectoralis muscle was not disturbed but a fixed volume implant, adjustable implant or temporary tissue expander completely or partially wrapped in mesh depending on surgeon preference and product selection, placed in the mastectomy cavity and sutured into place.

In all cases, peri and post-operative antibiotics and drains were used according to local policy or surgeon preference.

Complication and oncological data were collected by the clinical team at 30 days and 3 months following reconstruction by clinical and/or case-note review depending on whether the patient returned for follow up.

Participants were approached in clinic or during their hospital stay to obtain consent for patient-reported outcome (PRO) assessment at three months following surgery. The PRO was a modified version of the three-month questionnaire used in the UK National Mastectomy and Breast Reconstruction Audit (NMBRA) and included patient self-report of complications occurring in the three months following surgery24. Questionnaires were sent centrally by post or e-mail depending on patient preference with a reminder sent one month following the initial questionnaire if no response was received. Patient satisfaction was also assessed at 18 months following surgery20. Analyses are on-going and results will be reported elsewhere.

**Outcomes**

Four key outcomes were prospectively selected to assess the short-term safety of different approaches to IBBR based on published national quality standards for breast reconstruction derived from the NMBRA23. These were chosen as it was anticipated that a safety outcome may be the primary endpoint of a future trial and equivalence in a non-randomised study was important in informing selection of potential comparators for this study. Four outcomes of interest were included. These were defined a priori20 as: i) implant loss, the unplanned removal or loss of the implant as a result of infection or other complication; ii) infection, the presence of a hot, red breast requiring treatment; iii) readmission, any unplanned readmission to hospital following discharge for any complication of surgery and iv) re-operation, any return to the operating theatre for a complication within three months of the reconstruction procedure. Any implant loss, infection, readmission or re-operation occurring at any time-point within the first three months following the initial reconstruction assessed by clinical review or patient self-report was considered an event and included in the analysis.

Potential risk-factors on each of these key outcomes were identified through a prespecified exploratory risk-factor analysis. Specific variables of interest were identified a priori from the published literature and expert opinion and included patient and procedure-related factors, namely patient age; body mass index (BMI); smoking (current smokers vs others); previous radiotherapy to the ipsilateral breast (yes vs no); receipt of neoadjuvant chemotherapy (yes vs no); bilateral surgery; nipple-sparing vs other mastectomy types; use of fixed-volume vs adjustable implants/expanders and type of IBBR performed. Procedures were classified according to the mode of lower pole coverage as being i) submuscular or subfascial without mesh; ii) dermal-sling procedures using the patient’s own tissue, iii) biological mesh-assisted (including acellular dermal matrix and non-dermal biological products) iv) synthetic mesh-assisted, v) prepectoral if the implant was placed on top of the pectoralis muscle with or without mesh and vi) other if a combination of techniques was used e.g. dermal sling and mesh.

For quality assurance purposes, the principal investigator at each participating site was asked to independently validate the primary outcomes for all study participants at 3 months and to check complete case-ascertainment.

**Statistical analysis**

As this study aimed to inform a future RCT, it was powered to establish parameters required for a sample size calculation and to inform further aspects of trial design such as entry criteria for the future trial.

At the time of design, four clinical outcomes (implant loss, readmission, reoperation and infection) were considered potential primary outcomes in a main trial and a wide number of treatment approaches for IBBR were routinely offered22. A large sample was therefore required in order to (i) estimate with reasonable precision the incidence of four clinical outcomes (implant loss, readmission, reoperation and infection) within treatment approaches; and (ii) determine how implant procedures are performed and any variation in patient selection for each of these approaches. The study was therefore designed to recruit as many patients as possible and follow all to three months. To illustrate (i), the NMBRA24 observed that 9% of IBBR patients reported implant loss at three months. When designing a full trial, establishing this proportion with reasonable precision would be required. A sample size of 197 would allow a two-sided 95% confidence interval for a single proportion, assumed to be 0.09, extending from 0.05 to 0.13, using the large sample normal approximation. Allowing for the 15% loss to follow-up at three months reported in the NMBRA, analysis of implant loss at three months required at least 235 patients to be recruited inform a future trial with implant loss as a primary outcome. For (ii), centres participating in a National Practice Questionnaire (n=81)21,22 were eligible to participate. All centres were eligible as each unit was anticipated to vary in caseload and perform a relatively small number of procedures (4-40 per year).

Analysis was performed to a pre-specified statistical analysis plan approved by the trial steering group. Simple summary statistics were used to describe demographic, procedure, process and outcome data overall and by procedure type. Categorical data was summarised by counts and percentages. Continuous data was summarised by median, upper and lower quartiles and range. No formal statistical testing was performed.

The proportion of patients for each of the four key clinical outcomes was established, alongside the 95% confidence interval for each in order to compare our findings against those reported in the NMBRA24 and published national quality standards23.

The prespecified risk-factor analysis was performed using multivariable logistic regression. Variables of interest included patient age, BMI, smoking status, previous radiotherapy to the ipsilateral breast, receipt of neoadjuvant chemotherapy, bilateral surgery, nipple-sparing vs other mastectomy types, use of fixed-volume vs adjustable implants/expanders and type of IBBR performed.

Data were considered missing at random (Web appendix page 2) and therefore no missing data items were imputed. A complete case analysis was performed. This was considered unlikely to lead to bias as all included risk-factors were measured once per patient26. Linearity was checked for continuous variables for all four logistic models using (loess) smoothed line plots. These checks showed no obvious evidence of non-linearity for the effects of the three continuous variables. A p-value of <0.05 was deemed statistically significant and no adjustments were made for multiplicity. Instead relevant results from other studies were taken into account in the interpretation of results and the exploratory nature of this study emphasised. Statistical Analysis Software (SAS® 9.3; SAS Institute Inc., Cary, NC, USA) was used for all analyses.

This study was registered as an International Standard Randomised Controlled Trial, number ISRCTN37664281 and the protocol was published in 201620. This report has been prepared according to STROBE guidelines.

**Role of the funding source**

The funding source had no role in the study design, data collection, data analysis, data interpretation or writing of the report. The corresponding author (SP) had full access to the data in the study and has final responsibility for the decision to submit for publication.

**RESULTS**

Between 1st February 2014 and 30th June 2016, 2,217 records were entered onto the REDCap database. Of these, 109 (5%) of 2,217 were excluded: 34 patients underwent surgery outside the study period; 22 records did not include an operation date; 50 records provided no information regarding the type of surgery performed and 3 patients did not have an IBBR. Some 2,108 patients from 81 UK units were therefore included in the analysis (Figure 1). The median recruitment per unit was 14 cases (lower quartile [LQ] 6, upper quartile [UQ] 39). Further details on unit recruitment can be found in the web appendix (page 3).

Biological mesh-assisted reconstruction was the most commonly-performed procedure with over half (n=1,133 of 2,108, 53%) of all patients undergoing this technique. Fewer patients underwent synthetic mesh-assisted IBBR (n=243, 12% of 2,108) and a minority received traditional subpectoral reconstruction without mesh (n=181, 9% of 2,108). Subpectoral reconstruction with a dermal-sling was performed in approximately a fifth of patients (n=440, 21% of 2,108) and prepectoral reconstruction with mesh (n=42, 2%, of 2,108) was performed in the latter stages of the study. Some 64 patients received a combination of techniques (e.g. subpectoral reconstruction with dermal-sling and mesh) and for 15 patients, details of the technique were not reported. Strattice (LifeCell) or Surgimend (Integra) were used in 1,215 (66%) of the 1,830 mesh-assisted procedures but in total 14 different products were used during the course of the study with an increasing variety of products used as the study progressed (data not shown).

**Patient demographics, operative and oncological data**

Table 1 summarises the demographics of patients included in the study. The median age was 49 years (LQ 43; UQ 57). BMI was in the normal range (24.8 kg/m2; LQ 22.3 kg/m2; UQ 28.2 kg/m2) and higher overall in dermal-sling patients (28.0 kg/m2; LQ 24.8 UQ 32.3 kg/m2). One tenth of patients (n=206, 10% of 2,108) were current smokers and 7% (n=139 of 2,108) had received previous radiotherapy to the ipsilateral breast (table 1). The 2,108 patients underwent 2,655 implant-based reconstructive procedures. One-fifth were risk-reducing patients (n=411, 19% of 2,108) and 70% malignancy only (n=1505, 71% of 2,108). Of the 25% (n=547/2108) patients undergoing bilateral surgery, one-third (n=188/547) had a contralateral risk-reducing mastectomy at the time as their index cancer operation (table 2).

A one-stage reconstruction was planned in over three-quarters of patients (n=1,650, 78% of 2,108) and 60% (n=1,240, 59% of 2,108) had a definitive fixed-volume implant placed at the time of their surgery. Two-stage reconstruction with tissue-expanders or expandable implants (all patients: n=465, 22% of 2,108) was more commonly seen in patients having traditional submuscular procedures without mesh (n=104, 58% of 181) and those undergoing dermal-sling reconstruction (139, 32% of 440). Skin and nipple-sparing reconstruction was performed in one quarter of cases (n=507, 25% of 2,108) (table 2).

Post-operative oncological data and multidisciplinary team decision-making for adjuvant treatment is summarised in table 3. Approximately one-third of the 1693patients undergoing mastectomy and IBBR for malignancy were recommended chemotherapy (n=562/1693) or radiotherapy (n=495/1693) following their reconstruction. This did not appear to be related to the type of procedure performed, although more patients having standard subpectoral reconstruction without mesh were recommended for radiotherapy that patients having other procedure types.

**Short-term outcomes**

Of the 2108 patients recruited, 2081 (99%) were followed up to three months (median follow up 3 months, interquartile range [IQR] 3-3). The clinical outcomes of interest are summarised in table 4 overall and split by type of IBBR procedure. NMBRA data and quality standards for breast reconstruction23 are also included in this table for comparison.

Implant loss was experienced by 9% (n=182/2,081, 95% confidence interval [CI] 8%-10%) patients, greater than both the NMBRA published data (5%) and National Quality Standards (<5%). One in four patients (n=522/2,081, 25%: 95% CI 23-27%) experienced a post-operative infection requiring treatment and 372 patients were readmitted (18% of 2,081, 95% CI 16%-20%) for a complication of their reconstruction within three months. Both these results are consistent with results from the NMBRA23 (25% and 16% for infection and readmission respectively) and greater than the National Quality Standards (<10% and <5%). However, the percentage of patients requiring re-operation was greater than that in the NMBRA with almost 17% (n=370, of 2,081 95% CI 16%-20%) of this cohort requiring further surgery for complications of their reconstruction (table 4).

Multivariable logistic regression identified an association between BMI and smoking with all four clinical outcomes (table 5). This analysis also identified an association between infection and previous radiotherapy and reoperation and operative time. Neoadjuvant chemotherapy, bilateral surgery, indication for surgery, nipple-sparing procedures, insertion of a definitive fixed-volume implant and notably type of IBBR performed were not significant risk-factors for any of the key safety outcomes (table 5). Details of the number of events for each risk-factor can be found in the web appendix (page 8).

**DISCUSSION**

This national multicentre cohort study of 2,108 patients undergoing IBBR in 81 centres across the UK demonstrates that the short-term clinical outcomes of IBBR fall far short of the published aspirational quality standards for immediate breast reconstruction23 and have not improved in the 10 years since the NMBRA24. Despite recent published evidence demonstrating increased complication rates in mesh-assisted IBBR11, there was no association between type of mesh and short-term safety outcomes in this large non-randomised study. The optimum technique for IBBR is therefore unknown and more comparative data are needed. Indeed, a large-scale pragmatic RCT to identify the most clinically and cost-effective approach to IBBR will be required to truly answer this important question and provide information to inform clinical and health policy decisions.

Despite the lack of evidence, mesh-assisted single-stage DTI reconstruction using fixed-volume or adjustable implants has become the most widely-used procedure in the UK22, with less than 10% of patients undergoing traditional two-stage expander-implant procedures. This widespread adoption of mesh suggests that an RCT attempting to compare single-stage DTI reconstruction with mesh and the standard two-stage techniques would be very difficult due to surgeon preference. This study, however, shows little difference in the short-term clinical outcomes of biological and synthetic mesh-assisted IBBR and has highlighted the large number of products in current use. Prepectoral reconstruction was only performed in a minority of patients in this study although it is gaining popularity7. Despite the challenges associated with an RCT in breast reconstruction, methods have been developed and successfully used to overcome these issues and support surgeons to recruit into trials of very difference types of procedures where preferences may be strong27.

Although reconstructive technique does not appear to impact on short-term safety outcomes, patient factors including increasing BMI and current smoking are associated with increased risks of implant loss, infection, readmission and re-operation. Additionally, these results indicate that previous radiotherapy may be associated with a modest increase in the odds of developing a post-operative infection. Whilst this analysis was exploratory in nature, these results highlight the importance of careful patient selection and providing patients at high-risk with accurate information about the likelihood of post-operative complications to allow them to make more informed decisions. Operative time is another risk-factor associated with major complications. This may support dual surgeon operating for bilateral cancer cases or performing contralateral risk-reducing mastectomy (in those with unilateral malignancy) as a delayed procedure.

The percentages of patients experiencing implant loss, readmission and infection identified in this study remain unchanged since the 2008/9 NMBRA while the percentage of patients requiring re-operation has more than tripled24. Reasons for this are complex. Rates of IBBR have increased significantly since 2008/95,22 but there is no evidence to suggest that the indications for implant-based surgery have changed as the proportions of patients who smoke; have diabetes; a high BMI or ASA grades III/IV in the current study are largely consistent with the initial cohort24. Increased numbers of re-operations may reflect more aggressive management of complications when mesh is used, but this additional intervention does not appear to translate into a reduced percentage of implant loss. Although the percentages of implant loss and return to theatre in the current study are much lower than those reported in a recent randomised trial11,13, they are much higher than those reported in other large prospective observational studies14,15,28 and summarised in recent systematic reviews8,9. This large multicentre study is therefore more likely to reflect the ‘real world’ outcomes of IBBR and highlights the need for improvement.

This national prospective study adds significantly to the evidence base in IBBR but has several limitations. Firstly, it is a non-randomised study which will be subject to bias. Notably, patients undergoing dermal-sling reconstruction had higher BMIs that those in the other groups but other subtler differences may exist between patients undergoing different procedures that could not be appreciated in this study. Despite defining outcomes including implant loss a priori, practice changed during the study period. Of particular note was the introduction of implant salvage procedures whereby fixed-volume implants that were infected or exposed were debrided; washed out and replaced either with a new implant or a tissue expander. This was not considered an ‘implant loss’ in the study although the initial implant was removed. Infection was another controversial area. Any redness requiring treatment with antibiotics was included. We acknowledge that this may have overestimated the rate of implant infection but reported rates were consistent those in the NMBRA. Clear, unambiguous definitions of outcomes will therefore be needed for future studies. Smoking, BMI, operative time and previous radiotherapy were identified as risk-factors for complications in this study and this potential association may be informative when designing subsequent RCTs as a basis for balancing randomisation. The study was not powered to establish prognostic factors, however and the results should be confirmed in an external validation study but consistency between these results and those in other studies29,30 support these findings. Finally, complications were only assessed until 3 months. This would fail to capture complications such as infection which developed while patients were receiving chemotherapy or problems developing as a result of adjuvant radiotherapy for which a longer period of follow up would be required.

This large non-randomised study strongly supports the need for an RCT in IBBR and potential trial designs may include biological vs synthetic mesh or pre-pectoral vs subpectoral implant placement. Before embarking on a full trial, a pilot RCT to establish whether recruitment is possible is recommended. In addition, urgent work is also needed to improve outcomes for patients undergoing IBBR in the UK. The percentage of patients experiencing implant loss and infection and those requiring re-operation and readmission do not appear to have improved since NMBRA and do not meet published quality standards. Reasons for this are unclear, but non-compliance with best practice guidelines may be a contributory factor21 and further investigation of variation by centre is planned. This study provides further evidence that increasing BMI and smoking significantly increase the risk of complications. These are not immediately modifiable in the short-term, but neoadjuvant chemotherapy or endocrine therapy could be used as an effective strategy to provide patients with breast cancer the opportunity to lose weight or stop smoking prior to surgery. Bilateral risk-reducing surgery, however, could be delayed until these risk-factors had been addressed. An alternative solution would be to restrict the offer of IBBR to patients without risk-factors. This may not be practical or ethical and a more appropriate focus may be to develop effective strategies to help patients better understand the potential risks of surgery to allow them to make fully-informed decisions. Finally, reducing the observed variation may effectively improve outcomes and this will be the focus of the UK ‘Getting it Right First Time Initiative’ (http://gettingitrightfirsttime.co.uk/surgical-specialty/breast-surgery/). It is important however, that any standardisation of care reflects evidence-based best practice and further exploratory analysis of the iBRA cohort will support this.

There remains the need for high-quality randomised evidence to support the best practice of IBBR and the equivalence of different techniques in this non-randomised study supports a future RCT. The current outcomes of IBBR in the UK are poor and surgeons need to commit to robust evaluation if outcomes for patients are to be improved.

**Author contributions**

SP, CH, ST, JS, JMB, EJC, PRW and LW conceived and designed the study and data collection forms; EJC, PRW and JMB provided methodological support; SP, CH, JMB, PRW, EJC, RIC, MDG, AJ and ET secured funding for the project; SP, SM, CH, LW, RIC, MG and AJ provided clinical leadership and promoted unit participation and data collection; EJC, PRW and SP drafted the statistical analysis plan and analysed the data; All authors contributed to data interpretation. SP wrote the first draft of the paper. JMB provided strategic support for SP as SP led the whole study. SP is the guarantor. All authors reviewed and critically revised the manuscript and approved it prior to submission.

**Collaborators**

Local investigators and members of the iBRA Steering Group and the Breast Reconstruction Research Collaborative are PUBMED citable collaborators in this study and are listed in the Web appendix (page 1).

**Competing interests**

SP, CH, PRW AJ, LW report grants from NIHR Research for Patient Benefit Programme (see below) during conduct of the study. SP and AJ report grants from the Association of Breast Surgery and the British Association of Plastic Reconstructive and Aesthetic Surgeons (see below). SP reports grants from NIHR Clinician Scientist Award and non-financial support from MRC ConDucT-II Hub, during the conduct of the study. The remaining authors have nothing to disclose.

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**Data sharing statement**

Individual participant data (de-identified), the data dictionary and statistical analysis plan for this study will be available to researchers following methodological review of the proposed analysis plan by the iBRA steering group. Proposals may be submitted to the corresponding author (shelley.potter@bristol.ac.uk) from 12 months to 3 years following publication. To gain access, data requestors will need to sign a data access agreement.

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**Table 1 Patient demographics by type of implant-based reconstruction performed**

|  | **All patientsA****N=2108** | **Submusc/****subfascial (no mesh)****N=181 (9%)** | **Dermal sling****N=440 (21%)** | **Biological mesh****N=1133 (54%)** | **Synthetic mesh****N=243 (12%)** | **Pre-pec****N=42 (2%)** | **Other****N=64 (3%)** | **Not known****N=15 (1%)** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Age** (years)Median (LQ, UQ) (range) | 49 (43, 57) (16, 83) | 49 (43, 56) (16, 80) | 51 (45, 59) (24, 81) | 49 (42, 56) (20, 80) | 50 (43,58) (20, 83) | 48 (38, 52) (19, 73) | 49 (43, 58) (23, 74) | 46 (46, 52) (39, 63) |
| Not known | 13 | 0 | 2 | 4 | 1 | 0 | 0 | 6 |
| **BMI** (kg/m2)(median, LQ, UQ) (range) | 24.8 (22.3, 28.2) (14.4,54.0) | 24.0 (21.8, 27.7) (17, 51.6) | 28.0 (24.8, 32.2) (18.3,54.0) | 24.0 (21.9, 26.9) (14.4, 44.5) | 24.8 (22.1, 28.0) (17.3, 42.6) | 23.8 (22.2, 27.1) (18.7, 36.0) | 27.6 (23.8, 31.1) (18.0, 40.0) | 23.8 (23.4, 26.5) (18.8, 32.2) |
| Not obese (BMI<30 kg/m2) | 1613 (82) | 133 (80) | 247 (60) | 976 (90) | 184 (84) | 33 (79) | 44 (70) | 4 (80) |
| Obese (BMI>=30kg/m2) | 367 (18) | 34 (20) | 163 (40) | 107 (10) | 36 (16) | 9 (21) | 19 (30) | 1 (20) |
| Not known | 128 | 14 | 30 | 50 | 23 | 0 | 1 | 10 |
| **Smoking status** |  |  |  |  |  |  |  |  |
| Non-smoker | 1626 (78%) | 137 (77%) | 335 (77%) | 881 (79%) | 193 (79%) | 31 (76%) | 52 (85%) | 6 (100%) |
| Ex-smoker (stopped >6/52)  | 231 (11%) | 19 (11%) | 54 (12%) | 123 (11%) | 22 (9%) | 8 (20%) | 5 (8%) | 0 (0%) |
| Current smoker  | 206 (10%) | 22 (12%) | 42 (10%) | 111 (10%) | 26 (11%) | 2 (5%) | 4 (7%) | 0 (0%) |
| Nicotine replacement  | 10 (1%) | 0 (0%) | 3 (1%) | 5 (1%) | 2 (1%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Not known | 35 | 3 | 6 | 13 | 0 | 1 | 3 | 9 |
| **Diabetes** |  |  |  |  |  |  |  |  |
| Yes | 54 (3%) | 4 (2%) | 21 (5%) | 17 (2%) | 9 (4%) | 0 (0%) | 3 (5%) | 0 (0%) |
| No | 2013 (97%) | 174 (98%) | 408 (96%) | 1099 (98%) | 232 (96%) | 41 (100%) | 61 (95%) | 8 (100%) |
| Not known | 41 | 3 | 11 | 17 | 2 | 1 | 0 | 7 |
| **Previous radiotherapy to ipsilateral breast** |  |  |  |  |  |  |  |  |
| Yes | 139 (7%) | 14 (8%) | 26 (6%) | 76 (7%) | 17 (7%) | 2 (5%) | 5 (8%) | 1 (13%) |
| No | 1953 (93%) | 167 (92%) | 413 (94%) | 1052 (93%) | 223 (93%) | 40 (95%) | 59 (92%) | 7 (87%) |
| Not known | 16 | 0 | 1 | 5 | 3 | 0 | 0 | 7 |
| **Neo-adjuvant chemotherapy**  |  |  |  |  |  |  |  |  |
| Yes | 226 (11%) | 28 (16%) | 57 (13%) | 111 (10%) | 19 (8%) | 1 (2%) | 8 (13%) | 2 (22%) |
| No | 1853 (89%) | 150 (84%) | 381 (87%) | 1006 (90%) | 221 (92%) | 41 (98%) | 56 (87%) | 7 (78%) |
| Not known | 29 | 3 | 2 | 16 | 3 | 0 | 0 | 6 |
| **Neo-adjuvant endocrine therapy** |  |  |  |  |  |  |  |  |
| Yes | 78 (4%) | 11 (6%) | 21 (5%) | 37 (3%) | 8 (3%) | 1 (2%) | 2 (3%) | 1 (10%) |
| No | 1999 (96%) | 167 (94%) | 415 (95%) | 1079 (97%) | 233 (97%) | 41 (98%) | 61 (97%) | 9 (90%) |
| Not known | 31 | 3 | 4 | 17 | 2 | 0 | 1 | 5 |
| **Previous surgeries****Previous surgery to ipsilateral breast** |  |  |  |  |  |  |  |  |
| Yes | 654 (31%) | 61 (34%) | 113 (26%) | 371 (33%) | 80 (33%) | 8 (19%) | 23 (36%) | 4 (44%) |
| No | 1434 (67%) | 119 (66%) | 332 (74%) | 755 (67%) | 162 (67%) | 34 (81%) | 41 (64%) | 5 (56%) |
| Not known | 20 | 1 | 5 | 7 | 1 | 0 | 0 | 6 |
| **If yes to previous surgery, type of surgery(s) received** |  |  |  |  |  |  |  |  |
| Wide local excision | 375 (57%) | 29 (48%) | 60 (53%) | 218 (59%) | 49 (61%) | 3 (38%) | 16 (70%) | 3 (75%) |
|  With previous radiotherapy | 108 (29%) | 8 (28%) | 17 (28%) | 62 (29%) | 15 (31%) | 0 (0%) | 5 (31%) | 1 (33%) |
|  Without previous radiotherapy | 265 (71%) | 21 (72%) | 43 (72%) | 155 (71%) | 33 (69%) | 3 (100%) | 11 (69%) | 2 (67%) |
|  Not known | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| Sentinel node biopsy | 299 (46%) | 27 (44%) | 48 (43%) | 178 (48%) | 31 (39%) | 6 (75%) | 10 (44%) | 1 (25%) |
| Augmentation | 49 (8%) | 3 (5%) | 5 (4%) | 32 (9%) | 6 (8%) | 1 (13%) | 2 (9%) | 0 (0%) |
| Reduction | 28 (4%) | 1 (2%) | 5 (4%) | 13 (4%) | 6 (8%) | 2 (25%) | 3 (13%) | 0 (0%) |
| Other | 116 (18%) | 22 (36%) | 19 (17%) | 63 (17%) | 14 (18%) | 0 (0%) | 2 (9%) | 0 (0%) |
|  |  |  |  |  |  |  |  |  |

A For patients with two implant based reconstructions where mode differed by breast (n=10) these patients are summarised in both mode columns, depending on the mode used, and once in the overall column. Variations of approaches per breast within patient were: biological mesh and dermal sling (n=3); biological mesh and synthetic mesh (n=1); dermal sling and submuscular or subfacial (n=4); other and submuscular or subfacial (n=1); other and synthetic mesh (n=1)

B 1261 (60%) patients had none of the prior or neo-adjuvant treatments reported. 7 patients had missing data for all reported prior or neo-adjuvant treatments.

**Table 2 – Operative details by type of implant reconstruction performed**

|  | **All patientsA****n=2108** | **Submusc/ subfascial****n=181** | **Dermal sling****n=440** | **Biological mesh****n=1133** | **Synthetic mesh****n=243** | **Pre-pec****n=42** | **Other****n=64** | **Not known****n=15** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **ASA grade** |  |  |  |  |  |  |  |  |
| 1 | 1246 (60%) | 89 (50%) | 206 (48%) | 736 (65%) | 155 (64%) | 25 (60%) | 36 (57%) | 5 (71%) |
| 2 | 783 (38%) | 82 (46%) | 213 (49%) | 371 (33%) | 80 (33%) | 15 (36%) | 25 (40%) | 1 (14%) |
| 3 | 57 (3%) | 8 (5%) | 15 (5%) | 22 (2%) | 7 (3%) | 2 (5%) | 2 (3%) | 1 (14%) |
| 4 | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Not known | 22 | 2 | 6 | 4 | 1 | 0 | 1 | 8 |
| **Laterality** |  |  |  |  |  |  |  |  |
| Bilateral  | 547 (26%) | 40 (78%) | 299 (68%) | 866 (76%) | 176 (72%) | 21 (50%) | 45 (70%) | 15 (100%) |
| Unilateral | 1561(74%) | 40 (22%) | 141 (32%) | 267 (24%) | 69 (28%) | 21 (50%) | 19 (30%) | 0 (0%) |
| **IndicationB** |  |  |  |  |  |  |  |  |
| Malignancy  | 1505(72%) | 139 (76%) | 284 (65%) | 835 (74%) | 173 (71%) | 20 (48%) | 43 (68%) | 13 (100%) |
| Risk reduction | 411 (19%) | 27 (15%) | 94 (21%) | 209 (19%) | 48 (20%) | 18 (43%) | 17 (27%) | 0 (0%) |
| Malignancy and contralateral risk reducing surgery | 188 (9%) | 17 (9%) | 62 (14%) | 88 (8%) | 22 (9%) | 4 (10%) | 3 (5%) | 0 (0%) |
| Not known | 4 | 0 | 0 | 1 | 0 | 0 | 1 | 2 |
| **Planned procedureC** |  |  |  |  |  |  |  |  |
| One stage | 1638(78%) | 77 (43%) | 301(68%) | 969 (86%) | 200 (82%) | 36 (86%) | 52 (81%) | 7 (64%) |
| Two stage | 453 (21%) | 100 (55%) | 134 (31%) | 159 (14%) | 42 (17%) | 6 (14%) | 12 (19%) | 4 (36%) |
| Different approach per breast | 12 (1%) | 4 (2%) | 5 (1%) | 4 (0%) | 1 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Not known | 5 | 0 | 0 | 1 | 0 | 0 | 0 | 4 |
| **Type of mastectomyD,E** |  |  |  |  |  |  |  |  |
| Skin-sparing  | 1161(55%) | 117 (65%) | 96 (22%) | 756 (67%) | 149 (62%) | 15 (36%) | 24 (38%) | 5 (53%) |
| Skin and nipple-sparing | 486 (23%) | 41 (23%) | 21 (5%) | 308 (27%) | 81 (34%) | 22 (52%) | 15 (23%) | 1 (17%) |
| Reduction pattern | 398 (19%) | 7 (4%) | 308 (70%) | 51 (5%) | 6 (3%) | 5 (12%) | 22 (34%) | 0 (0%) |
| Other | 18 (1%) | 9 (5%) | 3 (1%) | 3 (0%) | 1 (0%) | 0 (0%) | 2 (3%) | 0 (0%) |
| Different type per breast | 32B (2%) | 7 (4%) | 12 (3%) | 13 (1%) | 4 (2%) | 0 (0%) | 1 (2%) | 0 (0%) |
| Not known | 13 | 0 | 0 | 2 | 2 | 0 | 0 | 9 |
| **IncisionF,G** |  |  |  |  |  |  |  |  |
| Peri-areolar | 127 (6%) | 10 (6%) | 3 (1%) | 90 (8%) | 16 (7%) | 3 (7%) | 5 (8%) | 0 (0%) |
| Lateral | 159 (8%) | 13 (7%) | 2 (1%) | 108 (10%) | 29 (12%) | 5 (12%) | 2 (3%) | 0 (0%) |
| Inframammary | 230 (11%) | 20 (11%) | 4 (1%) | 149 (13%) | 40 (17%) | 13 (31%) | 5 (8%) | 1 (25%) |
| Elipitical removing NAC | 936 (45%) | 106 (59%) | 13 (3%) | 665 (59%) | 123 (51%) | 11 (26%) | 17 (27%) | 2 (50%) |
| Wise pattern | 541 (26%) | 11 (6%) | 403 (92%) | 77 (7%) | 13 (5%) | 7 (17%) | 31 (48%) | 1 (50%) |
| Other | 78 (4%) | 16 (9%) | 6 (1%) | 36 (3%) | 16 (7%) | 2 (5%) | 3 (5%) | 0 (0%) |
| Different approaches | 19C (1%) | 5 (3%) | 6 (1%) | 7 (1%) | 3 (1%)  | 1 (2%) | 1 (2%) | 0 (0%) |
| Not known | 18 | 0 | 3 | 1 | 3 | 0 | 0 | 11 |
| **Mastectomy weight** (grams)H,I(median, LQ, UQ, range) | 390 (260, 583) (39, 2300) | 321 (208, 456) (68, 2300) | 665 (492, 915) (53, 2260) | 327 (229, 476) (39, 1480) | 383 (264, 540) (83, 2200) | 310(230, 527) (75., 1544) | 544 (332, 790) (166, 1505) | 280 (280,280) (280, 280) |
| Not known | 90 | 17 | 13 | 31 | 9 | 2 | 5 | 14 |
| **Prosthesis usedJ,K** |  |  |  |  |  |  |  |  |
| Fixed volume implant | 1235(59%) | 50 (28%) | 210 (48%) | 737 (65%) | 166 (69%) | 36 (88%) | 39 (61%) | 2 (67%) |
| Combined expander/implant  | 466E (22%) | 50 (28%) | 102 (23%) | 250 (22%) | 46 (19%) | 1 (2%) | 18 (28%) | 1 (33%) |
| Expander | 383 (18%) | 80 (44%) | 125 (29%) | 140 (12%) | 29 (12%) | 4 (10%) | 7 (11%) | 0 (0%) |
| Different approaches | 4 (0%) | 0 (0%) | 0 (0%) | 4 (0%) | 1 (0%) | 0 (0%) | 0 (0.0%) | 0 (0%) |
| Not known | 20 | 1 | 3 | 2 | 1 | 1 | 0 | 12 |
| **Axillary surgeryL,M** |  |  |  |  |  |  |  |  |
| None | 585 (28%) | 46 (25%) | 121 (28%) | 315 (28%) | 67 (28%) | 20 (48%) | 21 (33%) | 0 (0%) |
| SNB | 881 (42%) | 64 (35%) | 177 (40%) | 495 (47%)  | 106 (44%) | 11 (26%) | 23 (36%) | 5 (83%) |
| Axillary sample | 23 (1%) | 5 (3%) | 1 (0%) | 13 (1%) | 3 (1%) | 0 (0%) | 0 (0%) | 1 (17%) |
| Axillary clearance | 226 (11%) | 29 (16%) | 48 (11%) | 112 (10%) | 24 (10%) | 4 (10%) | 9 (14%) | 0 (0%) |
| SNB and ANC | 32 (2%) | 3 (2%) | 9 (2%) | 15 (1%) | 4 (2%) | 0 (0%) | 1 (2%) | 0 (0%) |
| Previous axillary staging  | 164 (8%) | 16 (9%) | 23 (5%) | 99 (9%) | 16 (7%) | 3 (7%) | 7 (11%) | 0 (0%) |
| Different approaches | 186 (9%) | 18 (10%) | 60 (14%) | 83 (7%) | 23 (10%) | 4 (10%) | 3 (5%) | 0 (0%) |
| Not known | 11 | 0 | 1 | 1 | 0 | 0 | 0 | 9 |
|  |  |  |  |  |  |  |  |  |
| **Operative time** (minutes)(median, LQ, UQ, range)Not known | 180(147-210)(60, 570)195 | 160(130-195)(60, 380)24 | 186(150-240)(62,530)37 | 180(150-210)(69, 570)97 | 165(135-187)(70, 410)4 | 180(147-240)(68, 380)17 | 180(150-246)(60, 480)3 | 149(118-180)(118, 180)13 |

A For patients with two implant based reconstructions where mode differed by breast (n=10) these patients are summarised in both mode columns, depending on the mode used, and once in the overall column. Variations of approaches per breast within patient were: biological mesh and dermal sling (n=3); biological mesh and synthetic mesh (n=1); dermal sling and submuscular or subfacial (n=4); other and submuscular or subfacial (n=1); other and synthetic mesh (n=1)

B This variable is collected on a per breast basis. For patients with two implant based reconstructions, with data for one breast and not the other, that patient is classified according to the non-missing data (n=6).

C This variable is collected on a per breast basis. For patients with two implant based reconstructions, with data for one breast and not the other, that patient is classified according to the non-missing data (n=1).

D This variable is collected on a per breast basis. For patients with two implant based reconstructions, with data for one breast and not the other, that patient is classified according to the non-missing data (n=5).

E Combinations of type of mastectomy within patients with two implant based reconstructions with different types per breast were: Skin sparing mastectomy and Skin and nipple preserving (n=15); Skin sparing mastectomy and Reduction (wise) pattern (n=7); Skin sparing mastectomy and Other (n=3); Skin and nipple preserving and Reduction (wise) pattern (n=2); Skin and nipple preserving and Other (n=4); Reduction (wise) pattern and Other (n=1).

F This variable is collected on a per breast basis. For patients with two implant based reconstructions, with data for one breast and not the other, that patient is classified according to the non-missing data (n=6).

G Combinations of location of incision within patients with two implant based reconstructions with different types per breast were: Elliptical removing NAC and Inframammary (n=1); Elliptical removing NAC and Lateral (n=4); Elliptical removing NAC and Other (n=3); Elliptical removing NAC and Peri-areolar (nipple preserving) (n=3); Elliptical removing NAC and Wise-pattern (n=1); Inframammary and Lateral (n=1); Inframammary and Other (n=2); Inframammary and Peri-areolar (nipple preserving) (n=1); Lateral and Peri-areolar (nipple preserving) (n=1); Other and Wise pattern (n=2).

H This variable is collected on a per breast basis. For patients with two implant based reconstructions, with data for one breast and not the other, that patient is classified according to the non-missing data (n=19).

I Where two patients have two implant based reconstructions with mastectomy weight data for both breasts (n=511), the average weight is given. The difference in weight between breasts varied from 0g to 463g (median 40g).

J This variable is collected on a per breast basis. For patients with two implant based reconstructions, with data for one breast and not the other, that patient is classified according to the non-missing data (n=7).

K Combinations of breast prosthesis used within patients with two implant based reconstructions with different types per breast were: Combined implant (Beckers) and Fixed volume implant (n=1); Fixed volume implant and Temporary expander (n=3).

L This variable is collected on a per breast basis. For patients with two implant based reconstructions, with data for one breast and not the other, that patient is classified according to the non-missing data (n=4).

M Combinations of axillary surgery within patients with two implant based reconstructions with different surgeries per breast were: Axillary clearance and None (n=41); Axillary clearance and Previous staging axillary surgery (n=1); Axillary clearance and sentinel node biopsy (n=10); Axillary sample and None (n=6); None and Previous staging axillary surgery (n=32); None and Sentinel node biopsy and immediate clearance (n=2); None and Sentinel node biopsy (n=46); Sentinel node biopsy and Previous staging axillary surgery (n=1).

**Table 3 Post-operative oncology data for patients undergoing mastectomy for oncological indications (n=1693)**

|  | **All patientsA****(n=1693)** | **Submuscular/ subfascial****(n=154)** | **Dermal sling (n=340)** | **Biological mesh (n=922)** | **Synthetic mesh (n=194)** | **Pre-pec (n=24)** | **Other (n=46)** | **Not known (n=13)** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Laterality** |  |  |  |  |  |  |  |  |
| Unilateral malignancy  | 1633 (97%) | 147 (96%) | 329 (97%) | 896 (97%) | 184 (95%) | 20 (83%) | 44 (86%) | 13 |
| Bilateral malignancy | 60 (3%) | 7 (4%) | 11 (3%) | 26 (3%) | 10 (5%) | 4 (17%) | 2 (4%) | 0 |
| **Invasive status** |  |  |  |  |  |  |  |  |
| Invasive | 1223(77%) | 113 (81%) | 244 (76%) | 656 (75%) | 144 (78%) | 22 (96%) | 34 (83%) | 10 |
| DCIS | 363 (23%) | 25 (18%) | 76 (24%) | 214 (24%) | 39 (21%) | 1 (4%) | 7 (17%) | 1 |
| Different status per breast | 11 (1%) | 1 (1%) | 1 (0%) | 8 (1%) | 1 (1%) | 0 (0%) | 0 (0%) | 0 |
| Not known | 96 | 15 | 19 | 44 | 10 | 1 | 5 | 2 |
| **Grade**  |  |  |  |  |  |  |  |  |
| Low grade/well-differentiated  | 131 (11%) | 7 (6%) | 20 (8%) | 81 (12%) | 15 (11%) | 2 (9%) | 3 (9%) | 3 |
| Intermediate grade/moderately differentiated  | 653 (54%) | 69 (62%) | 137 (57%) | 341 (52%) | 75 (53%) | 11 (50%) | 15 (44%) | 5 |
| High grade/poorly differentiated  | 418 (34%) | 35 (32%) | 80 (33%) | 230 (35%) | 50 (36%) | 6 (27%) | 15 (44%) | 2 |
| Different per breast | 14 (1%) | 0 (0%) | 4 (2%) | 5 (1%) | 1 (1%) | 3 (17%) | 1 (3%) | 0 |
| Not known | 477 | 43 | 99 | 265 | 53 | 2 | 12 | 3 |
| **Size of lesion (mm) (median, LQ, UQ, range)** | 21 (12 , 35) (0, 750) | 20 (16,50) (0, 114) | 23 (12 , 39) (0, 750) | 20 (12 , 31) (0, 125) | 28 (14 , 42) (0, 120) | 20 (14 , 36) (3, 80) | 20 (13 , 36) (0, 150) | 14 (7,19)(0, 65) |
| Not known | 480 | 43 | 98 | 265 | 54 | 2 | 15 | 3 |
| **Number of involved nodes (N, UQ,LQ, range)** | 0 (0,1)(0, 54) | 0 (0, 1)(0, 22) | 0 (0 , 1)(0, 28) | 0 (0 , 0)(0, 32) | 0 (0 , 1)(0, 54) | 0 (0 , 1)(0, 5) | 0 (0 , 1)(0, 25) | 0 (0 , 1)(0, 0) |
| Not known | 113 | 15 | 21 | 53 | 12 | 1 | 8 | 3 |
| **Planned ANC for node positive patients** |  |  |  |  |  |  |  |  |
| Yes | 193E (48%) | 28 (62%) | 34 (39%) | 99 (50%) | 29 (52%) | 1 (17%) | 2 (25%) | 0 (0.0%) |
| No | 206E( 52%) | 17 (38%) | 53 (61%) | 98 (50%) | 27 (48%) | 5 (83%) | 6 (75%) | 0 (0.0%) |
| Not applicable | 1268 | 107 | 249 | 709 | 136 | 18 | 36 | 13 |
| Not known | 26 | 2 | 4 | 16 | 2 | 0 | 2 | 0 |
| **MDT treatment recommendation** |  |  |  |  |  |  |  |  |
| **Adjuvant chemotherapy**  |  |  |  |  |  |  |  |  |
| Yes | 562 (36%) | 65 (47%) | 103 (33%) | 299 (35%) | 71 (39%) | 10 (44%) | 13 (33%) | 1 |
| No | 1002(64%) | 73 (53%) | 212 (67%) | 561 (65%) | 112 (61%) | 13 (57%) | 26 (67%) | 5 |
| Not known | 129 | 16 | 25 | 62 | 11 | 1 | 7 | 7 |
| **Adjuvant radiotherapy**  |  |  |  |  |  |  |  |  |
| Yes | 495 (32%) | 71 (52%) | 101 (32%) | 246 (28%) | 62 (34%) | 3 (13%) | 11 (28%) | 1 |
| No  | 1055(67%) | 63 (46%) | 210 (67%) | 613 (71%) | 118 (65%) | 18 (78%) | 28 (72%) | 5 |
| One breast only | 17 (1%) | 2 (2%) | 4 (1%) | 6 (1%) | 3 (2%) | 2 (9%) | 0 (0%) | 0 |
| Not known | 126 | 18 | 25 | 57 | 11 | 1 | 7 | 7 |
| **Adjuvant endocrine therapy** |  |  |  |  |  |  |  |  |
| Yes | 1081(69%) | 95 (70%) | 209 (66%) | 597 (69%) | 126 (69%) | 19 (83%) | 29 (74%) | 6 |
| No | 491 (31%) | 40 (30%) | 106 (34%) | 275 (32%) | 56 (31%) | 4 (17%) | 10 (26%) | 0 |
| Not known | 121 | 19 | 25 | 50 | 12 | 1 | 7 | 7 |

A Mode of lower pole coverage missing for 13 patients with at least one malignant breast, not included in type column, though included for Overall summary.

B Where two patients have two malignant breasts with lesions size data for both breasts (n=38), the average lesions size is given. Size of lesions between breasts within these patients varied from 0 to 70 (median 10).

C Where two patients have two malignant breasts with number of lymph nodes involved data for both breasts (n=53), the average number of nodes is given. The number of lymph nodes between breasts varied from 0 to 15 (median 0).

D Where two patients have two malignant breasts with number of lymph nodes removed data for both breasts (n=53), the average number of nodes is given. The number of lymph nodes removed between breasts varied from 0 to 20 (median 1).

E Where two patients have two malignant breasts with planned axillary clearance data available for one breast, patients are classified according to the breast for which there is data (yes: n=12; no: n=9).

**Table 4 Three month outcomes following implant-based breast reconstruction by procedure type compared to outcomes in the National Mastectomy and Breast Reconstruction Audit and UK National Quality Criteria for Breast Reconstruction**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **NMBRA outcomes at 3 monthsa** | **National Quality Standards** | **All patients in iBRA study****(n=2081)b** | **Submuscular/****Fascial (n=180)** | **Dermal sling (n=436)** | **Biological mesh (e.g. Strattice) (n=1121)** | **Synthetic mesh (e.g. TiLOOP)****(n=236)** | **Pre-pectoral (n=42)** | **Other** **(n=63)** |
| **Reoperation n (n/N%)[CI]** | 5% | <5% | 370 (18%)[16, 20] | 30 (17%)[12, 23] | 79 (18%)[15, 22] | 193 (17%)[15, 20] | 48 (20%)[15, 26] | 9 (21%)[10, 37] | 9 (14%)[7, 25] |
| **Readmission n (n/N%)[CI]** | 16% | <5% | 372 (18%)[16, 20] | 31 (17%)[12, 24] | 85 (20%)[16, 24] | 185 (17%)[14, 19] | 49 (21%)[15.8, 26.5] | 10 (25%)[12, 40] | 10 (116%)[8, 27] |
| **Infection n (n/N%)[CI]** | 25% | <10%c | 522 (25%)[23, 27] | 39 (22%)[16, 28] | 138 (32%)[27, 36] | 251 (22%)[20, 25] | 61 (26%)[20, 32] | 11 (26%)[14, 42] | 19 (30%)[19, 43] |
| **Implant loss n (n/N%)[CI]** | 9% | <5% | 182 (9%)[8,10] | 17 (10%)[6, 15] | 47 (111%)[8, 14] | 90 (8%)[7, 10] | 24 (10%)[7, 15] | 3 (7%)[2, 20] | 2 (3%)[0, 11] |

aNMBRA - National Mastectomy and Breast Reconstruction Audit

bOncoplastic Breast Reconstruction – Guidelines for Best Practice

cAcellular dermal matrix (ADM) assisted breast reconstruction procedures: Joint guidelines from the Association of Breast Surgery and the British Association of Plastic, Reconstructive and Aesthetic Surgeons

dOf the 2108 patients with implant based reconstruction, of which 2081 (99%) have been included in the outcome analysis:

* Complete outcome data (event data for all four key outcomes) is available for 2078 patients. These have been included in the analysis.
* Partial outcome data (event data for three of four outcomes) is available for 3 patients. These have been included in the analysis, assumed to not have had the event for the fourth missing outcome**.**
* 27 patients have no outcome data. These patients have been excluded from the analysis.

**Table 5 Logistic regression of risk factors for key outcomes**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Implant loss** | **Infection** | **Readmission** | **Reoperation** |
| N | 1722 | 1722 | 1722 | 1722 |
| Event | 143 | 437 | 302 | 305 |
| No event | 1579 | 1285 | 1420 | 1417 |
| Missinga | 359 | 359 | 359 | 359 |
| C statistic | 0.656 | 0.634 | 0.618 | 0.612 |
| **Variable** | ***OR*** | **95% CI** | **p value** | ***OR*** | **95% CI** | **p value** | ***OR*** | **95% CI** | **p value** | ***OR*** | **95% CI** | **p value** |
| **Age (years)** | 1.00 | 0.98, 1.02 | 0.87 | 1.01 | 1.00, 1.02 | 0.27 | 1.00 | 0.99, 1.01 | 0.77 | 0.99 | 0.98, 1.01 | 0.35 |
| **BMI (kg/m2)** | 1.07 | 1.03, 1.11 | <0.001 | 1.07 | 1.04,1.10 | <0.0001 | 1.05 | 1.03, 1.08 | <0.001 | 1.04 | 1.01, 1.07 | 0.0032 |
| **Operative time (minutes)** | 1.00 | 1.00, 1.01 | 0.049 | 1.00 | 1.00, 1.00 | 0.073 | 1.00 | 1.00, 1.00 | 0.049 | 1.00 | 1.00, 1.01 | 0.013 |
| **Smoking** |  |  |  |  |  |  |  |  |  |  |  |  |
| *No* | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . |
| *Yes* | 1.92 | 1.19, 3.09 | 0.0074 | 1.53 | 1.09, 2.17 | 0.015 | 1.92 | 1.33, 2.77 | <0.001 | 1.87 | 1.30, 2.70 | <0.001 |
| **Previous radiotherapy** |  |  |  |  |  |  |  | .. |  |  |  |  |
| *No* | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . |
| *Yes* | 1.35 | 0.70, 2.60 | 0.37 | 1.72 | 1.12, 2.62 | 0.013 | 1.15 | 0.69, 1.91 | 0.59 | 1.24 | 0.75, 2.03 | 0.41 |
| **Neoadjuvant chemotherapy** |  | .. |  |  | .. |  |  | . |  |  |  |  |
| *No* | Ref |  | . | Ref |  | . | Ref | Ref | . | Ref | Ref | . |
| *Yes* | 0.64 | 0.33, 1.21 | 0.17 | 0.72 | 0.48, 1.08 | 0.11 | 0.82 | 0.53, 1.28 | 0.38 | 0.73 | 0.47, 1.15 | 0.18 |
| **Bilateral surgery** |  |  |  |  |  |  |  |  |  |  |  |  |
| *No* | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . |
| *Yes* | 1.72 | 0.85, 3.47 | 0.13 | 1.27 | 0.81, 1.97 | 0.30 | 1.24 | 0.76, 2.03 | 0.39 | 1.15 | 0.70, 1.90 | 0.58 |
| **Nipple sparing mastectomy** |  | .. |  |  | .. |  |  |  |  |  |  |  |
| *No* | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . |
| *Yes* | 1.24 | 0.80, 1.92 | 0.33 | 1.09 | 0.82, 1.46 | 0.55 | 1.04 | 0.75, 1.44 | 0.81 | 1.20 | 0.88, 1.64 | 0.25 |
| **Risk reducing surgery** |  |  |  |  |  |  |  |  |  |  |  |  |
| *No* | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . |
| *Yes* | 0.87 | 0.37, 2.06 | 0.75 | 0.87 | 0.48, 1.56 | 0.64 | 1.13 | 0.59, 2.14 | 0.71 | 1.28 | 0.68, 2.41 | 0.45 |
| **Therapeutic mastectomy** |  |  |  |  |  |  |  |  |  |  |  |  |
| *No* | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . |
| *Yes* | 1.36 | 0.69, 2.69 | 0.38 | 0.80 | 0.49, 1.29 | 0.36 | 0.92 | 0.55, 1.54 | 0.74 | 1.11 | 0.67, 1.84 | 0.68 |
| **Fixed volume implant**  |  |  |  |  |  |  |  |  |  |  |  |  |
| *No* | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . |
| *Yes* | 0.87 | 0.60, 1.26 | 0.46 | 0.92 | 0.72, 1.16 | 0.46 | 0.86 | 0.66, 1.13 | 0.27 | 0.90 | 0.69, 1.18 | 0.45 |
| **Type of IBBR** |  |  |  |  |  |  |  |  |  |  |  |  |
| *Biological mesh* | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . | Ref | Ref | . |
| *Dermal sling* | 0.85 | 0.52, 1.38 | 0.50 | 1.21 | 0.89, 1.64 | 0.22 | 0.91 | 0.64, 1.30 | 0.60 | 0.85 | 0.59, 1.22 | 0.38 |
| *Other* | 0.17 | 0.02, 1.25 | 0.082 | 1.34 | 0.73, 2.46 | 0.34 | 0.82 | 0.39, 1.74 | 0.60 | 0.80 | 0.38, 1.70 | 0.56 |
| *Pre-pectoral*  | 0.91 | 0.20, 4.04 | 0.90 | 1.02 | 0.39, 2.66 | 0.96 | 1.92 | 0.76, 4.82 | 0.17 | 1.37 | 0.52, 3.60 | 0.52 |
| *Submuscular**/fascial* | 1.06 | 0.55, 2.08 | 0.86 | 0.89 | 0.56, 1.41 | 0.63 | 1.03 | 0.63, 1.70 | 0.90 | 1.00 | 0.61, 1.63 | 0.98 |
| *Synthetic mesh* | 1.12 | 0.66, 1.90 | 0.68 | 1.13 | 0.79, 1.61 | 0.50 | 1.20 | 0.81, 1.78 | 0.37 | 1.09 | 0.74, 1.62 | 0.66 |

aPatients with missing data for outcomes (n=27) and/or included covariates (n=359) were excluded from this risk factor analysis. Covariates with the most missing data were BMI (n=118, Table 1) and operative time (n=195, Table 2). All other covariates were missing in less than 30 patients (Table 1 and 2).

Linearity was checked for continuous variables for all four logistic models using (loess) smoothed line plots. These checks showed no obvious evidence of non-linearity for the effects of the three continuous variables