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Oncoplastic breast-conserving surgery for women with primary breast cancer (Review)

Nanda A, Hu J, Hodgkinson S, Ali S, Rainsbury R, Roy PG

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[Intervention Review]

Oncoplastic breast-conserving surgery for women with primary breast cancer

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ABSTRACT

Background

Oncoplastic breast-conserving surgery (O-BCS) involves removing the tumour in the breast and using plastic surgery techniques to reconstruct the breast. The adequacy of published evidence on the safety and efficacy of O-BCS for the treatment of breast cancer compared to other surgical options for breast cancer is still debatable. It is estimated that the local recurrence rate is similar to standard breast-conserving surgery (S-BCS) and also mastectomy, but the aesthetic and patient-reported outcomes may be improved with oncoplastic techniques.

Objectives

Our primary objective was to assess oncological control outcomes following O-BCS compared with other surgical options for women with breast cancer. Our secondary objective was to assess surgical complications, recall rates, need for further surgery to achieve adequate oncological resection, patient satisfaction through patient-reported outcomes, and cosmetic outcomes through objective measures or clinician-reported outcomes.

Search methods

We searched the Cochrane Breast Cancer Group's Specialized Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (via OVID), Embase (via OVID), the World Health Organization's International Clinical Trials Registry Platform and ClinicalTrials.gov on 7 August 2020. We did not apply any language restrictions.

Selection criteria

We selected randomised controlled trials (RCTs) and non-randomised comparative studies (cohort and case-control studies). Studies evaluated any O-BCS technique, including volume displacement techniques and partial breast volume replacement techniques compared to any other surgical treatment (partial resection or mastectomy) for the treatment of breast cancer.

Data collection and analysis

Four review authors performed data extraction and resolved disagreements. We used ROBINS-I to assess the risk of bias by outcome. We performed descriptive data analysis and meta-analysis and evaluated the quality of the evidence using GRADE criteria. The outcomes included local recurrence, breast cancer-specific disease-free survival, re-excision rates, complications, recall rates, and patient-reported outcome measures.

Main results

We included 78 non-randomised cohort studies evaluating 178,813 women. Overall, we assessed the risk of bias per outcome as being at serious risk of bias due to confounding; where studies adjusted for confounding, we deemed these at moderate risk.

Comparison 1: oncoplastic breast-conserving surgery (O-BCS) versus standard-BCS (S-BCS)

The evidence in the review found that O-BCS when compared to S-BCS, may make little or no difference to local recurrence; either when measured as local recurrence-free survival (hazard ratio (HR) 0.90, 95% confidence interval (CI) 0.61 to 1.34; 4 studies, 7600 participants; very low-certainty evidence) or local recurrence rate (HR 1.33, 95% CI 0.96 to 1.83; 4 studies, 2433 participants; low-certainty evidence), but the evidence is very uncertain due to most studies not controlling for confounding clinicopathological factors. O-BCS compared to S-BCS may make little to no difference to disease-free survival (HR 1.06, 95% CI 0.89 to 1.26; 7 studies, 5532 participants; low-certainty evidence). O-BCS may reduce the rate of re-excisions needed for oncological resection (risk ratio (RR) 0.76, 95% CI 0.69 to 0.85; 38 studies, 13,341 participants; very low-certainty evidence), but the evidence is very uncertain. O-BCS may increase the number of women who have at least one complication (RR 1.19, 95% CI 1.10 to 1.27; 20 studies, 118,005 participants; very low-certainty evidence) and increase the recall to biopsy rate (RR 2.39, 95% CI 1.67 to 3.42; 6 studies, 715 participants; low-certainty evidence). Meta-analysis was not possible when assessing patient-reported outcomes or cosmetic evaluation; in general, O-BCS reported a similar or more favourable result, however, the evidence is very uncertain due to risk of bias in the measurement methods.

Comparison 2: oncoplastic breast-conserving surgery (O-BCS) versus mastectomy alone

O-BCS may increase local recurrence-free survival compared to mastectomy but the evidence is very uncertain (HR 0.55, 95% CI 0.34 to 0.91; 2 studies, 4713 participants; very low-certainty evidence). The evidence is very uncertain about the effect of O-BCS on disease-free survival as there were only data from one study. O-BCS may reduce complications compared to mastectomy, but the evidence is very uncertain due to high risk of bias mainly resulting from confounding (RR 0.75, 95% CI 0.67 to 0.83; 4 studies, 4839 participants; very low-certainty evidence). Data on patient-reported outcome measures came from single studies; it was not possible to meta-analyse the data.

Comparison 3: oncoplastic breast-conserving surgery (O-BCS) versus mastectomy with reconstruction

O-BCS may make little or no difference to local recurrence-free survival (HR 1.37, 95% CI 0.72 to 2.62; 1 study, 3785 participants; very low-certainty evidence) or disease-free survival (HR 0.45, 95% CI 0.09 to 2.22; 1 study, 317 participants; very low-certainty evidence) when compared to mastectomy with reconstruction, but the evidence is very uncertain. O-BCS may reduce the complication rate compared to mastectomy with reconstruction (RR 0.49, 95% CI 0.45 to 0.54; 5 studies, 4973 participants; very low-certainty evidence) but the evidence is very uncertain due to high risk of bias from confounding and inconsistency of results. The evidence is very uncertain for patient-reported outcome measures and cosmetic evaluation.

Authors' conclusions

The evidence is very uncertain regarding oncological outcomes following O-BCS compared to S-BCS, though O-BCS has not been shown to be inferior. O-BCS may result in less need for a second re-excision surgery but may result in more complications and a greater recall rate than S-BCS. It seems that O-BCS may give better patient satisfaction and surgeon rating for the look of the breast, but the evidence for this is of poor quality, and due to lack of numerical data, it was not possible to pool the results of different studies. It seems O-BCS results in fewer complications compared with surgeries involving mastectomy.

Based on this review, no certain conclusions can be made to help inform policymakers. The surgical decision for what operation to proceed with should be made jointly between clinician and patient after an appropriate discussion about the risks and benefits of O-BCS personalised to the patient, taking into account clinicopathological factors. This review highlighted the deficiency of well-conducted studies to evaluate efficacy, safety and patient-reported outcomes following O-BCS.

PLAIN LANGUAGE SUMMARY

Oncoplastic breast-conserving surgery (O-BCS) for women with primary breast cancer

Background

Traditional surgery for early breast cancer is standard breast-conserving surgery (S-BCS) which aims to keep as much of the breast as possible. For women with large tumours compared to their breast size it can be difficult to conserve the breast whilst ensuring all the tumour is removed and may mean that mastectomy is needed. The most important part of surgical treatment for breast cancer is removing all cancer. In recent years, oncoplastic breast surgery techniques have been used to conserve the breast whilst removing breast cancer by applying the principles of plastic surgery, resulting in better cosmetic results. Oncoplastic breast-conserving surgery (O-BCS) may also result in better patient satisfaction and quality of life.

Traditionally, surgeons have either preserved the breast tissue by removing the cancerous lump (S-BCS) or reconstructing immediately after mastectomy. O-BCS involves removing cancer and either moving/adjusting the remaining breast tissue around (volume

displacement) or bringing in tissue from elsewhere to fill the defect after breast cancer removal (volume replacement). There are many techniques that fall under O-BCS that we have listed in full in other parts of the review; however, all are similar in their principle.

Review question

We reviewed the evidence about the effects of O-BCS (that is, removing some of the breast tissue and then reconstructing the remaining breast by either mobilising the breast tissue (mammaplasty or volume displacement) or bringing the tissue from elsewhere (partial breast reconstruction or volume replacement)) compared to other S-BCS (that is, removing the tumour in the breast without the need for further breast adjustment) or mastectomy (that is, removing all the breast tissue with or without reconstruction). We studied the effect on cancer-related (local recurrence, disease-free survival and overall survival), quality of life and cosmetic outcomes in women with breast cancer.

Study characteristics

The evidence is current to August 2020. We included 78 studies involving 178,813 patients with breast cancer. We split the studies into those that compared O-BCS to S-BCS, O-BCS to mastectomy alone and O-BCS to mastectomy with reconstruction. Some studies contributed to more than one comparison.

Key results

It seemed that O-BCS resulted in similar rates of local recurrence (that is, whether cancer returned in the same breast) and disease-free survival (free of any breast cancer after initial treatment) when compared to S-BCS, and resulted in less need for a second re-excision surgery (which may be required if the tumour is not fully removed in the first operation). O-BCS may result in more complications and more biopsies in the years after the surgery compared to S-BCS. It seems that O-BCS may give better patient satisfaction and surgeon rating for the look of the breast, but the evidence for this is of poor quality, and due to lack of numerical data, it was not possible to pool the results of different studies.

It was not possible to conclude whether or not cancer outcomes of local recurrence and disease-free survival for O-BCS were similar to mastectomy with or without reconstruction as there were not many good-quality studies. It seems O-BCS has fewer complications than surgeries involving mastectomy.

In practice, the decision to select O-BCS should be done through shared decision making with the surgeon, discussing the potential risks and benefits.

Certainty of evidence

The certainty of the evidence in this review was very low. The studies had several methodological flaws. Differences between groups in cancer stage and other cancer treatments that were used may have affected the results. This is likely to have an impact on the findings, and future research is needed to investigate the topic further.

Summary of findings 1. Any O-BCS compared to S-BCS for women with primary breast cancer

Any O-BCS compared to S-BCS for women with primary breast cancer

Patient or population: women with primary breast cancer
Setting: mixed multicentre/single-centre studies with initial inpatient procedure and outpatient follow-up
Intervention: any O-BCS
Comparison: S-BCS

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with S-BCS	Risk with any O-BCS				
Local recurrence-free survival (up to 5 years)	Study population		HR 0.90 (0.61 to 1.34)	7600 (4 observational studies)	⊕⊖⊖⊖ Very low[a,b]	We calculated estimates of risk with BCS using an average of non-adjusted baseline control rates from included studies.
	55 per 1000	50 per 1000 (34 to 73)				
Local recurrence rates (up to 5 years)	Study population		HR 1.33 (0.96 to 1.83)	2443 (4 observational studies)	⊕⊕⊖⊖ Low[b,c]	We calculated estimates of risk with BCS using an average of non-adjusted baseline control rates from included studies.
	57 per 1000	75 per 1000 (55 to 102)				
Disease-free survival (up to 5 years)	Study population		HR 1.06 (0.89 to 1.26)	5532 (7 observational studies)	⊕⊕⊖⊖ Low[b,c]	We calculated estimates of risk with BCS using an average of non-adjusted baseline control rates from included studies.
	98 per 1000	104 per 1000 (88 to 122)				
Re-excision rate: total re-excisions	Study population		RR 0.76 (0.69 to 0.85)	13,341 (38 observational studies)	⊕⊖⊖⊖ Very low[a,d,e]	We also assessed the risk of completion mastectomy (RR 1.00, 95% CI 0.85 to 1.15); O-BCS may have no effect on the completion mastectomy rate but the evidence is very uncertain.
	134 per 1000	101 per 1000 (92 to 114)				
Complications	Study population		RR 1.19 (1.10 to 1.27)	118,005 (20 observational studies)	⊕⊖⊖⊖ Very low[a,b,f]	O-BCS may increase or have no effect on the rate of complications but the evidence is very uncertain.
	34 per 1000	41 per 1000 (38 to 44)				
Recall rate	Study population		RR 2.39	715	⊕⊕⊖⊖	O-BCS may increase recall rate slightly.

	100 per 1000	240 per 1000 (167 to 343)	(1.67 to 3.42)	(6 observational studies)	Low[a]	
Patient-reported outcome measures	There is no significant difference in quality of life patient-reported outcome measures using BREAST-Q. However, there may be better patient-reported cosmetic satisfaction with O-BCS		-	5665 (24 observational studies)	⊕⊖⊖⊖ Very low[a,g]	The evidence is very uncertain about the effect of any O-BCS on patient-reported outcome measures.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: confidence interval; **HR:** hazard ratio; **O-BCS**: oncoplastic breast-conserving surgery; **RR:** risk ratio; **S-BCS**: standard breast-conserving surgery.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded by two levels due to study limitation: serious risk of bias due to confounding.
[b]Downgraded by one level due to imprecision: wide confidence levels crossing line of no effect.
[c]Downgraded by one level due to study limitation: moderate risk of bias due to confounding.
[d]Downgraded by one level due to heterogeneity: $I^2 = 43\%$, $P < 0.0001$.
[e]Downgraded by one level due to publication bias detected.
[f]Downgraded by one level due to heterogeneity: $I^2 = 60\%$, $P = 0.0003$.
[g]Downgraded by two levels due to study limitations: serious/critical risk due to measurement of outcome.

Summary of findings 2. Any O-BCS compared to mastectomy for women with primary breast cancer

Any O-BCS compared to mastectomy for women with primary breast cancer

Patient or population: women with primary breast cancer
Setting: mixed multicentre/single-centre studies with initial inpatient procedure and outpatient follow-up
Intervention: any O-BCS
Comparison: mastectomy

Outcomes	Anticipated absolute effects* (95% CI)	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments

	Risk with Mx	Risk with any O-BCS				
Local recurrence-free survival (up to 5 years)	Study population 161 per 1000	 92 per 1000 (58 to 148)	HR 0.55 (0.34 to 0.91)	4713 (2 observational studies)	⊕⊖⊖⊖ Very low[a,b]	Estimates of risk with BCS were calculated using an average of non-adjusted baseline control rates from included studies.
Cumulative local recurrence rate				(0 studies)	-	No studies evaluated local recurrence as cumulative rate
Disease-free survival	Study population 139 per 1000	 81 per 1000 (57 to 114)	RR 0.58 (0.41 to 0.82)	1193 (1 observational study)	⊕⊖⊖⊖ Very low[c,d]	Dichotomous data used as no studies reported time-to-event data
Re-excision rates				(0 studies)		Re-excisions are not often needed for mastectomy, therefore this outcome is not relevant for this comparison.
Complications	Study population 312 per 1000	 234 per 1000 (209 to 259)	RR 0.75 (0.67 to 0.83)	4839 (4 observational studies)	⊕⊖⊖⊖ Very low[c,e]	O-BCS may reduce complications compared to mastectomy but the evidence is very uncertain.
Recall rates				(0 studies)		Recall biopsies are not often needed for mastectomy, therefore this outcome is not relevant for this comparison.
Patient-reported outcome measures	There are insufficient data to make any conclusions		-	(1 observational study)	-	There are insufficient data to make any conclusions

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
BCS: breast-conserving surgery; **CI**: confidence interval; **HR:** hazard ratio;**Mx**: mastectomy; **O-BCS**: oncoplastic breast-conserving surgery; **RR:** risk ratio.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded by one level due to study limitation: moderate risk of bias due to confounding.
[b]Downgraded by two levels due to heterogeneity: $I^2 = 81\%$, P = 0.02.
[c]Downgraded by two levels due to study limitation: serious risk of bias due to confounding.
[d]Downgraded by one level due to imprecision: optimal size not met.
[e]Downgraded by two levels due to heterogeneity: $I^2 = 61\%$, P < 0.0001.

Summary of findings 3. Any O-BCS compared to mastectomy plus reconstruction for women with primary breast cancer

Any O-BCS compared to mastectomy plus reconstruction for women with primary breast cancer

Patient or population: women with primary breast cancer
Setting: mixed multicentre/single-centre studies with initial inpatient procedure and outpatient follow-up
Intervention: any O-BCS
Comparison: mastectomy plus reconstruction (Mx+R)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Mx+R	Risk with any O-BCS				
Local recurrence-free survival	Study population 43 per 1000	58 per 1000 (31 to 108)	HR 1.37 (0.72 to 2.62)	3785 (1 observational study)	⊕⊖⊖⊖ Very low[a,b]	Any O-BCS may result in little to no difference in local recurrence-free survival compared to Mx+R. Estimates of risk with BCS were calculated using an average of non-adjusted baseline control rates from included studies. Also calculated HR for LRR (local recurrence rates) for studies with a comparison of Mx+/-R where the vast majority were reconstructed; HR 1.59 (0.71 to 3.55)
Cumulative local recurrence rate				0 studies		Re-excisions are not often needed for mastectomy, therefore this outcome is not relevant for this comparison and therefore not studied.
Disease-free survival	Study population 189 per 1000	90 per 1000 (19 to 371)	HR 0.45 (0.09 to 2.22)	317 (1 observational study)	⊕⊖⊖⊖ Very low[a,c]	Estimates of risk with BCS were calculated using an average of non-adjusted baseline control rates from included studies. Also calculated HR for DFS for studies with a comparison of Mx+/-R where the vast majority were reconstructed; HR 1.03 (0.75 to 1.42)

Re-excision rates			0 studies	-	Re-excisions are not often needed for mastectomy, therefore this outcome is not relevant for this comparison.
Complications	Study population 492 per 1000	241 per 1000 (221 to 266)	RR 0.49 (0.45 to 0.54)	4973 (5 observational studies)	⊕⊖⊖⊖ Very low[a,d]	
Recall rates			0 studies	-	Recall biopsy is not often needed for mastectomy, therefore this outcome is not relevant for this comparison.
Patient-reported outcome measures	The evidence is too methodologically diverse and of high risk of bias due to measurement of outcomes to combine		-	(3 observational studies)	-	There is insufficient evidence to make a conclusion

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
BCS: breast-conserving surgery; **CI**: confidence interval; **DFS**: disease-free survival; **HR:** hazard ratio;**Mx**: mastectomy; **Mx+R**: mastectomy with reconstruction; **Mx+/-R**: mastectomy with or without reconstruction; **O-BCS**: oncoplastic breast-conserving surgery; **RR:** risk ratio.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded by two levels due to study limitation: serious risk of bias due to confounding.
[b]Downgraded by one level due to imprecision: optimal size not met.
[c]Downgraded by one level due to imprecision: 95% CI overlaps no effect.
[d]Downgraded by two levels due to heterogeneity: $I^2 = 85\%$, $P < 0.001$.

BACKGROUND

Description of the condition

Breast cancer is the most commonly diagnosed cancer in women worldwide (Bray 2018). Globally, incidence rates are increasing but mortality rates are decreasing with improved treatments, leaving many more breast cancer survivors (WHO 2010). In the UK an estimated 691,000 women are alive after a diagnosis of breast cancer, and this is predicted to rise to 840,000 women in 2020 (Breast Cancer Care 2020). There are over 3.8 million breast cancer survivors in the USA, including those who have finished treatment or are in the process of receiving treatment (BCRF 2019).

For the majority of women with primary breast cancer, the first treatment is breast surgery with curative intent (Breast Cancer Care 2020). As survival improves following breast cancer treatment, it has become imperative to improve quality of life, and long-term appearance and aesthetic outcomes after surgery have become increasingly relevant.

Description of the intervention

Surgery for breast cancer has evolved considerably over the years, from the radical mastectomy of Halsted 1894 to the development and acceptance of breast-conserving therapy as standard of care in recent years. Breast-conserving surgery (BCS) usually refers to lumpectomy or wide local excision (WLE). BCS followed by radiotherapy has been found to be equivalent in disease-free and overall survival when compared with mastectomy, and hence has become the standard of care for early-stage breast cancer (Agarwal 2014; Fisher 2002; Van Maaren 2016; Vila 2015). A WLE may be difficult for patients with a large tumour-to-breast-size ratio, resulting in poor cosmetic outcomes or patients may opt for a simple mastectomy (that is, the removal of the breast tissue up to the chest wall) (Regano 2009). There is large variation across countries in the rates of BCS (Munzone 2014; Sun 2018).

The primary goal of oncological surgery is cancer resection; that is, where the tumour, along with a margin of normal tissue is excised. There is also, however, increasing awareness that aesthetic outcomes of these procedures are extremely important. Patient expectations are increasing as they become aware that they need not be left with deformities after breast cancer surgery. Good aesthetic outcomes have been linked with significant improvements in patient satisfaction and quality of life (Kim 2015; Waljee 2008).

There are many breast reconstruction options for aesthetic improvement. Women being offered a mastectomy have the option of full breast reconstruction, using either implants or their own (autologous) tissue. Breast reconstruction can be done at the same time as the mastectomy (one-stage) or as a separate operation (two-stage). For women undergoing BCS for large tumours, the options include either volume displacement or partial volume replacement techniques using either implants or autologous tissue (ACS 2016).

Oncoplastic breast-conserving surgery (O-BCS) is the term used for oncological resection (breast tumour excisions) combined with plastic surgery techniques (Almasad 2008; Clough 2003; Rainsbury 2007; Regano 2009). O-BCS can be broadly divided into the two fundamentally different techniques: 1) volume displacement techniques use breast tissue (glandular or dermoglandular) from the same breast and places (redistributes) it into the surgical site (also known as mammoplasty); and 2) volume replacement techniques use tissue, other than the breast, to compensate for volume loss after breast tumours have been excised.

The uniting principle of these two techniques is to conserve the breast shape/size.

Volume displacement techniques can include various techniques (Holmes 2011), for example:

- wise pattern therapeutic mammaplasty;
- vertical scar mammaplasty (and its variations);
- circumareolar/Benelli's/round block mammoplasty;
- racquet handle/lateral mammaplasty.

Similarly, there are many techniques for autologous partial volume replacement techniques. The following techniques are recognised as partial volume replacement techniques, where the differentiating factor between which flap is used is usually the location of the tumour.

- Defects in the lower aspects of the breast can be addressed using local flaps such as:
  - abdominal adipofascial flaps (Kijima 2014; Ogawa 2007);
  - thoracoepigastric flaps (Hamdi 2014; Kijima 2011; Takeda 2005);
    - superior epigastric artery perforator flap;
    - medial intercostal artery perforator;
    - internal mammary artery perforator;
    - anterior intercostal artery perforator.
- Defects in the lateral half of the breast can be reconstituted with lateral chest wall perforator flaps such as:
  - lateral intercostal artery perforator (Hamdi 2006; Hu 2018);
  - lateral thoracic artery perforator (McCulley 2015);
  - thoracodorsal artery perforator flap (Munhoz 2011).
- Defects in any breast quadrant can be addressed using distant flaps. Most often these are pedicled flaps, but free flaps could also be used for partial breast reconstruction such as:
  - mini-latissimus dorsi (Raja 1997);
  - omental flaps (Zaha 2014);
  - other free flaps for partial breast reconstruction e.g. transverse upper gracilis flaps (McCulley 2011).

Many early-stage breast cancers can be successfully treated by WLE; however, the lesions with large tumour-to-breast-size ratio remain a challenge for breast surgeons to treat with BCS alone. O-BCS allows the excision of tumours that cannot be excised by, or would result in poor cosmetic outcomes from S-BCS. It allows these women to avoid mastectomy.

In this Cochrane Review, we will compare any O-BCS technique to other surgical techniques used for BCS because any of the aforementioned techniques may be offered to women with breast cancer under varying circumstances. For small cancers, it is likely that WLE with or without partial reconstruction (using either autologous tissue or an implant) will be offered. In contrast, for large cancers, the options could include WLE with or without partial reconstruction; or mastectomy with or without reconstruction.

How the intervention might work

For women with early-stage breast cancer, studies have shown that there is no detectable difference in overall survival or disease-free survival in those who have BCS plus radiotherapy and those who have a mastectomy (Poggi 2003; Van Maaren 2016). There has been increased adoption of the practice in many countries to facilitate breast-conserving therapy and avoid unnecessary mastectomies (Kaufman 2019). The emphasis remains on safe and adequate cancer resection, whilst aiming to achieve better aesthetic outcomes to improve quality of life.

There is evidence indicating that cosmesis, patient satisfaction and quality of life improve with BCS compared to mastectomy (Kim 2015; Waljee 2008). The options for surgical resection for breast cancer are dictated by the size of the tumour. There is an indirect correlation between the percentage of breast volume excised and cosmesis, which can have an impact on the satisfaction levels after BCS (Cochrane 2003). O-BCS techniques aim to keep the breast shape and size similar despite oncological resection; therefore it would be logical to expect better patient satisfaction.

Why it is important to do this review

Although oncoplastic surgery has rapidly gained acceptance and is widely practised, cohesive evidence is still lacking on both the short-term and long-term outcomes, particularly for partial breast reconstruction.

Since the most recent systematic review of oncoplastic breast surgery concluded its search in 2015 (Yiannakopoulou 2016), there have been over 30 articles published regarding partial breast reconstruction. A summary of evidence from this literature will help clinicians understand the indications and clinical, oncological and cosmetic outcomes of such techniques. This Cochrane Review will update our understanding of this rapidly evolving area of clinical practice and address the questions unexplored by previous reviews. In addition, this review will focus on volume displacement and replacement techniques as separate subsets of O-BCS, and compare these techniques with other alternatives.

OBJECTIVES

Our primary objective was to assess oncological control outcomes following O-BCS compared with other surgical options for women with breast cancer. Our secondary objective was to assess surgical complications, recall rates, need for further surgery to achieve adequate oncological resection, patient satisfaction through patient-reported outcomes, and cosmetic outcomes through objective measures or clinician-reported outcomes.

METHODS

Criteria for considering studies for this review

Types of studies

We planned to include all randomised controlled trials (RCTs) assessing oncoplastic breast-conserving surgery (O-BCS) but anticipated that there would be no RCTs on the topic. We, therefore, expanded the inclusion criteria to include comparative non-randomised studies (i.e. cohort studies, case-control studies and prospectively designed patient registries).

We included studies published in all languages from 1980 onwards as this is the date at which partial breast reconstruction was introduced.

We excluded single-arm studies, expert opinion and duplicate studies.

Types of participants

We included women with primary breast cancer who underwent any O-BCS using either volume displacement or partial replacement breast reconstruction for cancer compared with women who underwent any other surgical technique for cancer.

We excluded men and people who have undergone surgery for benign breast conditions.

Types of interventions

Experimental interventions

Any oncoplastic breast-conserving surgery techniques including:

- volume displacement techniques
  - wise pattern therapeutic mammaplasty
  - vertical scar mammaplasty (and its variations)
  - circumareolar/Benelli's/Round block mammoplasty
  - racquet handle/lateral mammaplasty
- partial volume replacement techniques
  - abdominal adipofascial flaps/advancement flaps
  - lateral chest wall perforator flaps
    - lateral intercostal artery perforator flap
    - lateral thoracic artery perforator
    - thoracodorsal artery perforator flap
  - latissimus dorsi mini-flap
  - thoracoepigastric flaps
    - superior epigastric artery perforator flap
    - medial intercostal artery perforator
    - internal mammary artery perforator
    - anterior intercostal artery perforator
  - omental flaps
  - free flaps for partial breast reconstruction

We included any other techniques if mentioned in the literature.

Comparator interventions

Any other surgical treatment. The comparators were stratified into partial resection and mastectomy. These include:

- standard breast-conserving surgery (S-BCS) e.g. wide local excision (WLE), quadrantectomy, segmentectomy, partial mastectomy;
- partial volume replacement using non-autologous tissue;
- mastectomy with no reconstruction;
- mastectomy with breast reconstruction using an implant alone;
- mastectomy with breast reconstruction using autologous tissue including pedicled and free flaps.

The main analyses were:

- any O-BCS versus S-BCS

- any O-BCS versus mastectomy without reconstruction
- any O-BCS versus mastectomy with reconstruction procedures

Co-interventions

We recognised that some women with breast cancer may also undergo hormonal therapy, chemotherapy or radiotherapy, or a combination of therapies. We collected data on whether patients received these co-interventions; we did not, however, conduct a subgroup analysis as no study reported outcomes based on these. This information can be found in Table 1, which describes confounding variables; differences in these co-interventions informed the risk of bias for each study.

Types of outcome measures

Primary outcomes

The primary outcomes focused on oncological control by O-BCS by assessing the following.

- Local recurrence: locoregional recurrence (that is, ipsilateral breast tumour recurrence), defined as cancer detected in the same breast where cancer had been diagnosed. Some studies reported this as local recurrence-free survival - defined as the time from the date of treatment to the first date of local relapse.
- Disease-free survival: breast cancer-specific disease-free survival, defined as the time from the date of completing initial treatment (that is, completing the surgical procedure) to the first date of a local, regional, or distant relapse, diagnosis of a second primary breast cancer, or death due to this.
- Overall survival: overall survival, defined as the time from the date of treatment to death from any cause, or number of deaths from any cause.

Follow-up was described as 1 year, 1 to 5 years, 5 years, and 10 years if reported as dichotomous outcomes; or longest reported follow-up if hazard ratios were reported.

Secondary outcomes

The secondary outcomes focused on oncological, surgical and cosmetic outcomes by assessing the following.

- Re-excision rates: need for further breast surgery due to inadequate cancer resection (for example, re-excision for further margin resection or completion mastectomy).
- Complications: surgical complications, for example, flap necrosis, infection, wound dehiscence and any other complications reported in the literature.
- Recall rates: defined as abnormal surveillance on mammogram resulting in additional imaging or biopsy.
- Time to adjuvant therapy: time in days from surgery to initiation of adjuvant chemotherapy and/or radiotherapy.
- Patient-reported outcome measures: such as patient satisfaction, that derive from validated questionnaires (for example, Breast-Q; Cohen 2016).
- Cosmetic evaluation: surgeon-reported cosmetic outcomes that derive from subjective or objective validated scales (for example, the Harris scale and Breast Analyzing Tool; Harris 1979; Krois 2017).

Search methods for identification of studies

Electronic searches

We searched the following databases on 7 August 2020.

- The Cochrane Breast Cancer's Specialised Register. Details of the search strategies used by the Group for the identification of studies and the procedure used to code references are outlined on the Group's website (breastcancer.cochrane.org/sites/breastcancer.cochrane.org/files/public/uploads/specialised_register_details.pdf). We extracted trials with the following key words and considered them for inclusion in the review: abdominal adipofascial flaps, lateral chest wall perforator flaps, lateral intercostal artery perforator flap, latissimus dorsi mini-flap, omental flaps, thoracoepigastric flaps, superior epigastric artery perforator flap, medical intercostal artery perforator, internal mammary artery perforator, anterior intercostal artery perforator, advancement/random pattern or rotation flaps, free flaps for partial breast reconstruction, breast-conserving surgery, oncoplastic breast surgery, partial volume replacement breast, partial breast reconstruction and partial mastectomy. We will search for papers including women with breast cancer who are undergoing any kind of oncoplastic breast-conserving surgery, as it is often the case for breast-conserving surgeries to be grouped together.
- CENTRAL (in the Cochrane Library, August 2020). See Appendix 1.
- MEDLINE (via Ovid SP) from 1980 to August 2020. See Appendix 2.
- Embase (via Ovid SP) from 1980 to August 2020. See Appendix 3.
- The World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal (apps.who.int/trialsearch/Default.aspx) for all prospectively registered and ongoing trials. See Appendix 4.
- ClinicalTrials.gov. See Appendix 5.

Searching other resources

Bibliographic searching

We screened the studies in the reference lists of identified relevant trials or reviews (for example Chen 2018; De La Cruz 2016; Haloua 2013; Losken 2014; Yoon 2016). We obtained a copy of the full-text article for each reference reporting a potentially eligible study.

Data collection and analysis

Selection of studies

We uploaded our references into Covidence. Two review authors (AN and JH) independently examined each title and abstract to determine whether reports appear to meet the inclusion criteria based on the protocol, and resolved any differences by discussion. For those studies with multiple publications of duplicate data sets, the study with the shorter follow-up time or fewer participant numbers for outcomes of interest was excluded so as not to duplicate data in the analysis.

We obtained copies of potentially eligible reports and two review authors (AN and JH) examined the full-text articles independently. We used Cochrane Task Exchange to help with translations for six studies (2 Spanish, 1 French, 1 Hungarian and 2 Chinese (Mandarin)). We did not have any potentially relevant studies that

we were unable to translate. The review author team reviewed all potentially eligible reports and decided which studies should be included in the review. We recorded the selection process in a PRISMA flow diagram (Page 2021); we recorded excluded studies in the 'Characteristics of excluded studies table.

Data extraction and management

The review author team designed and agreed upon the uniform criteria for data extraction and create a standardised form in Excel prior to review commencement. Three review authors (AN, JH and SA) independently undertook data extraction, with at least two authors reviewing each study. Any differences were resolved by discussion, and when needed we consulted a fourth review author (PR) to help resolve any disagreements. For those studies with more than one publication, we extracted data from all publications and considered the version with the longest follow-up as the primary reference for the study and excluded the other from the analysis.

We tabulated the study characteristics for each included study to determine whether we were able to synthesise these data and present them in text or tabular form. We included the following information from the individual studies on standardised data extraction forms.

- General Information
  - Author names, countries and year of publication
  - Study design and level of evidence
  - Conflicts of interest and funding
- Demographics
  - Number of participants
  - Number of breasts treated
  - Age of participants
  - Smoking history
  - History of diabetes
  - History of steroid intake or immunosuppression
  - body mass index (BMI)
- Breast factors
  - Preoperative breast/bra size
  - Oncological parameters
    - Type of cancer (invasive or in situ)
    - Grade
    - Stage
    - Axillary nodal status
    - Hormone receptor status (oestrogen receptor, progesterone receptor), HER2 status
    - Size of tumour including any associated additional foci
    - Location of tumour (which quadrant)
  - Tumour–nipple distance
    - Solitary, multifocal or multicentric
    - Presence of lymphovascular invasion
- Cancer treatment
  - Adjuvant radiotherapy
  - Prior neoadjuvant or adjuvant chemotherapy
  - Previous breast surgery
- Technical surgical details
  - Incision used
  - Reconstruction performed
  - Flap included a skin paddle used to reconstruct a skin defect
- Postsurgical details
  - Median follow-up duration
  - Loss to follow-up expressed as a percentage
- Primary outcomes as described above
  - Local recurrence
  - Survival (for example, disease-specific (breast cancer) and overall survival)
- Secondary outcomes, as described above
  - Patient-reported outcome measures (for example, patient satisfaction)
  - Time to adjuvant therapy (days)
  - Surgical complications
  - Recall rates
  - Need for further surgery to address aesthetics/symmetry
  - Surgeon-reported cosmetic outcomes
- Surgical outcomes
  - Early complications, for example:
    - completion mastectomy rates
    - flap necrosis
    - infection
    - readmission
    - generic surgical complications
  - Late complications, for example:
    - correction of symmetry (contralateral augmentation/reduction or nipple reconstruction)
    - correction of deformity (lipomodelling, scar revision etc.)
    - any other breast procedures
- Cosmetic outcomes
  - Clinician-reported
  - Patient-reported outcome measures, such as satisfaction and quality of life
  - Any symmetrisation surgery
- For non-randomised studies
  - Methods used to control for confounders
  - Adjusted and unadjusted outcome measures
  - List of variables included in analyses for adjusted estimates

If reports related to the same study appear in multiple publications, we combined them under the overall study ID.

Assessment of risk of bias in included studies

We planned to use Cochrane's risk of bias tool for RCTs (RoB 1; Higgins 2011) and the ROBINS-I tool for non-randomised studies (Sterne 2016). We planned to compare study protocols with final papers where possible and would have noted if key information was missing across all study types. However, there were no RCTs in this review nor any protocols.

Non-randomised studies

Three review authors (AN, SA and JH) applied the ROBINS-I tool, as described in Sterne 2016, to assess the risk of bias of effect of assignment in the results of non-randomised studies that compare health effects of two or more interventions. We resolved disagreements by discussion. We used the ROBINS-I tool for cohort studies, case-control studies and prospective patient registries. We completed separate ROBINS-I tables to generate an overall risk

of bias for each outcome: local recurrence, disease-free survival, overall survival, re-excision rates, complications, recall rates, time to adjuvant therapy, cosmetic evaluation, and patient-reported outcome measures. We assessed the risk of bias according to the following domains.

Pre-intervention bias

- Due to confounding: for example comorbidities of patients, associated ductal carcinoma in situ, the predominance of small tumour size or small tumour:breast ratio (no established cut-offs exist for defining size), lack of pathology reporting in published literature, smoking status, age, ethnicity, genetic risk for breast cancer.
  - For oncological outcomes (local recurrence, disease-free survival and overall survival we would expect the following confounders to be controlled for: oncological parameters of tumour (type, size, grade, stage, nodal status, hormonal status) and cancer treatment.
  - For re-excision rates we would expect the following confounders to be controlled for: oncological parameters of tumour (especially tumour size and location) and cancer treatment.
  - For complication rates we would expect the following confounders to be controlled for: age, comorbidities, oncological parameters of tumour (especially stage and size) and cancer treatment (especially axillary surgery and adjuvant radiotherapy).
  - For time to adjuvant therapy we would expect the following confounders to be controlled for: comorbidities and cancer treatment.
  - For patient-reported outcome measures we would expect the following confounders to be controlled for: oncological parameters of tumour (especially tumour size and location) and cancer treatment.
  - For cosmetic evaluation, we would expect the following confounders to be controlled for: oncological parameters of tumour (especially tumour size and location) and cancer treatment.
- In the selection of participants into the study

At-intervention bias

- In the classification of the intervention

Post-intervention bias

- Due to deviations from the intended intervention
  - This includes bias due to differences in surgeon technique and experience between control and intervention within studies.
- Due to missing data
- In the measurement of outcomes: for example, cosmetic assessment being subjective and not using validated anonymised questionnaires
- In the selection of the reported results

We scored each of these domains as having low, moderate, serious, or critical risk of bias. Based on these scores, we determined an overall risk of bias for each study per outcome. If we graded any domain as serious, we deemed the overall risk of bias as serious.

We summarised the risk of bias judgements across different studies for each of the domains listed and summarised results in separate risk of bias tables (Table 2; Table 3; Table 4; Table 5; Table 6; Table 7; Table 8; Table 9; Table 10).

When considering treatment effects, we took into account the risk of bias for studies that contribute to each outcome.

Confounding and adjustment

We identified the confounding factors that the researchers had considered, recorded whether they had been measured and what researchers had done to control for bias. That is, any design features used for this purpose (for example, matching or restriction to particular subgroups) and the methods of analysis (for example, stratification, regression modelling with propensity scores or covariates). We have displayed as a table a list of confounders mentioned by the studies (Table 1), and detail how the studies dealt with them; for example, restricted participant selection, demonstrated a balance between groups for the confounder, matched on the confounder or adjusted for the confounder in statistical analyses to quantify the effect size.

Measures of treatment effect

We reported time-to-event outcomes (that is, local recurrence, overall survival) as hazard ratios (HRs) with 95% confidence intervals (CIs). We estimated HRs using the methods of Parmar 1998 if possible. We used this method to extract HRs for local recurrence from three studies (Niinikoski 2019 (2); Piper 2016; Ren 2014), for disease-free survival from four studies (DeLorenzi 2018; Mazouni 2013; Ozmen 2020; Vieira 2016), and for overall survival from six studies (DeLorenzi 2018; Gulcelik 2013; Mazouni 2013; Ozmen 2020; Ren 2014; Vieira 2016). We were unable to estimate HRs from three studies as there were not enough data to calculate the HR (Acea-Nebril 2017; Chakravorty 2012; Lee 2018).

For local recurrence, the data were reported as either local recurrence rate or local recurrence-free survival. We extracted both, but were not able to combine these two outcomes. If it was not possible to estimate HRs from all studies, we treated the number of events (that is, recurrences, deaths) from treatment date to 1 year, from treatment date to between 1 year and < 5 years, from treatment date to 5 years, and from treatment date to 10 years of follow-up as dichotomous outcomes.

We reported continuous outcomes (that is, patient-reported outcome measures, quality of life) as mean differences (MDs) with 95% CIs.

We reported dichotomous outcomes (that is, re-excision rates, local or distant recurrence (if not a time-to-event outcome), any complications of surgery) as risk ratios (RRs) with 95% CIs.

Unit of analysis issues

The unit of analysis was the study as this systematic review used aggregated data and not individual data. We planned to exclude cross-over and cluster-RCTs but there were none.

Dealing with missing data

When studies reported one primary outcome but other primary outcome data were missing, we contacted the authors to request further information. If data were missing to the extent that we

could not include the study in a meta-analysis and our attempts to retrieve data have been exhausted, we would present the results in the review and discuss in the context of the findings. We planned to discuss the impact of missing data and imputation methods in the Discussion section of the review, and if necessary conduct a sensitivity analysis.

Assessment of heterogeneity

If we could combine results in a meta-analysis, we assessed heterogeneity using the I^2 statistic (Higgins 2003), and interpreted this according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2021).

- 0% to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity*
- 50% to 90%: may represent substantial heterogeneity*
- 75% to 100%: considerable heterogeneity*

* In cases of moderate or high heterogeneity, we explored potential sources of heterogeneity by performing sensitivity analyses.

Assessment of reporting biases

We searched for protocols of included studies using PubMed and other trial registries, when possible. If more than 10 trials were included in a meta-analysis, we assessed publication bias and other reporting biases by visual inspection of funnel plots for primary outcomes (Higgins 2021).

Data synthesis

If it was appropriate to perform a meta-analysis (wherein the population, intervention, comparison and outcomes are deemed similar enough to pool), we synthesised data using RevMan Web (RevMan5). We used a fixed-effect model for data synthesis and explored the impact of model choice through sensitivity analysis. We pooled HRs using the generic inverse variance method.

When meta-analysis was not possible, we considered other methods of analysis following guidance from the *Cochrane Handbook* on synthesising and presenting data using other methods (McKenzie 2021). When results provided a direction of effect we used the vote counting method. This method provides no information on the magnitude of effects nor does it account for differences in the relative sizes of the studies.

If the data were too diverse to permit combining of effect sizes in a meaningful or valid manner, we presented the results of individual studies in table and graphical formats and used a narrative approach to summarise the data. We provided a narrative synthesis of the findings from the included studies, structured around the type of intervention, target population characteristics, type of outcome and intervention content. We followed the Cochrane guidelines for a narrative summary (Ryan 2013).

If sufficient evidence of high certainty were available for local recurrence rates, we planned to compare the results to a typical non-inferiority standard of "less than 5% ipsilateral breast tumour recurrence at 5 years follow-up", which is set for any breast conservation therapy by the Association of Breast Surgery (UK) at the British Association of Surgical Oncology (BASO) 'Surgical guidelines for the management of breast cancer' (Association of Breast Surgery 2012).

Subgroup analysis and investigation of heterogeneity

We conducted a subgroup analysis comparing and discussing the two main techniques of O-BCS — volume displacement and partial volume replacement — with any other options in BCS (if there were a minimum of 5 studies). This meant we conducted the following further analyses.

- Volume displacement techniques versus S-BCS
- Volume displacement versus mastectomy alone
- Volume displacement versus mastectomy plus reconstruction
- Volume replacement techniques versus S-BCS
- Volume replacement versus mastectomy alone
- Volume replacement versus mastectomy plus reconstruction

We planned that if data were available, we would present one particular technique of O-BCS versus any other available option for breast cancer surgery. In addition, we planned to present data from studies that compare the various types of O-BCS with each other, specifically relating to those listed in the experimental interventions section, but there were no data for this. Further subgroup analysis may be possible in future reviews.

Sensitivity analysis

We conducted the following sensitivity analyses.

- Quality assessment of included studies (removing studies that are at high risk of bias for RCTs or critical risk of bias for non-randomised studies from the meta-analysis, whilst noting all studies in a narrative synthesis)
- Fixed-effect model versus random-effects model

We commented if sensitivity analysis changed any of the meta-analysis in the main analysis that had moderate or high heterogeneity.

Summary of findings and assessment of the certainty of the evidence

We used the GRADE approach to assess the certainty of the evidence of the main outcomes. We used the overall ROBINS-I judgement to feed into the GRADE assessment. We calculated the estimate of absolute risk for outcomes displayed as HRs using an average of unadjusted baseline control event rates from the included studies. Two review authors (AN and SH) used GRADEpro GDT software to develop the summary of findings tables using the following main outcomes.

- Local recurrence at 5 years: shown as local recurrence-free survival and local recurrence rate
- Breast cancer-specific disease-free survival at 5 years
- Re-excisions: need for further breast surgery due to inadequate cancer resection
- Complications
- Recall rates: number of biopsies needed in follow-up period
- Patient-reported outcome measures, such as patient satisfaction

RESULTS

Description of studies

Results of the search

We identified 7910 references through our electronic and manual searches. After removing duplicate records, we retrieved 7902 references. After screening the full text, we identified the 78 observational studies to include in the review. Searching of the reference lists of eligible publications did not reveal additional publications for inclusion. Summarised in Figure 1.

Figure 1. Study flow diagram

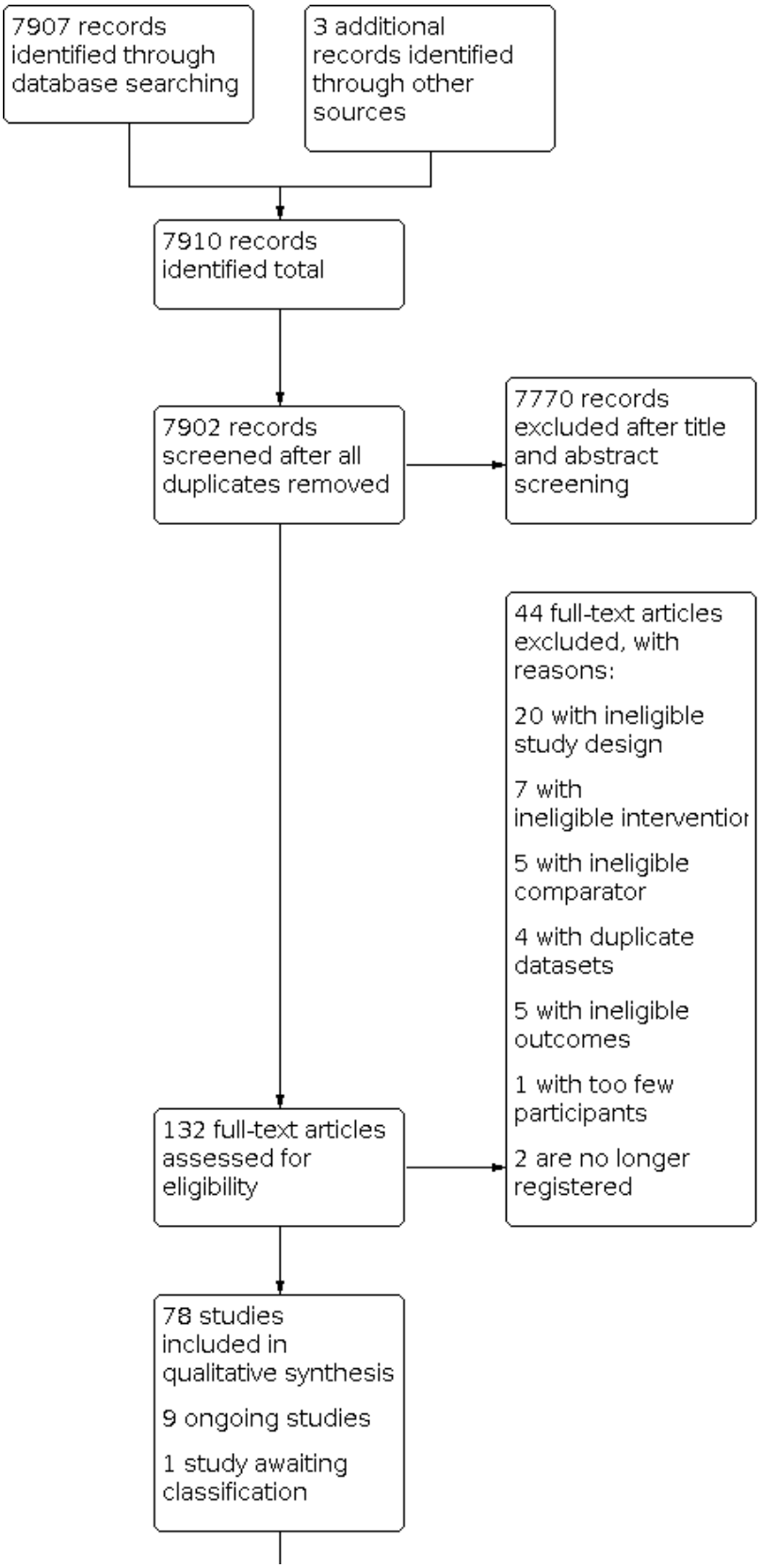
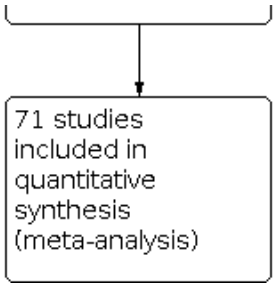


Figure 1. (Continued)



We excluded three publications (Angarita 2019; Kelemen 2016; Niinikoski 2019 (1)) because they were published as conference abstracts and then later published as journal articles (Angarita 2020; Keleman 2019; Niinikoski 2019 (2)). One publication Cil 2016 was an earlier dataset of Angarita 2020, which was a larger more recent dataset. Data were extracted from these publications but they were excluded from analyses to avoid duplication of results.

Included studies

Design

All 78 included studies were non-randomised cohort studies. Four studies were described as case controls, but according to the *Cochrane Handbook* (Higgins 2021), they were cohort studies due to selecting participants based on intervention rather than outcome (Atallah 2015; Ozmen 2016; PlaFarnos 2018; Vieira 2016). Sixty studies were retrospective (77%) and 18 (23%) prospective studies.

Setting

The majority of the studies were based in the USA and UK. For a full breakdown of the countries see Table 11. Sixty-three studies were single-centre (81%), ten (13%) were multi-centre and five (6%) were large international/national database reviews.

Most articles were published in English. Six papers were translated into English from Mandarin (Jiang 2015; Tang 2016); Hungarian (Matrai 2014); Spanish (Acea-Nebril 2005; Sherwell-Cabello 2006), and French (Gicalone 2015).

Population

We included 78 observational studies with 178,813 participants in the review. All participants were patients with primary breast cancer. The details of inclusion and exclusion can be found in the individual study details. Some papers only included subsets of patients with primary breast cancer, such as those with certain histological types of cancer (e.g. DeLorenzi 2018) or size (e.g. Di Micco 2017) or location (e.g. Gulcelik 2013) or co-intervention (e.g.Chauhan 2016 (1); Chauhan 2016 (2)), but we did not differentiate and included all studies of patients with breast cancer that had a surgical intervention as part of their treatment. The age range was 23 to 86 years in the intervention group and 23 to 90 years in the comparison group. The relationship of clinicopathological factors of participants within studies varied, which is displayed in detail in Table 1. Future reviews may consider evaluating these differences as subgroups.

Intervention

We identified two distinct types of intervention: volume replacement and volume displacement O-BCS. Some studies did not differentiate these methods and combined the techniques as O-BCS.

Twenty-one studies combined volume displacement techniques, and we assumed one study (Farooqi 2019), where the details were unclear, to be in this category (27%). Two studies (3%) analysed both volume displacement and replacement techniques and analysed them separately (Bali 2018; Lee 2018 3%).

We classified 44 studies (56%) as volume displacement O-BCS only. Borm 2019 involved 288 participants that underwent volume displacement surgery and one participant underwent volume replacement. Therefore, we classified this study in the volume displacement category. The breakdown of techniques is displayed in the Characteristics of included studies tables.

We classified 11 (14%) studies as volume replacement O-BCS only. Seven of these studies evaluated the latissimus dorsi mini-flap (Fan 2019; Hashimoto 2019; Mustonen 2004; Ozmen 2016; Ozmen 2020; Ren 2014; Zhou 2019). The breakdown of techniques in all studies is displayed in the Characteristics of included studies tables.

The co-interventions varied among studies and were determined by local guidance and cancer multidisciplinary team decisions. The relationship within the studies is shown in Table 1.

Comparison

We identified three distinct types of control: BCS, mastectomy alone and mastectomy with reconstruction. The breakdown of techniques in all studies is displayed in the Characteristics of included studies tables; some had multiple groups of comparison. The combinations of intervention and comparisons can be seen in Table 12.

- **O-BCS versus S-BCS:** 16 studies compared any O-BCS (volume displacement and replacement together) to a form of BCS (Angarita 2020; Chauhan 2016 (1); Chauhan 2016 (2); DeLorenzi 2016 (1); DeLorenzi 2018; Dolan 2015; Down 2013; Farooqi 2019; Hamdi 2008; Mukhtar 2018; Palsodittlir 2018; Rose 2019; Rose 2020; Tang 2016; Viega 2010; Viega 2011). These studies contributed to the main analysis of O-BCS versus S-BCS. One study compared O-BCS to BCS and analysed volume displacement and replacement techniques separately (Bali 2018), and so contributed to both the main analysis of O-BCS versus S-BCS and both subgroup analyses. Thirty-six studies compared volume displacement O-BCS only compared to S-BCS (Acea-Nebril 2017; Acosta-Marin 2014; Amitai 2018; Atallah 2015; Borm 2019; Cassi 2016; Chakravorty 2012; Crown 2015; Crown 2019; Di Micco 2017; Eichler 2013; Gicalone 2007 (1); Gicalone 2007 (2); Gicalone 2015; Gulcelik 2013; Hilli-Betz 2014;

Jiang 2015; Keleman 2019; Kimball 2018; Lansu 2014; Losken 2009; Losken 2014; Malhaire 2015; Matrai 2014; Mazouni 2013; Niinikoski 2019 (2); Ojala 2017; Palsodittlir 2018; Piper 2016; Santos 2015; Scheter 2019; Sherwell-Cabello 2006; Tenofsky 2014; Vieira 2016; Wijgman 2017; Wong 2017), and contributed to the main analysis of O-BCS versus S-BCS and the subgroup analysis of volume displacement O-BCS versus S-BCS. Six studies compared volume replacement O-BCS to S-BCS (Fan 2019; Hashimoto 2019; Hu 2019; Nakada 2019; Ozmen 2016; Zhou 2019), and so contributed to the main analysis of O-BCS versus S-BCS and the subgroup analysis of volume replacement O-BCS versus S-BCS.

- **O-BCS** versus**mastectomy (Mx)**: three studies compared volume replacement O-BCS to mastectomy without reconstruction (Gendy 2003; Nakagomi 2019; Ren 2014), and contributed to the main analysis of O-BCS versus mastectomy without reconstruction and the subgroup analysis of volume replacement O-BCS versus mastectomy.
- **O-BCS** versus**mastectomy + reconstruction (Mx + R):** one study compared any O-BCS (volume displacement and replacement together) to mastectomy with reconstruction (Kelsall 2017), and contributed to the main analysis of O-BCS versus mastectomy with reconstruction. Three studies compared volume displacement only to mastectomy with reconstruction (Hart 2015; Peled 2014; Tong 2016), and contributed to the main analysis of O-BCS versus mastectomy with reconstruction and the subgroup analysis of volume displacement O-BCS versus mastectomy plus reconstruction. Two studies compared volume replacement only to mastectomy with reconstruction (Mustonen 2004; Ozmen 2020), and contributed to the main analysis of O-BCS versus mastectomy with reconstruction and the subgroup analysis of volume replacement O-BCS versus mastectomy plus reconstruction.
- **O-BCS** versus**mastectomy with or without reconstruction (Mx +/- R)**: one study compared any O-BCS (volume displacement and replacement together) to mastectomy with or without reconstruction (DeLorenzi 2016 (2)). We have included these studies in the main analyses of O-BCS versus mastectomy and O-BCS versus mastectomy with reconstruction, but given they combine mastectomy with and without reconstruction as a control group they are separated when pooling.
- **O-BCS** versus**BCS/Mx:** one study compared any O-BCS (volume displacement and replacement together) to S-BCS and mastectomy without reconstruction (Klit 2017). One study compared volume displacement O-BCS to S-BCS and mastectomy without reconstruction (Acea-Nebril 2005), and contributed to both the main analyses of O-BCS versus S-BCS and O-BCS versus mastectomy as well as the subgroup analyses of volume displacement O-BCS versus S-BCS and versus mastectomy.
- **O-BCS** versus**BCS/Mx +/- R:** two studies compared any O-BCS (volume displacement and replacement together) to BCS and mastectomy with or without reconstruction combined (Mansell 2015; Mansell 2017). We have included these studies in the main analyses of O-BCS versus mastectomy and O-BCS versus mastectomy with reconstruction, but given they combine mastectomy with and without reconstruction as a control group they are separated when pooling.
- **O-BCS** versus**Mx/Mx + R:** one study compared volume displacement O-BCS with mastectomy with and without reconstruction (Potter 2020), and so contributed to O-BCS versus mastectomy and O-BCS versus mastectomy with reconstruction.
- **O-BCS** versus**BCS/Mx/Mx + R:** two studies compared any O-BCS (volume displacement and replacement together) to S-BCS, mastectomy alone and mastectomy with reconstruction (Carter 2016; Kahn 2013), so contributed to all three main analyses. One study compared any O-BCS to S-BCS, mastectomy alone and mastectomy with reconstruction and analysed volume displacement and replacement techniques separately (Lee 2018), so contributed to all three main analyses and both subgroup analyses. One study compared volume displacement O-BCS to S-BCS, mastectomy alone and mastectomy with reconstruction (Morrow 2019), and contributed to all three main analyses and the subgroup analyses of volume displacement.

Primary outcomes

Local recurrence was evaluated in 30 studies (38%), disease-free survival in 13 studies (16%), and overall survival in 17 studies (22%). We wrote to all authors of studies that reported one of the primary outcomes but not others. We received four responses, but nobody was able to provide further data.

Secondary outcomes

Re-excision rates were evaluated in 42 studies (53%), complications in 41 studies (52%), and recall rates were evaluated in 7 studies (9%). Time to adjuvant therapy was evaluated in 16 studies (20%), patient-reported outcomes in 28 studies (35%), and aesthetic outcomes in 11 studies (14%).

Ongoing studies

Of the nine ongoing studies, one is a RCT based in the UK (ACTRN12612000638831), planning to compare O-BCS with S-BCS. It was last updated in 2016 and may no longer be ongoing; we contacted the authors for further information.

There are three trials registered in Egypt by the same author and institution which planned to compare O-BCS with S-BCS (NCT02901223; NCT02923635; NCT03012152). They planned to measure the outcome of margins in all specimens and patient-reported outcome measures. All three trials were last updated in 2017 with no published results. It appears there are similarities between the studies. We contacted authors for further information.

The remaining six studies are observational studies.

One is in China (NCT04030845) comparing O-BCS with any other breast reconstruction reporting local recurrence, overall survival, complications and patient-reported outcomes using a visual analogue scale.

Two are in the Netherlands (Catsman 2018; NTR6901), both comparing O-BCS with S-BCS. Catsman 2018 will evaluate re-excisions and patient-reported outcome measures with patient questionnaires (Breast-Q; Cohen 2016), EORTC-QLQ (European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire; Aaronson 1993) and aesthetic outcome with photographs of the breast given to a panel and analysed with BCCT.core software (BCCT.core). NTR6901 will analyse patient satisfaction and postoperative complications.

One study based in Austria (NCT01396993), will compare O-BCS with S-BCS and assess patient-reported local recurrence, disease-

free survival, overall survival, patient-reported outcome measures (using a breast image scale, BREAST-Q; Cohen 2016), complications and aesthetic outcome (using the breast symmetry index; Fitzal 2007).

One study based in Denmark (NCT02159274), will compare O-BCS with S-BCS and assess patient-reported outcomes focusing on shoulder function and lymphoedema. They will also compare aesthetic outcomes (using the breast retraction assessment; Pezner 1985).

Studies awaiting classification

One study describes itself to be a RCT (Srivastava 2018), however as insufficient information on methods was available, we decided to categorise this as awaiting classification. The study has not been published as a full study to our knowledge.

Excluded studies

We excluded 45 studies during the full-text review, amongst which 20 had study designs that did not meet eligibility criteria, seven had interventions that were not eligible, and five had comparators that were not eligible. For further information see Figure 1.

Risk of bias in included studies

We assessed risk of bias for all studies using ROBINS-I (Sterne 2016). We have displayed each risk of bias assessment divided into each outcome studied as per the tool. The summary and details can be found per outcome in the corresponding figures and tables.

- Local recurrence - Figure 2, Table 2
- Disease-free survival - Figure 3, Table 3
- Overall survival - Figure 4, Table 4
- Re-excision rates - Figure 5, Table 5
- Complications - Figure 6, Table 6
- Recall rates - Figure 7, Table 7
- Time to adjuvant therapy - Figure 8, Table 8
- Patient-reported outcome measures - Figure 9, Table 10
- Cosmetic evaluation - Figure 10, Table 9

Figure 2. ROBINS-1 risk of bias for local recurrence

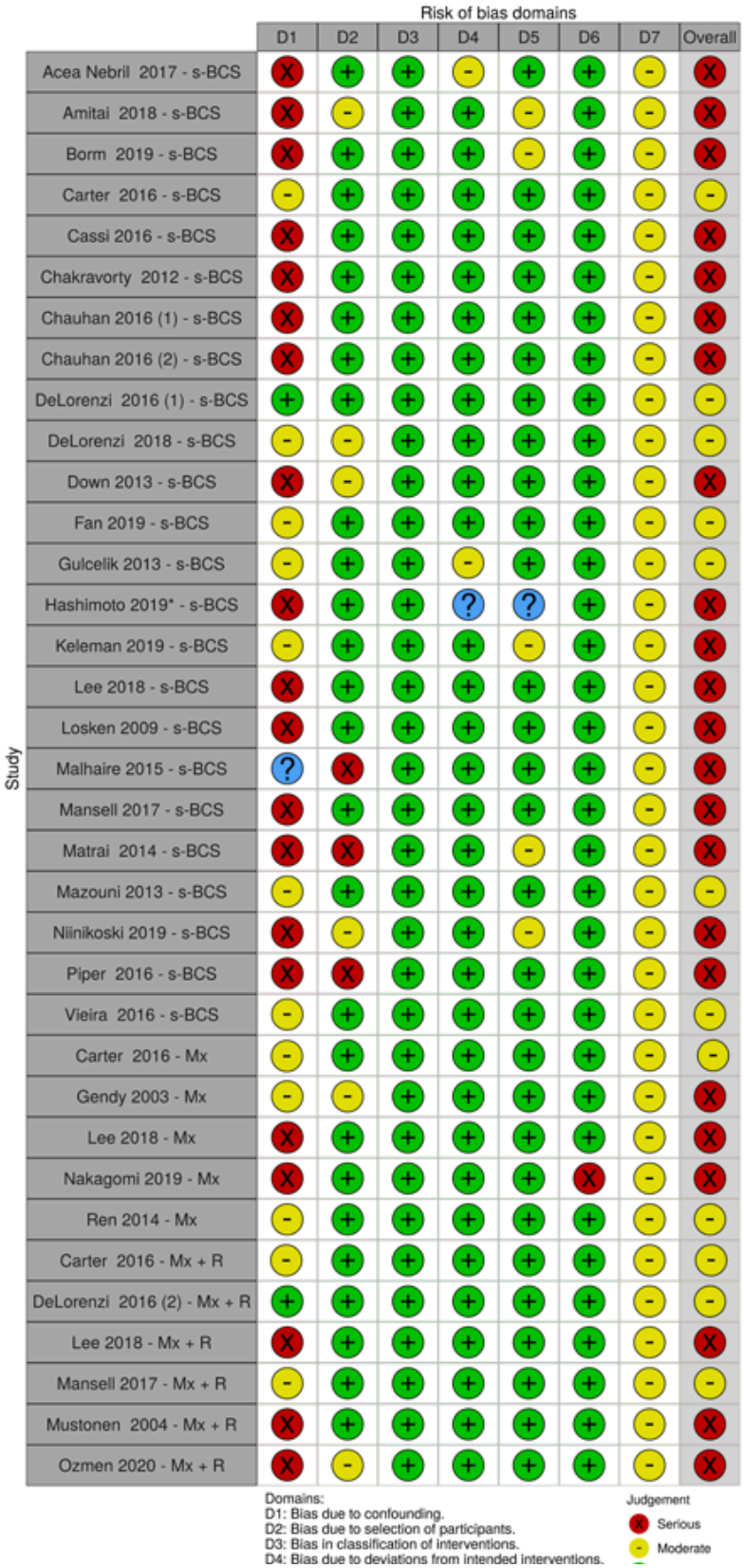


Figure 2. (Continued)

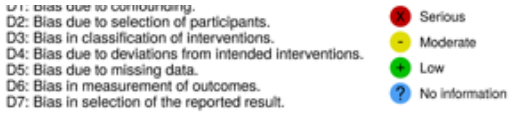


Figure 3. ROBINS-1 risk of bias for disease-free survival

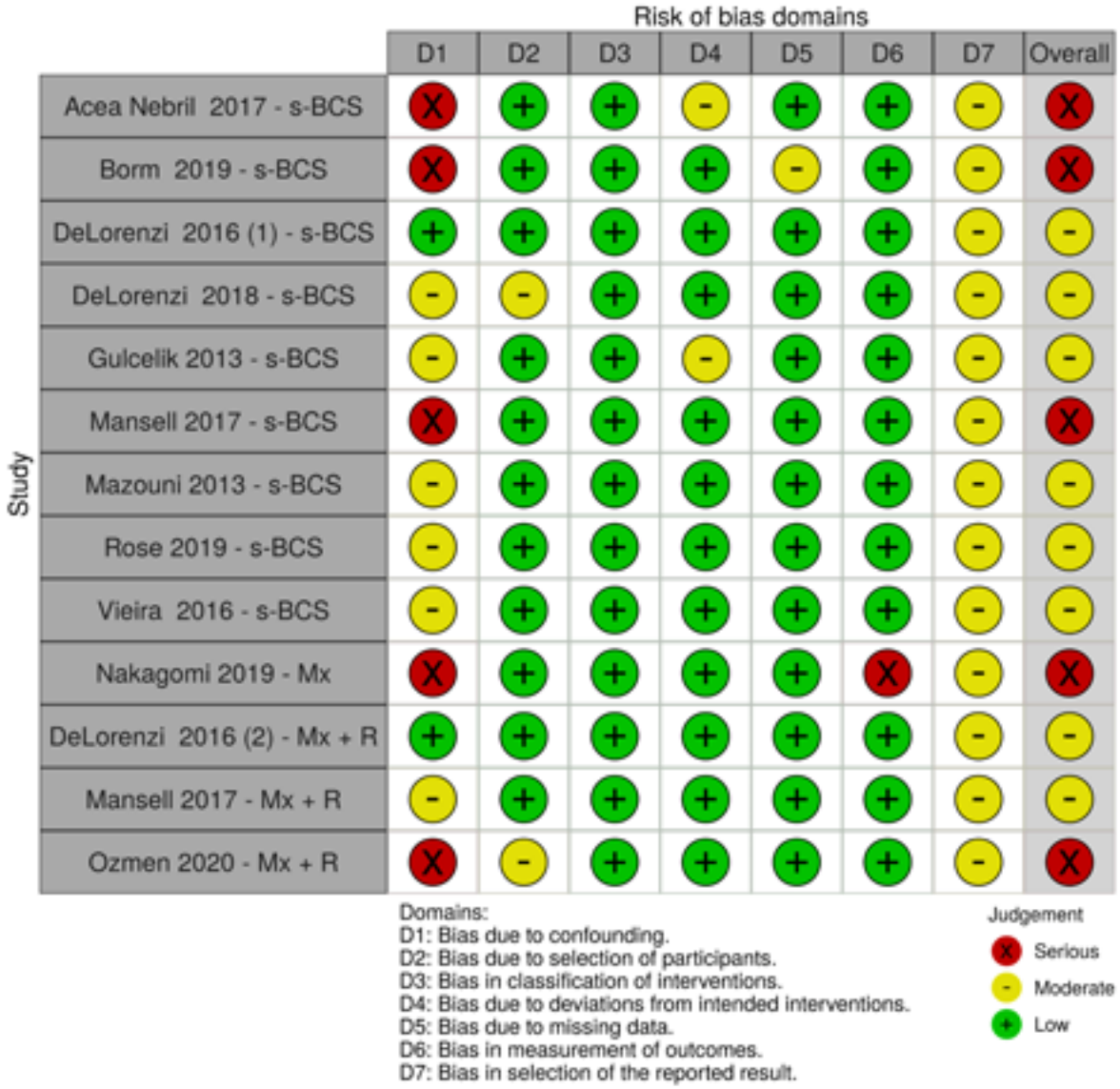


Figure 4. ROBINS-1 risk of bias for overall survival

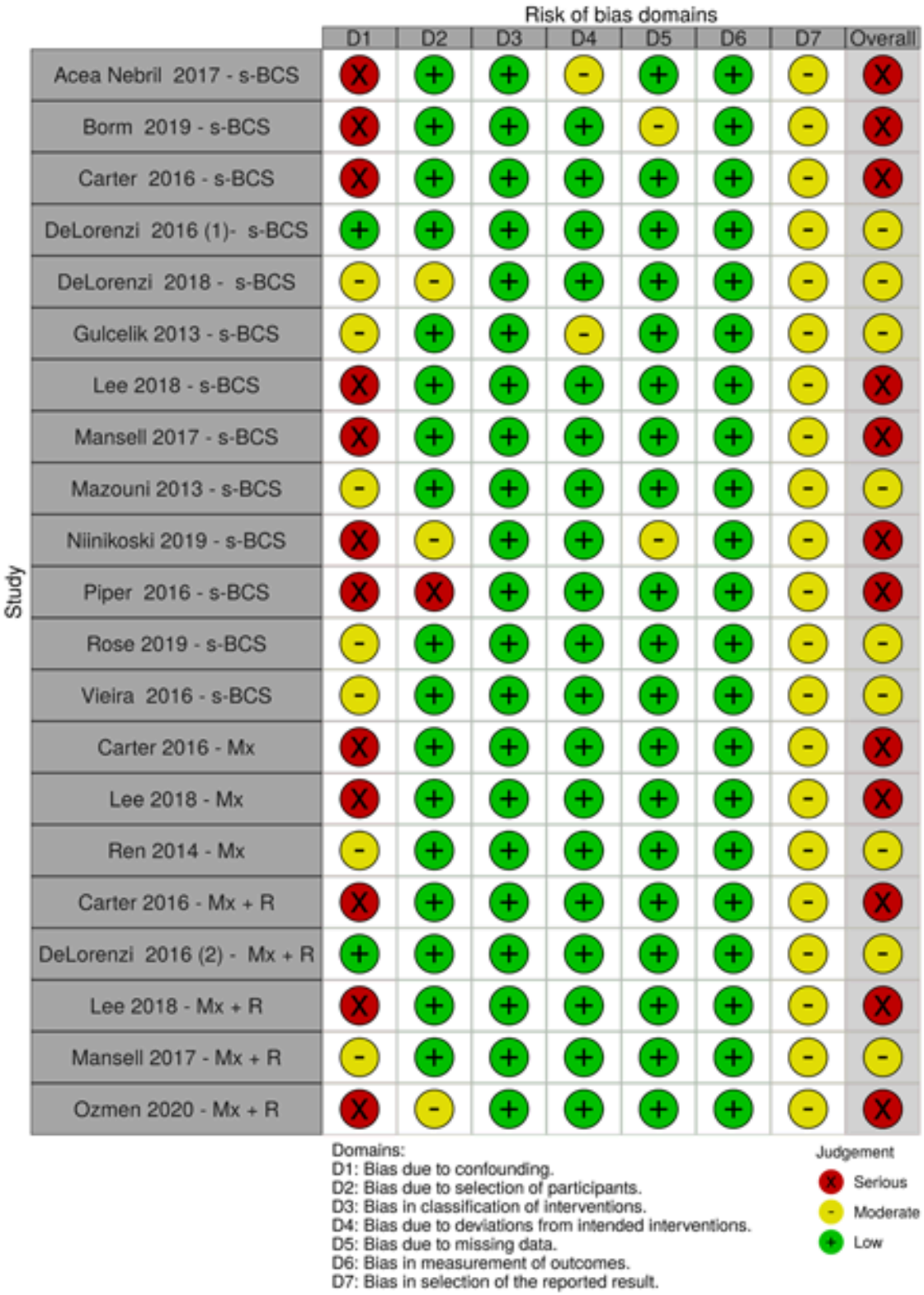


Figure 5. ROBINS-1 risk of bias for re-excisions

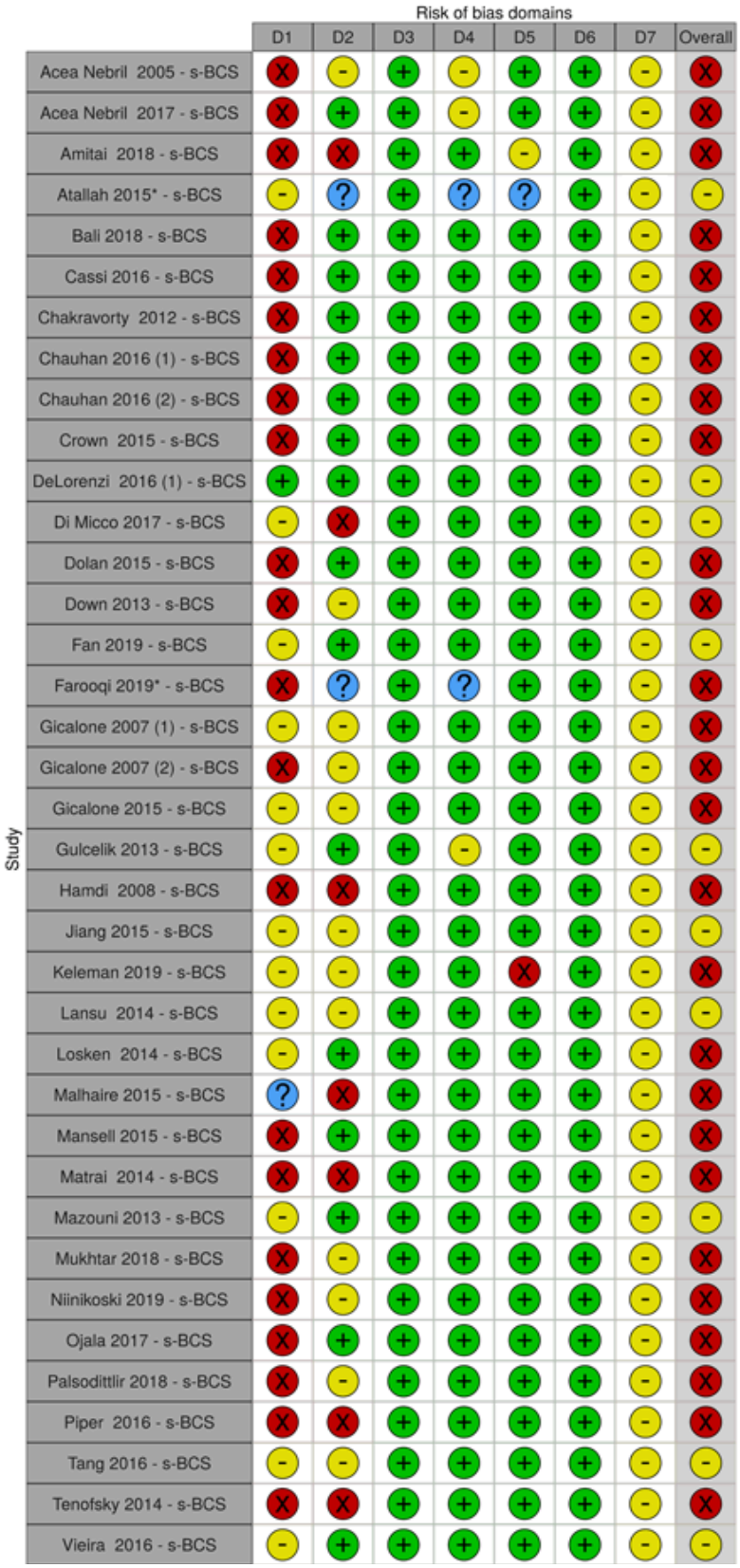


Figure 5. (Continued)

Figure 6. ROBINS-1 risk of bias for complications

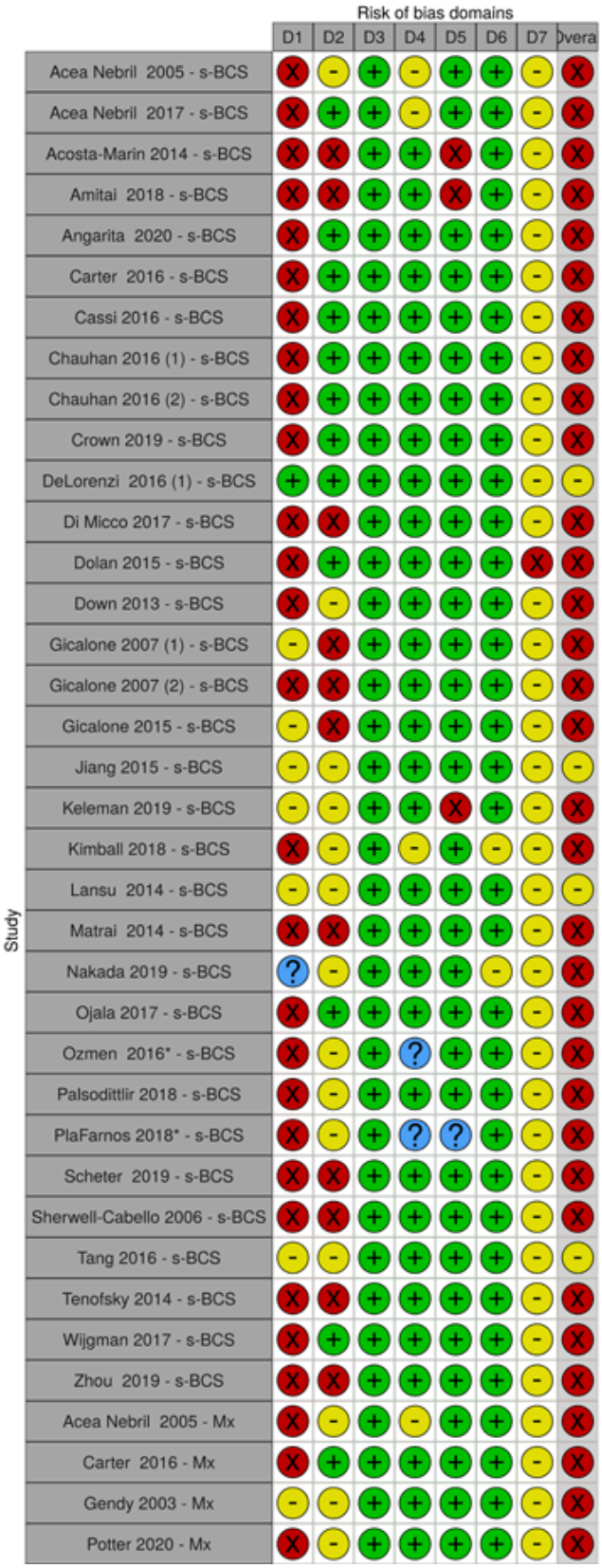


Figure 6. (Continued)

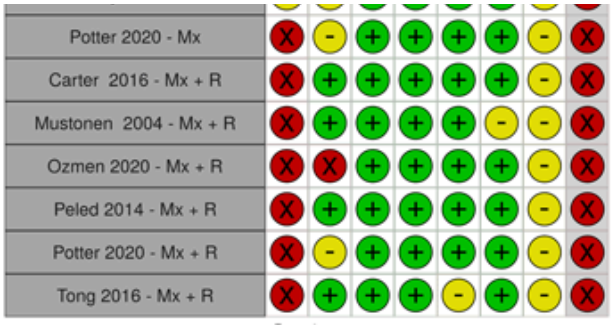


Figure 7. ROBINS-1 risk of bias for recall rates

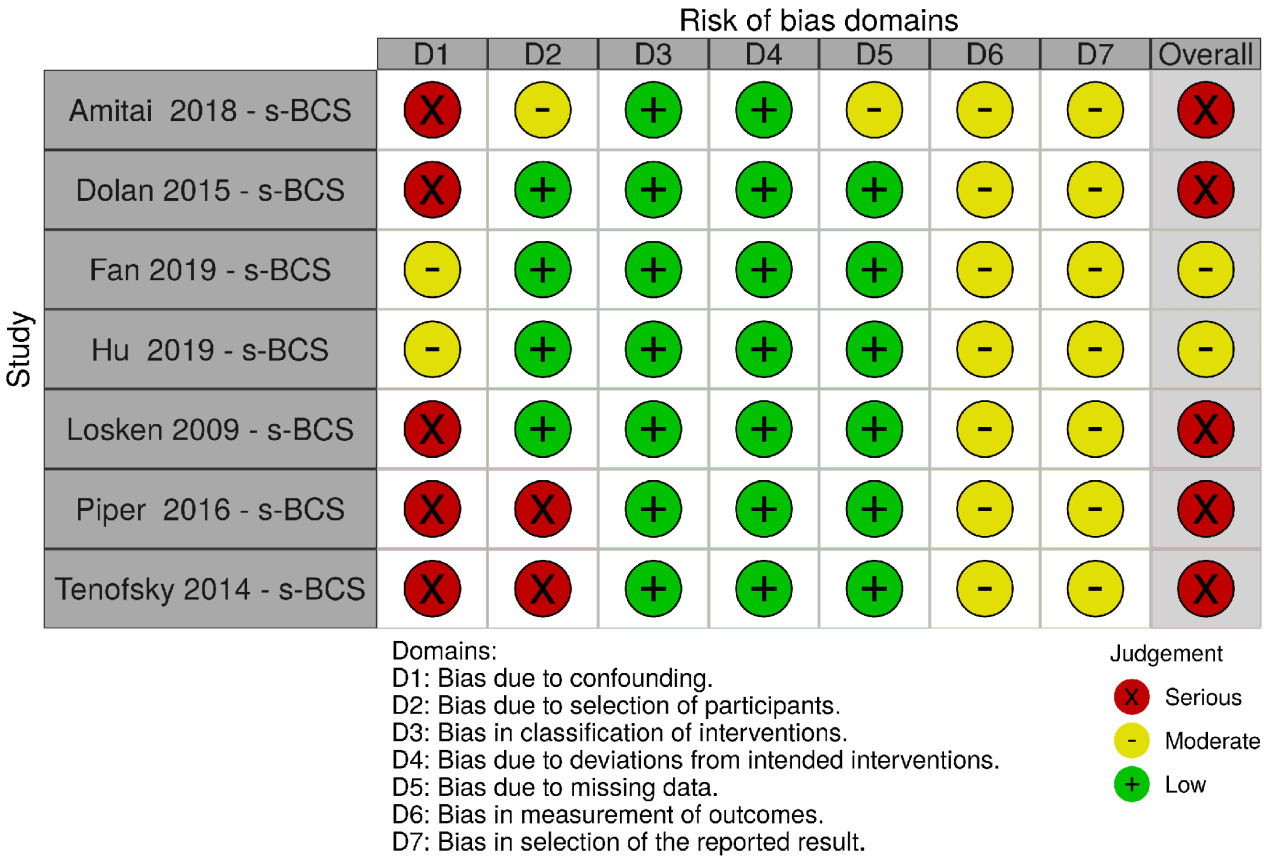


Figure 8. ROBINS-1 risk of bias for time to adjuvant therapy

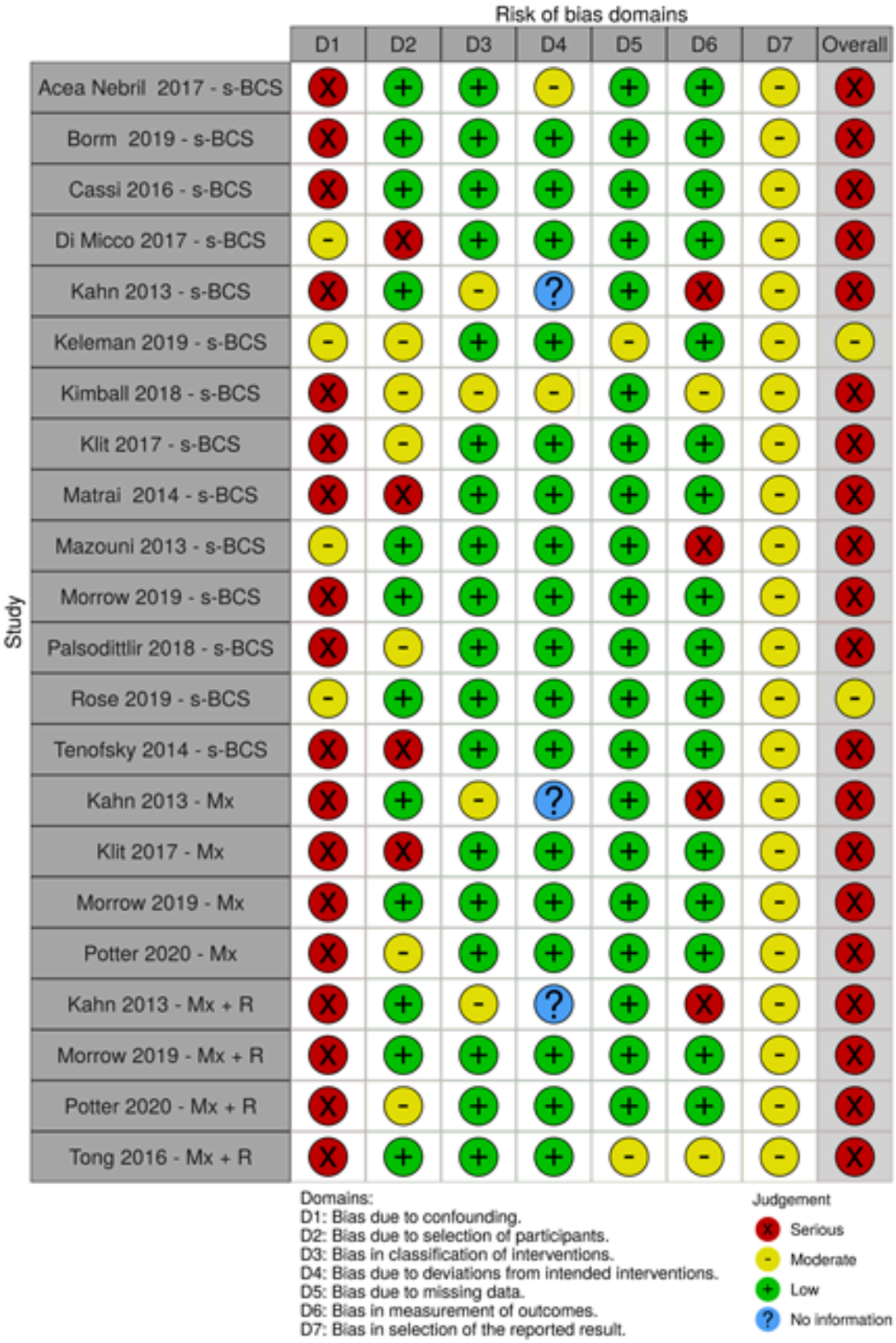


Figure 9. ROBINS-1 risk of bias for patient reported outcome measures

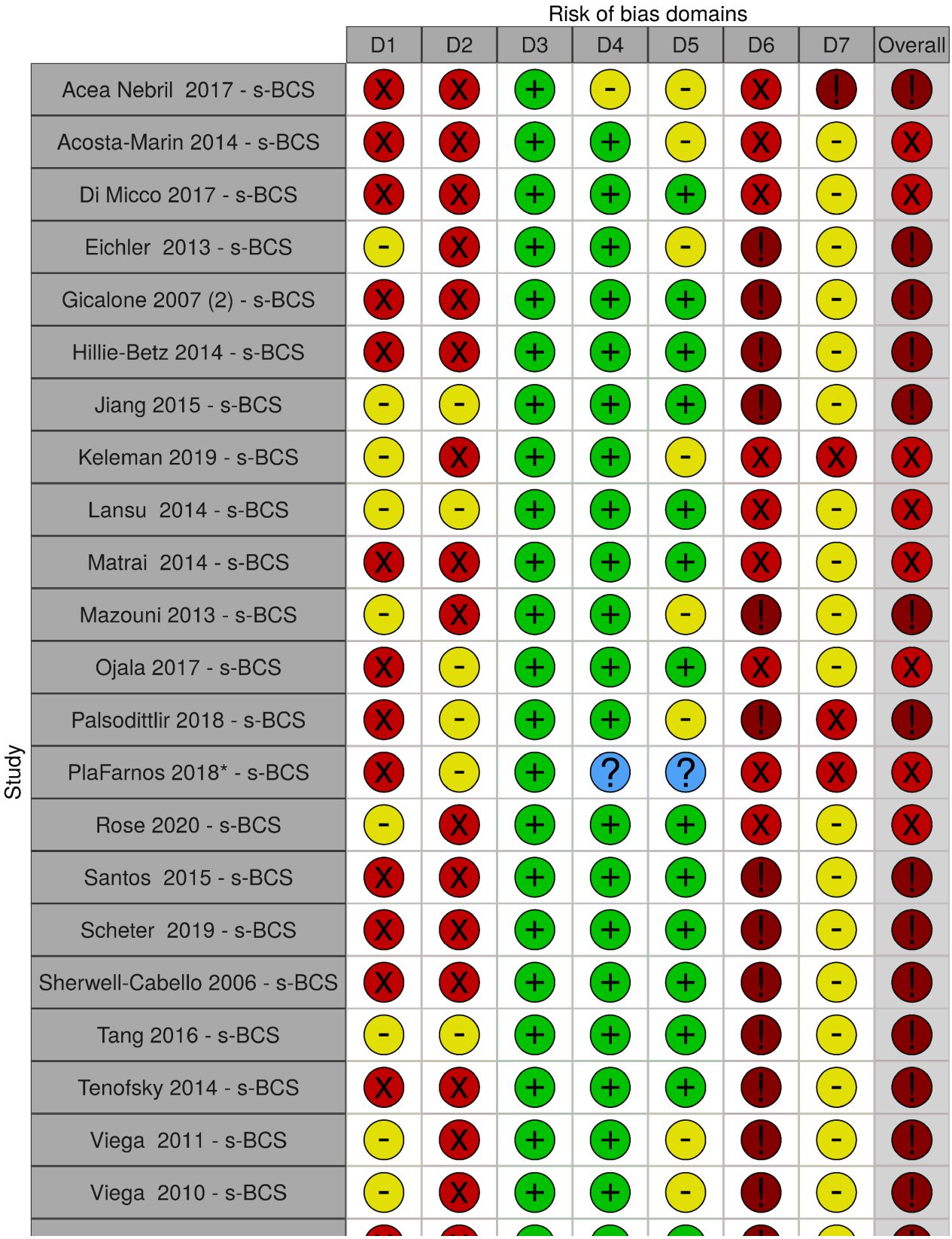


Figure 9. (Continued)

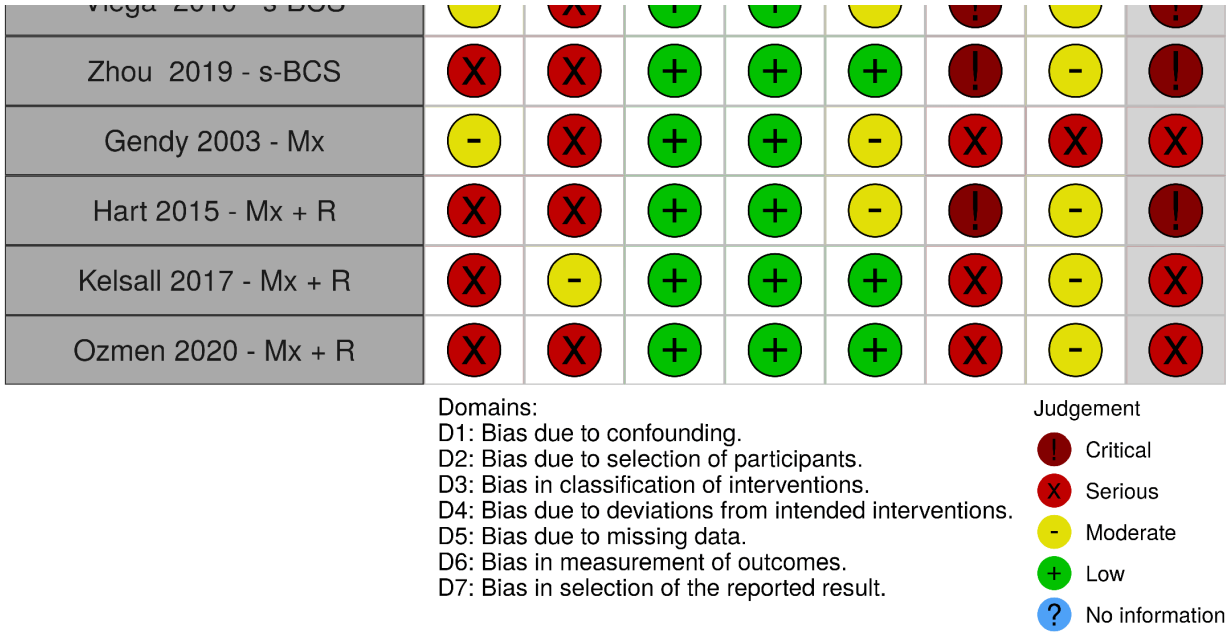
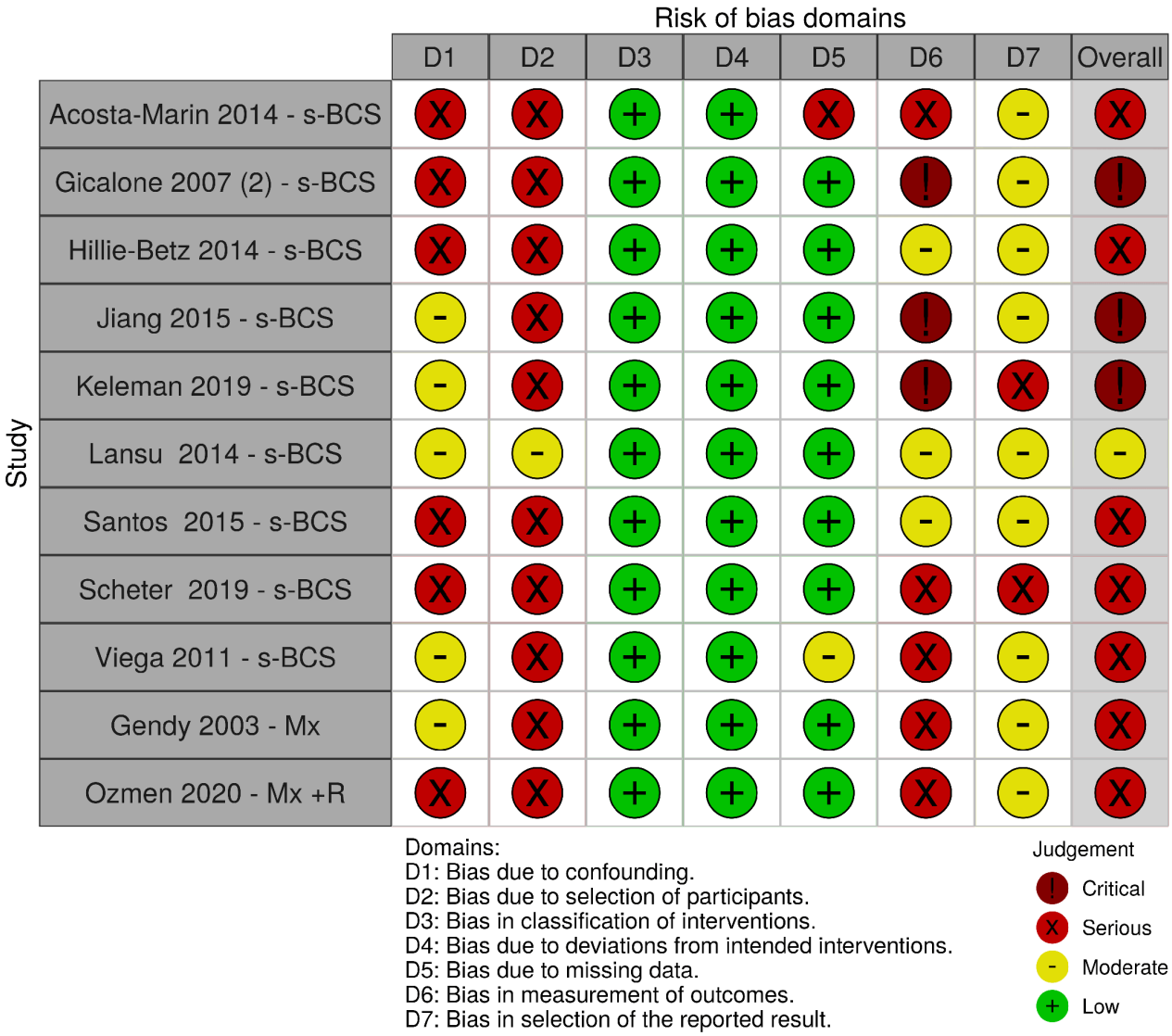


Figure 10. ROBINS-1 risk of bias for cosmetic evaluation



Overall

Overall we rated the risk of bias for local recurrence (Figure 2, Table 2), disease-free survival (Figure 3, Table 3), overall survival (Figure 4, Table 4), re-excision rates (Figure 5, Table 5), complications (Figure 6, Table 6), recall rates (Figure 7, Table 7), and time to adjuvant therapy (Figure 8, Table 8) as serious in most studies. The major implication for risk of bias was confounding bias with details of confounding in Table 1.

For patient-reported outcome measures (Figure 9, Table 10) and cosmetic evaluation (Figure 10, Table 9) overall, we rated the risk of bias for recall rates as serious/critical in most studies. For those with critical risk of bias, the major implication for risk of bias was measurement of outcome bias due to the use of unvalidated tools. If validated but still subjective tools were used then we deemed risk of bias serious due to knowledge of the intervention impacting the outcome.

Bias due to confounding

We judged the risk of bias due to confounding to be serious in most studies for most outcomes. This is due to differences in clinicopathological factors and co-interventions, e.g. radiotherapy, chemotherapy and endocrine therapy; details are displayed in Table 1.

For local recurrence (Figure 2, Table 2), disease-free survival (Figure 3, Table 3), and overall survival (Figure 4, Table 4), if comparisons differed in clinicopathological factors, such as tumour stage, size and grade (e.g. Lee 2018; Mansell 2017; Piper 2016), or co-interventions (e.g. Carter 2016; Keleman 2019; Mansell 2017), we deemed them at serious risk of bias. We deemed some studies

at low risk of bias (e.g. DeLorenzi 2016 (1); DeLorenzi 2016 (2)), as important clinicopathological factors were matched for and co-interventions were balanced across the groups. We deemed studies moderate (e.g. Fan 2019; Mazouni 2013; Vieira 2016) if they demonstrated balance in some clinicopathological and co-interventions across the studies. It should be noted that Mazouni 2013 includes only patients undergoing surgery following primary systemic treatments; given that this was balanced between the O-BCS and control group, we deemed this at moderate risk of bias. Differences in adjuvant radiotherapy are more significant (higher risk of bias) for the comparison O-BCS versus S-BCS, as it is usually standard practice to give radiotherapy with BCS, whereas radiotherapy can be avoided with mastectomies.

For re-excisions (Figure 5, Table 5), if clinicopathological factors, especially tumour size and tumour location were different across the groups, then we deemed studies at serious risk of bias (e.g. Chakravorty 2012; Hamdi 2008; Wijgman 2017).

For complications (Figure 6, Table 6) if clinicopathological factors especially tumour stage and patient comorbidities/factors (e.g. Crown 2019; Gicalone 2007 (1); Ozmen 2016) and co-interventions, especially axillary surgery and adjuvant radiotherapy (Di Micco 2017; Kimball 2018; Tang 2016) were imbalanced, we deemed studies at serious risk of bias.

For patient-reported outcome measures (Figure 9, Table 10) and cosmetic evaluation (Figure 10, Table 9), we judged the risk of bias due to confounding to be serious in most studies, especially if differences in size and location (e.g. Lee 2018; Mansell 2017; Piper 2016) or co-interventions, especially radiotherapy (e.g. Carter 2016; Keleman 2019; Mansell 2017).

Bias due to selection of participants

We judged the selection bias to be low in most outcomes as all/most eligible participants in a period of time were included. We deemed some studies (Amitai 2018; DeLorenzi 2018; Niinikoski 2019 (2); Ren 2014 etc.) at moderate risk of bias as some participants were not included or controlled for in a way that could have affected the selection, e.g. excluding patients that needed mastectomy eventually and women choosing after being counselled on potential outcomes. If studies excluded patients based on needing mastectomy, eventually we deemed the risk of bias moderate for oncological outcomes, recall rates and time to adjuvant therapy (as these outcomes would be slightly affected by the exclusion of such patients) but serious for re-excision rates, complications, patient-reported outcome measures and cosmetic evaluation, given patients who had a mastectomy have had a re-excision, may have had it due to a complication, will have their overall satisfaction and cosmesis affected by the intervention initially chosen. We deemed some studies at serious risk of bias (e.g. Malhaire 2015; Matrai 2014; Piper 2016) for reasons such as: patients were selected to certain arms as selection was based on localisation techniques or it was unclear why these patients were selected, or patients without negative margins were excluded. For patient-reported outcome measures (Figure 9, Table 10) and cosmetic evaluation (Figure 10, Table 9), we judged the selection bias to be serious in most cases as there is a natural bias in those patients that respond to questionnaires.

Bias due to classification of interventions

We judged risk of bias to be low in all studies as classification of interventions was clear and determined at the start of the intervention.

Bias due to deviation from intended intervention

We judged risk of bias to be low/moderate in all studies as there was no evidence of deviation from the intended operation as these studies were cohort studies and were selected based on their intervention. Acea-Nebril 2017 mentioned a deviation from the intended co-intervention (time to adjuvant therapy) in the intervention group.

We evaluated surgeon experience and whether the study had taken into account learning curves after the introduction of a new technique in the study. Most studies did not comment on this. The study period for Crown 2015 and Crown 2019 began after allowing time for the surgeons to adapt to the new O-BCS technique accounting for confounding created by learning curves, therefore we judged them to be at low risk of bias. Some studies, such as Gicalone 2007 (1), Keleman 2019 and Tenofsky 2014 ensured all surgeries were done by or under the supervision of experienced surgeons in the operations studied. We deemed two studies at moderate risk of bias due to the study period starting from the beginning of uptake of O-BCS and for including centres with varying levels of experience in O-BCS (Gulcelik 2013; Kimball 2018).

Bias due to missing data

We judged risk of bias due to missing data to be low because in most studies all patients enrolled were followed up. Some studies reported some loss to follow-up, but with similar numbers in both groups, so the impact may be similar across groups (Amitai 2018; Borm 2019; Gendy 2003; Gulcelik 2013; Keleman 2019).

Bias in measurement of outcomes

We judged risk of bias to be low in all cases for local recurrence (Figure 2, Table 2), disease-free survival (Figure 3, Table 3), overall survival (Figure 4, Table 4), re-excision rates (Figure 5, Table 5), and complications (Figure 6, Table 6) as all are an objective outcome measure. For disease-free survival, length of follow-up time details were not clear for Nakagomi 2019 and so we deemed this to be at serious risk of bias. For complications, some studies reported difficulties in recording complications in large databases (e.g. Angarita 2020), so we judged these to be at moderate risk of bias. For recall rates we judged risk of bias to be moderate in all cases as recall rates are usually based on radiological imaging, which can be subject to bias. Four studies used the BI-RADS (Breast Imaging-Reporting and Data System) scale to reduce this risk of bias (Amitai 2018; Dolan 2015; Fan 2019; Hu 2019).

For time to adjuvant therapy, we judged risk of bias to be low in most cases as time to adjuvant therapy is an objective outcome measure in days. However, we deemed Tong 2016 at critical risk of bias as they reported a general 'delay in time to adjuvant therapy', which was poorly defined.

We judged risk of bias to be serious when patient-reported outcome measures were measured used a validated reporting tool (e.g. BREAST-Q; Cohen 2016) (Acea-Nebril 2017; Di Micco 2017; PlaFarnos 2018) or EORTC (Aaronson 1993) (Keleman 2019; Lansu 2014 etc.) but this is still very vulnerable to bias from subjective knowledge

of the intervention. We deemed studies at critical risk of bias that used non-validated tools (e.g. Eichler 2013; Jiang 2015; Palsodittlir 2018).

For cosmetic evaluation, we judged risk of bias to be moderate when aesthetic outcome was judged by the objective BCCT.core software (Hilli-Betz 2014; Lansu 2014; Santos 2015). We judged those with a large panel who were unaware of the surgery with validated scoring tools at serious risk of bias (it is very difficult to actually blind surgeons) (e.g. Scheter 2019). We deemed those with small unblinded panels with self-designed tools judging cosmetic outcome to have a critical risk of bias (e.g. Viega 2011).

Bias in the selection of the reported results

For local recurrence (Figure 2, Table 2), disease-free survival (Figure 3, Table 3), overall survival (Figure 4, Table 4), re-excision rates (Figure 5, Table 5), complications (Figure 6, Table 6), recall rates (Figure 7, Table 7), and time to adjuvant therapy (Figure 8, Table 8), we judged the selection of reported results as moderate in all cases as there was no indication of selected reporting and no indication that an outcome would have been logically collected (given what is reported in the study) but then not reported. There was no difference between the methods sections and results reported in any of the papers, but no study had a prior protocol. For patient-reported outcome measures (Figure 9, Table 10), and cosmetic evaluation (Figure 10, Table 9), we judged selection of reported results as moderate in most cases as there was no indication of selected reporting, but no study had a prior protocol. There were a few that did not report all outcomes that we deemed serious (e.g. Keleman 2019; Palsodittlir 2018; Gendy 2003).

Effects of interventions

See: **Summary of findings 1** Any O-BCS compared to S-BCS for women with primary breast cancer; **Summary of findings 2** Any O-BCS compared to mastectomy for women with primary breast cancer; **Summary of findings 3** Any O-BCS compared to mastectomy plus reconstruction for women with primary breast cancer

The 78 studies with 92 comparisons, enrolled 178,813 women. The matrix of different comparisons can be found in Table 12. The certainty of evidence ratings for the main outcomes are presented in Summary of findings 1, Summary of findings 2 and Summary of findings 3.

Comparison 1: O-BCS versus S-BCS

Primary outcomes

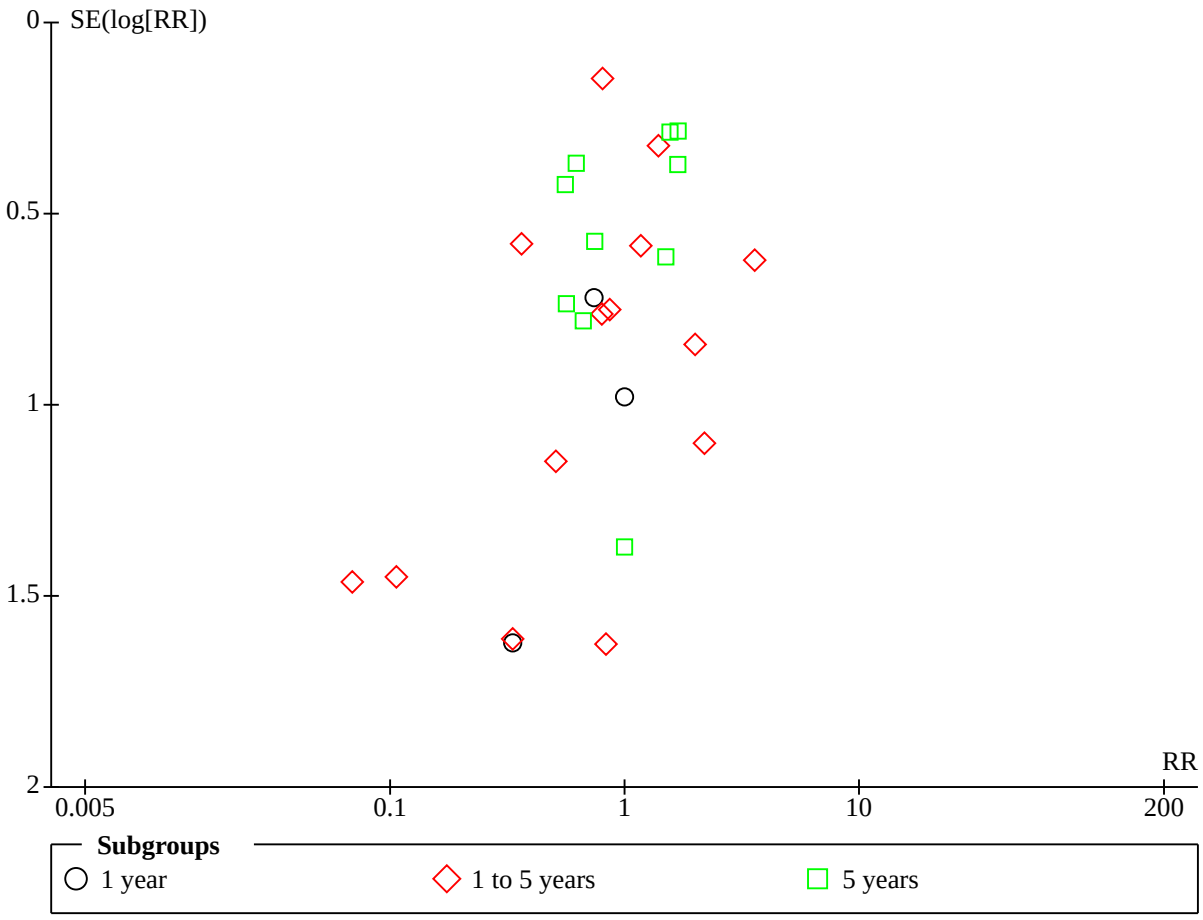
Local recurrence

Twenty-four studies involving 16,126 participants evaluated local recurrence for oncoplastic breast-conserving surgery (O-BCS) versus standard breast-conserving surgery (S-BCS). One study evaluated local recurrence (Atallah 2015) but we did not include it in the analysis due to a lack of follow-up time.

For seven of these studies, including 10,043 participants, we were able to extract hazard ratios (HRs). Four of the studies reported local recurrence-free survival and the HR was 0.90 (95% confidence interval (CI) 0.61 to 1.34; I^2 = 0%, P = 0.77; 4 studies, 7600 participants; very-low certainty evidence; Analysis 1.1). We downgraded the certainty of evidence two levels due to high risk of bias due to confounding in most of the studies and one level due to imprecision, as the 95% CI overlaps the line of no effect. Four studies reported local recurrence rates and the HR was 1.33 (95% CI 0.96 to 1.83; I^2 = 0%, P = 0.68; 4 studies, 2443 participants; low-certainty evidence; Analysis 1.1). We downgraded the certainty of evidence by one level due to confounding and one level due to imprecision as the 95% CI overlaps the line of no effect.

To see the impact of the studies where data were not extractable as HRs, we extracted the data as dichotomous event rates and analysed with time points of 1 year (risk ratio (RR) 0.73, 95% CI 0.25 to 2.10; I^2 = 0%, P = 0.84; 3 studies, 637 participants;); 1 to 5 years (RR 0.83, 95% CI 0.66 to 1.04; ; I^2 = 27%, P = 0.16; 15 studies, 9014 participants); and 5-year follow-up (RR 1.07, 95% CI 0.82 to 1.39; I^2 = 26%, P = 0.2; 10 studies, 6672 participants) in Analysis 1.2. We created a funnel plot for these studies, which suggests publication bias (Figure 11).

Figure 11. Funnel plot of comparison: 1 Any O-BCS versus breast-conserving surgery, outcome: 1.3 Local recurrence: O-BCS versus S-BCS.



Disease-free survival

Eight studies involving 6411 participants evaluated disease-free survival for O-BCS versus S-BCS. One study (Lee 2018) evaluated disease-free survival (DFS) but no data were extractable.

For seven of these studies, we were able to extract HRs for DFS and the HR was 1.06 (95% CI 0.89 to 1.26; I^2 = 18%; P = 0.29; 7 studies, 5532 participants; low-certainty evidence; Analysis 1.3). We downgraded the level of evidence by one level due to imprecision as the 95% CI overlaps the line of no effect and one level due to confounding.

To see if extracting the data as dichotomous event rates changed the analysis, we analysed at time points of 1 to 5 years (RR 0.99, 95% CI 0.74 to 1.34; ; I^2 = 0%, P = 0.49; 3 studies, 946 participants), 5 years (RR 1.19, 95% CI 0.99 to 1.44; I^2 = 41%, P = 0.13; 6 studies, 5054 participants) and 10 years (RR 1.21, 95% CI 1.04 to 1.40; I^2 = 0%, P = 0.33; 2 studies, 2163 participants; Analysis 1.4).

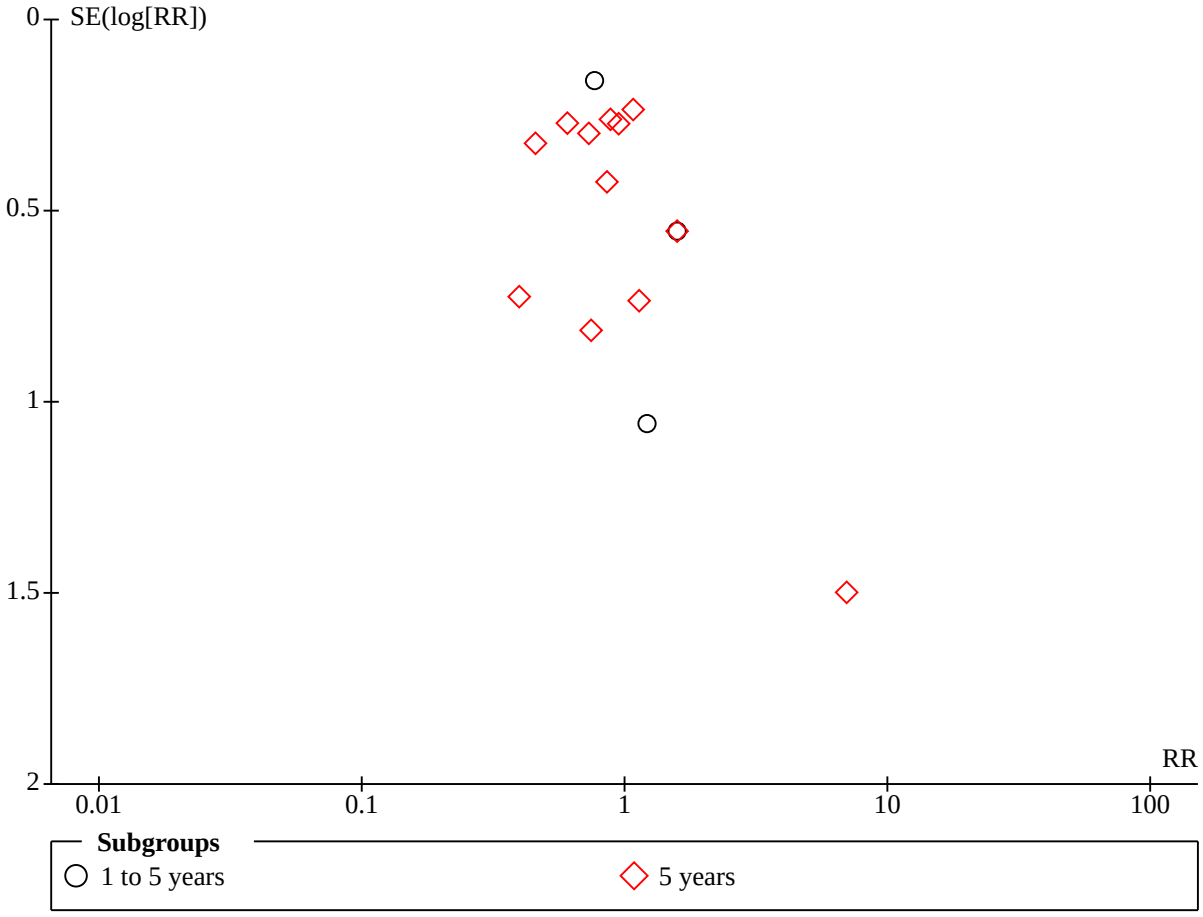
Overall survival

Thirteen studies involving 13,887 participants evaluated overall survival for O-BCS versus S-BCS. One study evaluated overall survival (OS) (Chakravorty 2012), but no data were extractable.

For eight of these studies, we were able to extract HRs for OS and the HR was 1.02 (95% CI 0.82 to 1.28;I^2 = 0%; P = 0.95; 8 studies, 10,078 participants; Analysis 1.5).

To see if extracting the data as dichotomous event rates changed the analysis, we analysed with time points of 1 to 5 years (RR 0.82, 95% CI 0.61 to 1.10; I^2 = 0%, P = 0.42; 3 studies, 4970 participants) and 5 years (RR 0.82, 95% CI 0.67 to 1.00; I^2 = 1%, P = 0.43; 12 studies, 8730 participants; Analysis 1.6). We created a funnel plot for these studies, which suggests publication bias (Figure 12).

Figure 12. Funnel plot of comparison: 1 Any O-BCSversus breast-conserving surgery, outcome: 1.7 Overall survival: O-BCS versus S-BCS.



Secondary outcomes

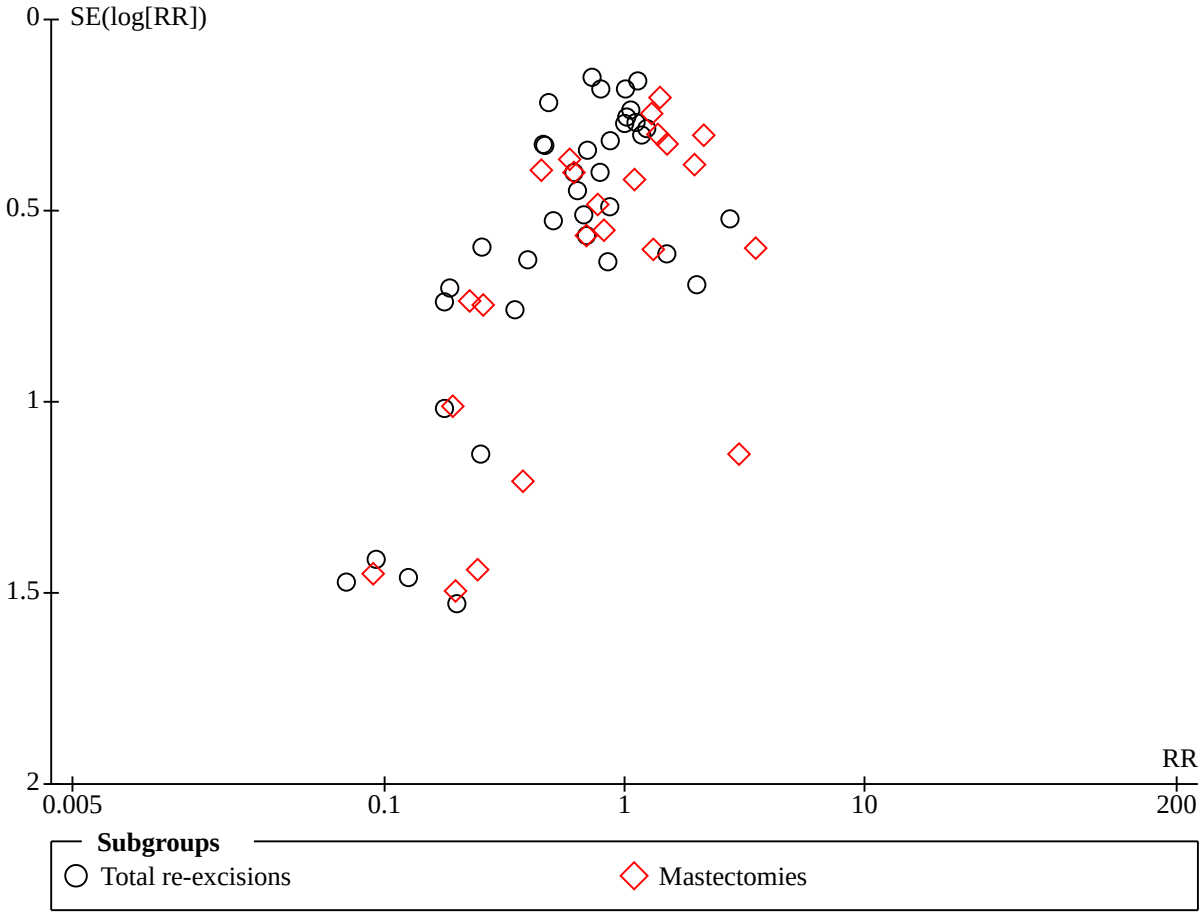
Re-excision rates

Thirty-eight studies evaluated participants that need further surgery due to inadequate cancer resection. Fifteen studies reported the total number of women that underwent any further surgery (Amitai 2018; Atallah 2015; Cassi 2016; Di Micco 2017; Fan 2019; Farooqi 2019; Hamdi 2008; Jiang 2015; Lansu 2014; Matrai 2014; Ojala 2017; Tang 2016; Tenofsky 2014; Vieira 2016; Wong 2017). Eighteen studies evaluated women that eventually had further partial re-excisions or total mastectomy separately (Chakravorty 2012; Chauhan 2016 (1); Chauhan 2016 (2); Dolan 2015; Down 2013; Gicalone 2007 (1); Gicalone 2007 (2); Gicalone 2015; Gulcelik 2013; Keleman 2019; Malhaire 2015; Mansell 2015; Mazouni 2013; Mukhtar 2018; Niinikoski 2019 (2); Palsodittlir 2018; Piper 2016; Wijgman 2017). In four studies (Acea-Nebril 2017; Bali 2018; Crown 2015; Losken 2014) they reported women who initially underwent partial re-excision and some went on to have a mastectomy, the total number of women that underwent any surgery was extracted so as not to duplicate participants in the results. DeLorenzi 2016 (1) reported women who underwent mastectomy only.

Four studies also evaluated re-excision rates but we did not include them in the analysis; we excluded Acea-Nebril 2005, Crown 2019 and Mansell 2017 as they were the publications of subsets of participants (those with sufficient follow-up) of studies already included in the analysis (Acea-Nebril 2017; Crown 2015; Mansell 2015). We excluded Kahn 2013 as they reported re-excisions for the intervention alone.

The RR for O-BCS for needing any further surgery due to inadequate cancer resection compared to S-BCS was 0.76 (95% CI 0.69 to 0.85; I^2 = 43%, P = 0.003; 38 studies, 13,341 participants; very-low certainty; Analysis 1.7). We downgraded the certainty of evidence by one level each for risk of bias due to confounding, inconsistency of the results due to heterogeneity and publication bias. The RR for O-BCS for needing completion mastectomy compared to O-BCS was 1.00 (95% CI 0.85 to 1.18; I^2 = 50%; P = 0.003; 24 studies, 10,863 participants). We created a funnel plot for these studies, which suggests publication bias (Figure 13).

Figure 13. Funnel plot of comparison: 1 Any O-BCS versus breast-conserving surgery, outcome: 1.8 Re-excision rates: O-BCS versus S-BCS.



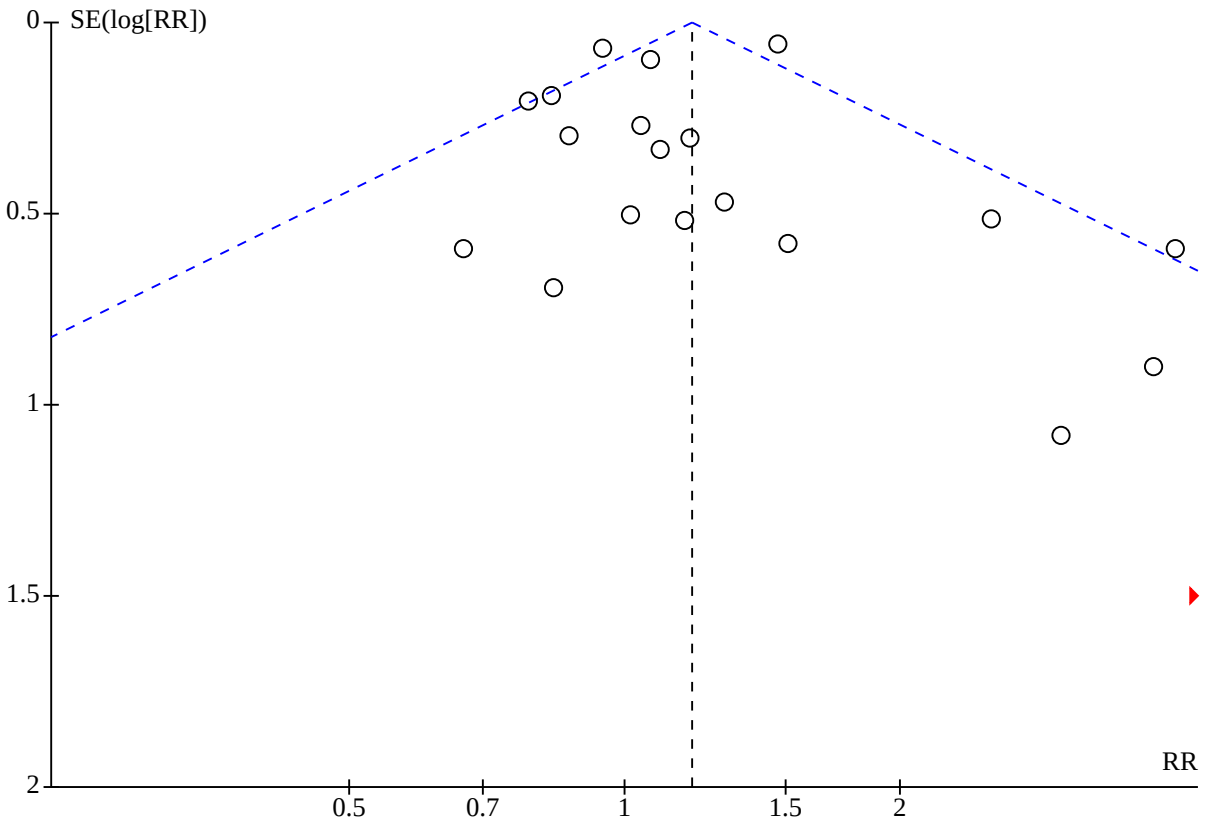
Complications

Thirty-four studies evaluated complications in O-BCS versus S-BCS. Crown 2015 reported complications for the intervention but we excluded it from the analysis as it was the same cohort as Crown 2019.

Amitai 2018 and Nakada 2019 reported fat necrosis rates only. Dolan 2015, Ojala 2017 and Zhou 2019 reported women who required reoperation for complications only. Hilli-Betz 2014 reported postoperative pain only. Six studies (Down 2013; Gicalone 2007 (1); Gicalone 2007 (2); Kimball 2018; Tang 2016; Tenofsky 2014) reported a breakdown of certain complications but not the total rate of complications. DeLorenzi 2016 (1) reported complications for the intervention only.

Twenty-six studies reported a breakdown of the complications - we presented these in Table 13 and Table 14. Twenty of these studies reported the rate of complications; we included these in the meta-analysis. The RR was 1.19 (95% CI 1.10 to 1.27; I^2 = 60%, P = 0.0003; 20 studies, 118,005 participants; very-low certainty evidence; Analysis 1.8). We created a funnel plot for these studies, which suggests publication bias (Figure 14). We downgraded the certainty of evidence by one level each due to risk of bias due to confounding, inconsistency due to heterogeneity of the results, imprecision and publication bias.

Figure 14. Funnel plot of comparison: 1 Any O-BCS versus breast-conserving surgery, outcome: 1.9 Complications: O-BCS versus S-BCS.



Recall rates

Seven studies evaluated recall rates (Amitai 2018; Dolan 2015; Fan 2019; Hu 2019; Losken 2009; Piper 2016; Tenofsky 2014). All studies evaluated the requirement for biopsies and we were able to extract dichotomous data from all but Tenofsky 2014, which reported a mean number of biopsies per woman. The risk ratio was 2.39 (95% CI 1.67 to 3.42 ; I^2 = 0% P = 0.53; 6 studies, 715 participants; low-certainty evidence; Analysis 1.9). We downgraded the certainty of evidence by two levels to low due to serious risk of bias. Details on recall imaging in studies were too methodologically diverse to combine and are summarised in Table 15.

Time to adjuvant therapy

Fourteen studies evaluated time to adjuvant therapy. Twelve studies defined this as from initial surgery to first adjuvant therapy appointment. Of these, three studies reported time to any adjuvant therapy (Keleman 2019; Matrai 2014; Palsodittlir 2018), six reported time to chemotherapy and radiotherapy separately (Acea-Nebril 2017; Borm 2019; Di Micco 2017; Kimball 2018; Morrow 2019; Rose 2019), one reported time to chemotherapy only (Klit 2017), and two reported time to radiotherapy alone (Cassi 2016; Tenofsky 2014). Mazouni 2013 was found to have an unclear definition of when the timing began and Kahn 2013 defined it as from multidisciplinary team meeting, which is an unreliable time point. Therefore, we excluded these studies from the analysis.

Of these, seven studies provided extractable mean and standard deviation (SD) data (Acea-Nebril 2017; Borm 2019; Cassi 2016; Klit 2017; Matrai 2014; Rose 2019; Tenofsky 2014) and contributed to Analysis 1.10. For time to any adjuvant therapy, the mean difference (MD) was 2.60 days (95% CI -5.48 to 10.68; 1 study, 120 participants). For time to adjuvant chemotherapy, the MD was -1.13 days (95% CI -2.55 to 0.29; I^2 = 56%, P = 0.08; 4 studies, 4566 participants). For time to adjuvant radiotherapy, the MD was 9.67 days (95% CI 7.21 to 12.14; I^2 = 54%, P = 0.07; 5 studies, 3720 participants).

The studies that reported data as the median number of days to adjuvant therapy are shown in Table 16.

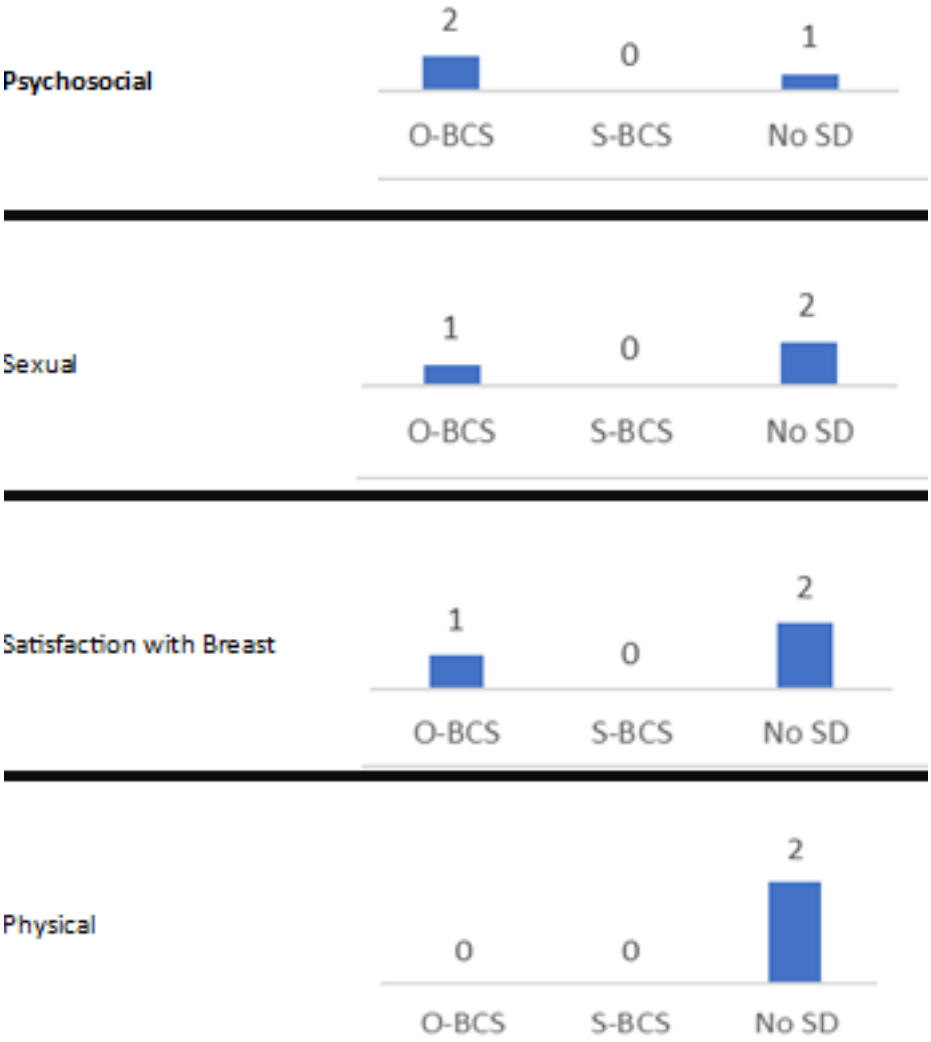
Patient-reported outcome measures

Twenty-three studies, evaluating 5665 participants reported outcomes for O-BCS versus S-BCS.

Five studies (Acea-Nebril 2017; Di Micco 2017; PlaFarnos 2018; Rose 2020; Scheter 2019) used the validated Breast-Q questionnaire (Cohen 2016). Of these Acea-Nebril 2017 and PlaFarnos 2018 gave details about Breast-Q for the intervention only. The comparative studies were synthesised using the vote-counting method per BREAST-Q(Cohen 2016) domain (Figure 15). The outcomes were measured/given in various ways and so we extracted the direction of effect for each Breast-Q component, taking into account whether the study authors found the result significant or not. We

downgraded these results to very low due to the very high risk of bias due to confounding and measurement of outcome.

Figure 15. Harvest plot for vote counting: O-BCS versus S-BCS - PROMs (Breast-Q). Each column represents the number of studies that significantly favoured either O-BCS, S-BCS or found no significant difference for each Breast-Q component.



Three studies used some form of the European Organisation for Research and Treatment of Cancer (EORTC) (Aaronson 1993) Breast questionnaires (Keleman 2019; Lansu 2014; Matrai 2014). Keleman 2019 and Matrai 2014 only reported some scales and we, therefore, deemed these at critical risk of bias.

Two studies used other validated patient-reported outcome measures scales: Ojala 2017 used the Breast Cancer Treatment Outcome Scale (Stanton 2001), and Viega 2010 used the short-form 36 (Garratt 1993) and Rosenberg EPM self-esteem score (Rosenberg 1989). These studies are summarised in Table 17.

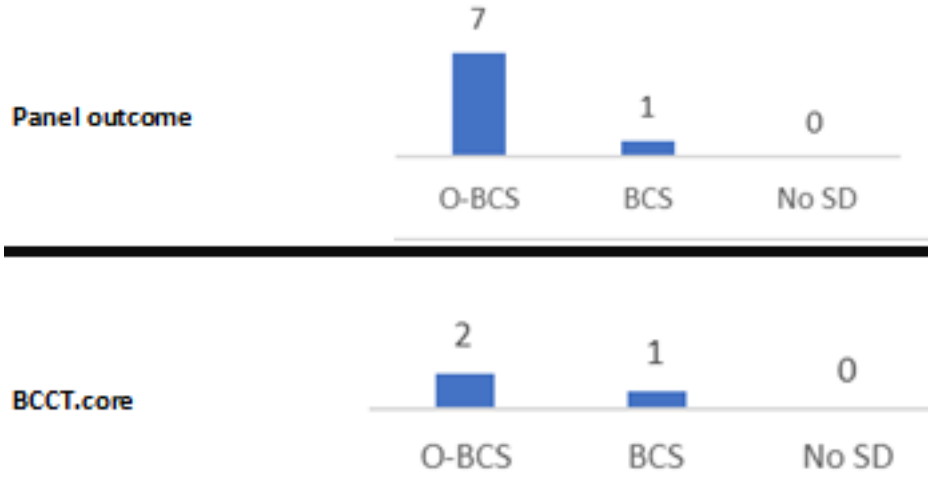
Thirteen studies (Acosta-Marin 2014; Eichler 2013; Gicalone 2007 (2); Hilli-Betz 2014; Jiang 2015; Mazouni 2013; Palsodittlir 2018; Santos 2015; Sherwell-Cabello 2006; Tang 2016; Tenofsky 2014; Viega 2011; Zhou 2019) used self-designed unvalidated questionnaires to assess patient-reported outcome measures. The results of these studies are also summarised in Table 17. We deemed these studies to have too high risk of bias and methodological diversity to synthesise in any form. We downgraded these results to very low due to very high risk of bias and inconsistent results.

Cosmetic evaluation

Nine studies evaluating 1461 participants reported a cosmetic evaluation for O-BCS versus S-BCS (Acosta-Marin 2014; Gicalone 2007 (2); Hilli-Betz 2014; Jiang 2015; Keleman 2019; Lansu 2014; Santos 2015; Scheter 2019; Viega 2011).

Three studies used the computer programme BCCT.core to objectively assess aesthetic outcomes (Hilli-Betz 2014; Lansu 2014; Santos 2015). We synthesised these studies using the vote-counting method (Figure 16).

Figure 16. Harvest plot for vote counting: O-BCS versus S-BCS - cosmetic evaluation. Each column represents the number of studies that significantly favoured either O-BCS, S-BCS or found no significant difference for BCCT.core scores or panel assessment.



Eight studies used an expert panel and self-designed assessment of aesthetic outcome (Acosta-Marin 2014; Gicalone 2007 (1); Hilli-Betz 2014; Keleman 2019; Lansu 2014; Santos 2015; Scheter 2019; Viega 2011) and results are provided in Table 18. These studies have a lot of methodological diversity but we deemed it appropriate to use the vote-counting method to synthesise results in Figure 16.

Comparison 2: O-BCS versus mastectomy without reconstruction

Primary outcomes

Local recurrence

Five studies involving 6682 participants evaluated disease-free survival for O-BCS versus mastectomy alone. It was possible to extract HRs for two studies, both of which reported local recurrence-free survival (Ren 2014; Carter 2016) (HR 0.55; 95% CI 0.34 to 0.91; I^2 = 81%, P = 0.02; 2 studies, 4713 participants; very-low uncertainty evidence Analysis 2.1). We downgraded the evidence by one level for risk of bias due to confounding and two levels due to inconsistency.

To see the impact of the studies where data were not extractable as HRs, we extracted the data as dichotomous event rates and analysed with time points of 1 to 5 years (RR 0.32, 95% CI 0.24 to 0.41; I^2 = 64%, P = 0.1; 2 studies, 4025 participants), 5 years (RR 0.84, 95% CI 0.41 to 1.75; I^2 = 33%, P = 0.22; 2 studies, 942 participants) and 10 years follow-up (RR 6.52, 95% CI 1.42 to 30.06; 1 study, 1193 participants; Analysis 2.2).

Disease-free survival

One study involving 1193 participants evaluated disease-free survival for O-BCS versus mastectomy alone (Nakagomi 2019). It reported significantly better disease-free survival in the intervention group (Analysis 2.3). However, this study was at serious risk of bias due to confounding from clinicopathological factors and uneven distribution of co-interventions. One study evaluated disease-free survival (Lee 2018), but no data were extractable from it. Therefore, no studies reported HR and so were unable to contribute to this analysis; there were insufficient data to make any conclusions.

Overall survival

Three studies involving 5382 participants evaluated overall survival for O-BCS versus mastectomy alone (Carter 2016; Lee 2018; Ren 2014). It was possible to extract HRs for two studies (Carter 2016; Ren 2014). The HR for OS was 0.39 (95% CI 0.30 to 0.51; I^2 = 71%, P = 0.06; 2 studies, 4713 participants).

To see the impact of the studies where data were not extractable as HRs, we extracted the data as dichotomous event rates and analysed with time points of 1 to 5 years (RR 0.30, 95% CI 0.22 to 0.40; 1 study, 3924 participants) and 5-year follow-up (RR 1.71, 95% CI 0.79 to 3.69; I^2 = 88%, P = 0.004; 2 studies, 932 participants) (Analysis 2.5).

Secondary outcomes

Re-excision rates

Re-excisions for oncological margin control are not often performed when a mastectomy is undertaken, therefore this outcome is not relevant for this comparison.

Complications

Four studies evaluated complications in O-BCS versus mastectomy without reconstruction (Acea-Nebril 2005; Carter 2016; Gendy 2003; Potter 2020). The RR of developing a complication compared to mastectomy was 0.75 (95% CI 0.67 to 0.83; I^2 = 61%, P = 0.05; 4 studies, 4839 participants; very-low certainty evidence). We downgraded the certainty of evidence two levels due to risk of bias (confounding) and two levels due to inconsistency of the results.

Acea-Nebril 2005 and Carter 2016 mentioned a breakdown of complications. This is found in Table 19 and Table 20.

Recall rates

Recall biopsy after mastectomy is often not needed, therefore this outcome is not relevant for this comparison.

Time to adjuvant therapy

Four studies including 5093 participants evaluated time to adjuvant therapy for O-BCS versus mastectomy alone. Three studies ((Kahn 2013; Morrow 2019; Potter 2020) defined this as from initial surgery to first adjuvant therapy appointment. Klit 2017 reported time to chemotherapy. Morrow 2019 and Potter 2020 reported time to chemotherapy and radiotherapy separately. Kahn 2013 defined it as from multidisciplinary team meeting, which is an unreliable time point. Potter 2020 defined this as from the final surgery and reported time to chemotherapy and radiotherapy separately. Therefore, we excluded this study from the analysis.

Klit 2017 provided extractable mean and SD data and contributed to Analysis 2.7. This showed no difference between the groups in time to adjuvant therapy, and no conclusions can be made from the results due to the lack of studies reporting outcome data. The studies that reported data as medians and provided P values are shown in Appendix Table 21.

Patient-reported outcome measures

One study compared aesthetic outcomes between O-BCS (49 participants) and mastectomy without reconstruction (58 participants; Gendy 2003). The authors used the Hopwood Body Image score (Hopwood 2001), hospital anxiety and depression scale (Zigmond 1983) and Rosenberg self-esteem scale (Jordan 2020) to assess patient outcomes. They found objectively and subjectively significantly better sensation in the intervention group. Body image based on the Hopwood Body Image score (Hopwood 2001) was significantly better in the intervention group. There was no significant difference in anxiety/depression. We deemed the study to have a serious risk of bias due to confounding, selection bias and measurement and reporting of the outcome. No conclusions can be made due to the lack of studies reporting this outcome for this comparison.

Cosmetic evaluation

One study involving 107 participants, reported this outcome (Gendy 2003). The authors used a self-designed questionnaire given to a panel of five surgeons to mark the breasts' aesthetic outcome out of five. They found O-BCS to be better (median (range) 3.8/5 (1.2 to 5)) than mastectomy alone (2.9 (1 to 4.4)). We deemed the study to have a critical risk of bias due to the measurement of the outcome. No conclusions can be made due to the lack of studies reporting this outcome for this comparison.

Comparison 3: O-BCS versus mastectomy with reconstruction (Mx+R)

Primary outcomes

Local recurrence

Six studies involving 6337 participants evaluated disease-free survival for O-BCS versus mastectomy with reconstruction (Carter 2016; DeLorenzi 2016 (2); Lee 2018; Mansell 2017; Mustonen 2004; Ozmen 2020). It was possible to extract HR for three studies of which one reported local recurrence-free survival compared to the control group Mx+R alone (Carter 2016), and two reported local recurrence compared to the control group Mx with or without reconstruction (DeLorenzi 2016 (2); Mansell 2017; Analysis 3.1). The HR for local recurrence-free survival was 1.37 (95% CI 0.72 to 2.62; 1 study, 3785 participants; very low-certainty evidence) and for local recurrence rate was 1.03 (95% CI 0.75 to 1.42; 2 studies, 1001 participants). We downgraded the evidence by two levels due to high risk of bias due to confounding and one level due to imprecision as the optimal size was not met.

To see the impact of the studies where data were not extractable as HRs, we extracted the data as dichotomous event rates and analysed with time points of 1 to 5 years (RR 1.19, 95% CI 0.87 to 1.64; I^2 = 0%, P = 0.43; 2 studies, 3449 participants), 5 years with the comparator Mx+R alone (RR 0.53, 95% CI 0.19 to 1.44; I^2 = 0%, P = 0.87; 2 studies, 830 participants) and 5 years with the comparator Mx+/-R (RR 1.54, 95% CI 0.74 to 3.21; I^2 = 14%, P = 0.28; 2 studies, 1001 participants) in Analysis 3.2.

Disease-free survival

Three studies involving 1318 participants evaluated disease-free survival for O-BCS versus mastectomy with reconstruction (DeLorenzi 2016 (2); Mansell 2017; Ozmen 2020). Lee 2018 evaluated disease-free survival, but we were not able to extract data. It was possible to extract HRs for all other studies (Analysis 3.3): O-BCS versus Mx+R alone (HR 0.45, 95% CI 0.09 to 2.22; 1 study, 317 participants; very-low certainty evidence); O-BCS versus Mx+/-R (HR 1.03, 95% CI 0.75 to 1.42; 2 studies, 1001 participants). We downgraded the evidence to very low certainty due to the study design, high risk of bias and inconsistency.

To see the impact of the studies if we extracted the data as dichotomous event rates, we analysed that available data at time points of 5 years follow-up with the comparator Mx+R alone (RR 0.74, 95% CI 0.27 to 2.04; 1 study, 317 participants) and 5 years with the comparator Mx+/-R (RR 0.88, 95% CI 0.66 to 1.18; I^2 = 4%, P = 0.31; 2 studies, 1001 participants) in Analysis 3.4.

Overall survival

Five studies involving 5616 participants evaluated overall survival for O-BCS versus mastectomy with reconstruction. It was possible to extract HRs for four studies (Carter 2016; DeLorenzi 2016 (2); Mansell 2017; Ozmen 2020): O-BSC versus Mx+R alone (HR 1.74, 95% CI 1.23 to 2.47; I^2 = 0%, P = 0.5; 2 studies, 4102 participants; Analysis 3.5) and O-BCS versus Mx+/-R (HR 0.65, 95% CI 0.40 to 1.07; I^2 = 85%, P = 0.01; 2 studies, 1001 participants; Analysis 3.5).

To see the impact of the studies where data were not extractable as HRs, we extracted the data as dichotomous event rates and analysed with time points of 1 to 5 years (RR 1.39, 95% CI 0.97 to 1.98; 1 study, 3387 participants), 5-year follow-up with the comparator Mx+R alone (RR 0.52, 95% CI 0.33 to 0.84; I^2 = 0%, P = 0.49; 2 studies, 1001 participants) and 5-year follow-up with the comparator Mx+/-R (RR 0.52, 95% CI 0.33 to 0.84; I^2 = 87%, P = 0.006; 2 studies, 1001 participants) in Analysis 3.6.

Secondary outcomes

Re-excision rates

Re-excisions for oncological margin control are not often performed when a mastectomy is undertaken, therefore this outcome is not relevant for this comparison.

Complications

Six studies evaluated complications in O-BCS versus mastectomy with reconstruction (Carter 2016; Mustonen 2004; Ozmen 2020; Peled 2014; Potter 2020; Tong 2016). The combined RR was 0.49 (95% CI 0.45 to 0.54; I^2 = 87%, P < 0.0001; 5 studies, 4973 participants; very-low certainty evidence) with critical heterogeneity. We downgraded the certainty of evidence to very low due to high risk of bias due to confounding and heterogeneity of the results. All studies mentioned a breakdown of complications and are recorded in Table 19 and Table 20.

Recall rates

Recall after mastectomy is often not needed, therefore this outcome is not relevant for this comparison.

Time to adjuvant therapy

Four studies including 2766 participants evaluated time to adjuvant therapy for O-BCS versus mastectomy plus reconstruction (Kahn 2013; Morrow 2019; Potter 2020; Tong 2016).

Only Morrow 2019 defined this as from initial surgery to first adjuvant therapy appointment and data are reported in Table 21. Potter 2020 defined this as from the final surgery and reported time to chemotherapy and radiotherapy separately. Kahn 2013 defined it as from multidisciplinary team meeting, which is an unreliable time point. Tong 2016 reported how many patients had complications that resulted in a delay to receiving adjuvant therapy. Therefore, we excluded these three studies from the analysis.

Patient-reported outcome measures

Three studies evaluated patient-reported outcomes in O-BCS compared to mastectomy and reconstruction (Hart 2015; Kelsall 2017; Ozmen 2020), and results are presented in Table 22. Studies were all of serious risk of bias due to measurement of outcome. They are too methodologically diverse to synthesise.

Cosmetic evaluation

One study compared aesthetic outcome between O-BCS (242 participants) and mastectomy with reconstruction (75 participants) (Ozmen 2020). Authors used the Japanese Breast Cancer Society Cosmetic Evaluation Scale (Kijima 2011) assessed by a panel. They found O-BCS had a significantly better cosmetic outcome. We deemed the study to have serious risk of bias due to selection bias and measurement of the outcome. No conclusions can be made due to the lack of studies reporting this outcome for this comparison.

Subgroup analysis

For each outcome, we evaluated how many evaluated the subgroups of volume displacement and volume replacement techniques to see if this changed the conclusions. Most of the studies used volume displacement techniques only or did not evaluate the techniques separately.

Comparison 1: O-BCS versus S-BCS

Local recurrence

Of the 24 studies evaluating local recurrence, 15 studies (62.5%) evaluated local recurrence for the volume displacement subgroup (Acea-Nebril 2017; Amitai 2018; Borm 2019; Cassi 2016; Chakravorty 2012; Gulcelik 2013; Keleman 2019; Lee 2018; Losken 2009; Malhaire 2015; Matrai 2014; Mazouni 2013; Niinikoski 2019 (2); Piper 2016; Vieira 2016), and three studies (12.5%) evaluated local recurrence for the volume replacement subgroup (Fan 2019; Hashimoto 2019; Lee 2018).

Out of the seven studies we were able to extract HRs from, three studies were volume displacement (Borm 2019; Niinikoski 2019 (2); Piper 2016), and none were volume replacement. Therefore, insufficient evidence was available to conduct a subgroup analysis.

It was possible to see the impact of volume displacement O-BCS on local recurrence when data were extracted as dichotomous event rates and analysed with time points of 1 to 5 years (RR 0.84, 95% CI 0.51 to 1.39; 8 studies, 2578 participants) and 5-year follow-up (RR 0.90, 95% CI 0.63 to 1.27; 8 studies, 4729 participants) in Analysis 4.1.

Disease-free survival

Of the nine studies that evaluated disease-free survival, five studies (56%) evaluated volume displacement techniques (Acea-Nebril 2017; Borm 2019; Gulcelik 2013; Mazouni 2013; Vieira 2016), whilst none evaluated volume replacement techniques alone. Of these, we were able to extract HRs from four studies (Borm 2019; Gulcelik 2013; Mazouni 2013; Vieira 2016), therefore, insufficient evidence was available to conduct a subgroup analysis.

Overall survival

Of the 13 studies that evaluated overall survival, eight studies (62%) evaluated volume displacement techniques (Acea-Nebril 2017; Borm 2019; Gulcelik 2013; Lee 2018; Mazouni 2013; Niinikoski 2019 (2); Piper 2016; Vieira 2016). One study (8%) evaluated volume replacement techniques (Lee 2018). For three volume displacement studies, we were able to extract HRs (Borm 2019; Mazouni 2013; Vieira 2016), therefore, insufficient evidence was available to conduct a subgroup analysis. We analysed those studies that were extracted as dichotomous data with sufficient data for the 5-year time point (RR (non-event) 0.76, 95% CI 0.59 to 0.98; 7 studies, 4373 participants) in Analysis 4.2. There were insufficient data to comment on volume replacement techniques.

Re-excision rates

Of the 38 studies that evaluated participants that need further surgery due to inadequate cancer resection, 27 studies (69%) evaluated volume displacement techniques (Acea-Nebril 2017; Amitai 2018; Atallah 2015; Bali 2018; Cassi 2016; Chakravorty 2012; Crown 2015; Di Micco 2017; Gicalone 2007 (1); Gicalone 2007 (2); Gicalone 2015; Gulcelik 2013; Hamdi 2008; Jiang 2015; Keleman 2019; Lansu 2014; Losken 2014; Malhaire 2015; Mansell 2015; Matrai 2014; Mazouni 2013; Niinikoski 2019 (2); Ojala 2017; Piper 2016; Tenofsky 2014; Vieira 2016; Wijgman 2017; Wong 2017) and two studies (5%) evaluated volume replacement techniques (Bali 2018; Fan 2019). For total re-excisions in these studies of volume displacement techniques, the RR was 0.77 (95% CI 0.69 to 0.87; 27 studies, 9076 participants) and for total mastectomy, the RR was 1.05 (95% CI 0.86 to 1.28; 16 studies, 7078 participants; Analysis 4.3).

There were insufficient data to comment on volume replacement techniques.

Complications

Of the 33 studies that evaluated complications, 21 studies (64%) evaluated volume displacement techniques (Acea-Nebril 2005; Acea-Nebril 2017; Acosta-Marin 2014; Amitai 2018; Cassi 2016; Crown 2019; Di Micco 2017; Gicalone 2007 (1); Gicalone 2007 (2); Gicalone 2015; Jiang 2015; Keleman 2019; Kimball 2018; Lansu 2014; Matrai 2014; Ojala 2017; PlaFarnos 2018; Scheter 2019; Sherwell-Cabello 2006; Tang 2016; Tenofsky 2014; Wijgman 2017) and three studies (9%) evaluated volume replacement techniques (Nakada 2019; Ozmen 2020; Zhou 2019).

Of the 21 studies that reported the rate of complications included in the meta-analysis, 14 studies evaluated volume displacement techniques (Acea-Nebril 2017; Acosta-Marin 2014; Cassi 2016; Crown 2019; Di Micco 2017; Gicalone 2015; Jiang 2015; Keleman 2019; Lansu 2014; Matrai 2014; PlaFarnos 2018; Scheter 2019; Sherwell-Cabello 2006; Wijgman 2017) and one study evaluated volume replacement techniques (Ozmen 2016). For volume displacement techniques, the RR was 1.03 (95% CI 0.9 to 1.18; 14 studies, 4083 participants; Analysis 4.4). There were insufficient data to comment on volume replacement techniques.

Recall rates

Of the six studies that evaluated recall rates, three studies (50%) evaluated volume displacement techniques (Amitai 2018; Losken 2009; Piper 2016) and two studies (33%) evaluated volume replacement techniques (Fan 2019; Hu 2019). There were insufficient data to comment on both volume displacement and replacement techniques.

Time to adjuvant therapy

Of the seven studies that provided extractable mean and SD data, four of them evaluated volume displacement techniques (Acea-Nebril 2017; Cassi 2016; Matrai 2014; Tenofsky 2014), and none reported volume replacement techniques. There were insufficient data to comment on both volume displacement and replacement techniques.

Patient-reported outcome measures

Of the 24 studies that evaluated patient-reported outcomes, 18 studies (75%) evaluated volume displacement techniques and one study (4%) evaluated volume replacement techniques. Due to the high risk of bias and methodological diversity, it was not possible to conduct a subgroup analysis. The results of each study along with their intervention method are presented in Analysis 1.11 and Table 17.

Cosmetic evaluation

Of the nine studies evaluating cosmetic evaluation, eight studies evaluated volume displacement techniques only (Acosta-Marin 2014; Gicalone 2007 (2); Hilli-Betz 2014; Jiang 2015; Keleman 2019; Lansu 2014; Santos 2015; Scheter 2019). Due to the high risk of bias and methodological diversity it was not possible to conduct a subgroup analysis.

Comparison 2: O-BCS versus mastectomy without reconstruction

Local recurrence

Of the five studies that evaluated local recurrence for O-BCS versus mastectomy alone, four studies (80%) evaluated volume replacement only (Gendy 2003; Lee 2018; Nakagomi 2019; Ren 2014) and one study evaluated volume displacement (Lee 2018). There were insufficient data to comment on both volume displacement and replacement techniques.

Disease-free survival

No studies evaluated volume displacement or replacement alone for disease-free survival.

Overall survival

Of the three studies that evaluated overall survival for O-BCS versus mastectomy alone, two studies (66%) evaluated volume replacement (Lee 2018; Ren 2014) and one study evaluated volume displacement (Lee 2018). There were insufficient data to comment on both volume displacement and replacement techniques.

Complications

Of the four studies that evaluated complications in O-BCS versus mastectomy alone, two studies (50%) evaluated volume displacement techniques (Acea-Nebril 2005; Potter 2020) and one study (25%) evaluated volume replacement techniques (Gendy 2003). There were insufficient data to comment on both volume displacement and replacement techniques.

Time to adjuvant therapy

No studies evaluated any subgroup alone and provided extractable mean and SD data. Morrow 2019 and Potter 2020 both extracted volume displacement only, details of which can be shown in Table 21. There were insufficient data to comment on both volume displacement and replacement techniques.

Patient-reported outcome measures

The one study that compared aesthetic outcome between O-BCS and mastectomy alone analysed volume replacement techniques (Gendy 2003). There were insufficient data for analysis.

Cosmetic evaluation

The one study that compared aesthetic outcome between O-BCS and mastectomy alone analysed volume replacement techniques (Gendy 2003). There were insufficient data for analysis.

Comparison 3: O-BCS versus mastectomy with reconstruction

Local recurrence

Of the six studies that evaluated local recurrence for O-BCS versus mastectomy with reconstruction, three studies (50%) evaluated volume replacement techniques (Lee 2018; Mustonen 2004; Ozmen 2020). There were insufficient data to comment on both volume displacement and replacement techniques.

Disease-free survival

Of the three studies that evaluated disease-free survival for O-BCS versus mastectomy with reconstruction, one study evaluated volume replacement techniques alone (Ozmen 2020); there were no studies for volume displacement techniques. There were insufficient data for analysis.

Overall survival

Of the four studies that provided HR data for overall survival, two studies evaluated volume replacement techniques (Lee 2018; Ozmen 2020). There were insufficient data for analysis.

Complications

Of the five studies that evaluated total complications in O-BCS versus mastectomy with reconstruction, three studies evaluated volume displacement techniques (Peled 2014; Potter 2020; Tong 2016) and one evaluated volume replacement techniques (Ozmen 2020). There were insufficient data to comment on both volume displacement and replacement techniques.

Time to adjuvant therapy

We included one study in this analysis evaluating volume displacement techniques (Morrow 2019; Table 21). There were insufficient data to conduct a subgroup analysis of this outcome.

Patient-reported outcome measures

Three studies evaluated patient-reported outcomes (Hart 2015; Kelsall 2017; Ozmen 2020), and results are summarised in Table 22. Hart 2015 evaluated volume displacement techniques only and Ozmen 2020 evaluated volume replacement techniques only. There were insufficient data to comment on both volume displacement and replacement techniques.

Cosmetic evaluation

The one study comparing aesthetic outcome with mastectomy with reconstruction (Ozmen 2020), evaluated volume replacement techniques only. No conclusions can be made due to the lack of studies reporting this outcome for this comparison.

Sensitivity analysis

It was not possible to conduct a sensitivity analysis of studies at low risk of bias as all studies were viewed with at least a moderate/serious risk of bias.

We used the fixed-effect model and conducted sensitivity analyses for all the comparisons using the random-effects model. Most analyses were robust and did not change the conclusions drawn from the findings except in the following cases.

- Comparison 1: O-BCS versus S-BCS
  - Overall survival (5 years)
    - fixed-effect: 0.79 (0.65 to 0.96)
    - random-effects: 0.82 (0.67 to 1.00)
  - Complication rate
    - fixed-effect: 1.19 (1.10 to 1.27)
    - random-effects: 1.12 (0.94 to1.33)
- Comparison 2: O-BCS versus mastectomy alone
  - Local recurrence HR
    - fixed-effect: 0.55 (0.34 to 0.91)
    - random-effects: 0.87 (0.18 to 4.11)
- Comparison 3: O-BCS versus mastectomy plus reconstruction
  - Overall survival HR
    - fixed-effect 0.39 (0.30 to 0.51)
    - random-effects 0.58 (0.18 to 1.85)
- Subgroup analysis
  - Overall survival
    - fixed-effect 0.76 (0.59 to 0.98)
    - random-effects 0.77 (0.54 to 1.09)

DISCUSSION

Summary of main results

In general, the results were inconclusive as many studies included in the analyses did not account for confounding or were downgraded due to inconsistency or imprecision.

O-BCS versus S-BCS

When comparing O-BCS to S-BCS, there may be little or no difference in local recurrence-free survival, local recurrence rate or disease-free survival based on very-low certainty of evidence. There may be little to no effect on overall survival. O-BCS may reduce the rate of re-excision based on very low-certainty evidence due to the risk of bias from confounding and inconsistent results. This result, however, is plausible as O-BCS allows larger resections. O-BCS may increase the number of women who have at least one complication and this is based on very low-certainty evidence. This result may be due to the novelty of the technique or that it is a more intensive surgical procedure. The evidence from the review suggests that O-BCS may increase the recall to biopsy rate and this may be due to changes in follow-up imaging due to the surgery and mobilisation of the breast. The review suggests that days to adjuvant therapy may be increased, only for time to adjuvant radiotherapy, by the use of O-BCS compared to S-BCS. This may be explained by delays due to complications. The delay to adjuvant radiotherapy is of the order of 7.21 to 12.1 days, which may be clinically significant.

The results were inconclusive as to whether there was a difference in patient-reported outcomes between O-BCS and S-BCS. Little or no difference was found in the overall quality of life measured by the BREAST-Q. However, cosmesis, psychosocial well-being and satisfaction with the breast reported by patients were at times significantly better after O-BCS. The review was inconclusive about the difference in cosmetic evaluation between O-BCS and S-BCS. Two out of three studies reported better BCCT.core scores after O-BCS, whilst one favoured S-BCS. Panel assessments favoured the aesthetic outcome of O-BCS, however, these studies had a critical risk of bias with measurement of outcome methods.

O-BCS versus mastectomy alone

Evidence from two studies suggests O-BCS may increase local recurrence-free survival, but the evidence is very uncertain. No conclusion could be made about disease-free survival as there were data from only one eligible study. O-BCS may reduce complications compared to mastectomy, but the evidence is very uncertain due to the high risk of bias mainly due to confounding. There were insufficient data to draw conclusions on time to adjuvant therapy, patient-reported outcome measures and cosmetic evaluation, as each subgroup was reported in one study only.

O-BCS versus mastectomy with reconstruction

The results of the review found that O-BCS may result in little or no difference in recurrence or disease-free survival when compared to mastectomy with reconstruction. The evidence is very uncertain due to the high risk of bias, inconsistency and imprecision among studies. O-BCS may reduce the complication rate compared to mastectomy plus reconstruction, but the evidence is very uncertain

due to the high risk of bias due to confounding and inconsistency of the results. There were insufficient data to make any conclusions on time to adjuvant therapy, patient-reported outcome measures and cosmetic evaluation as each subgroup was reported in one study only.

Overall completeness and applicability of evidence

In this systematic review, the evidence was incomplete due to a lack of good-quality studies in this area that used appropriate methods to adjust for confounding. Additional research is likely to have an important impact on the estimated effect. Decisions regarding choice of surgical method should be made jointly by the surgeon and patient after extensive information on the risks and benefits is provided. Careful consideration of patients for whom to offer O-BCS is needed.

Strengths of the review

- We compared O-BCS to all other surgical alternatives for breast cancer, which has not been done before.
- Our search strategy was comprehensive where the electronic search included publications of relevant studies irrespective of language. We also conducted a manual search of reference lists of relevant studies and screened trial registries.
- We categorised interventions, comparators and outcomes as per clinical relevance.
- When it was not possible to count the outcome in the main analyses, we presented the results as appendices (for full transparency).
- We analysed subgroups and conducted sensitivity analyses to ensure rigorous data analysis that informed our conclusions.
- At least two or three review authors checked all data extraction and input to minimise errors.
- Our results were assessed carefully with application of the ROBINS-I tool and GRADE criteria for each of the relevant outcomes.

Main limitations

The main limitations of this systematic review are due to the limited strength of the evidence due to methodological deficiencies of the existing studies.

- The evidence in this review came from observational studies (mostly retrospective and of low-methodological quality), subject to important biases which increased the uncertainty of the results and limited the quality of existing evidence.
- It was not possible to calculate the HR for the assessment of survival data for all studies because many studies did not report time-to-event analyses in sufficient detail.
- We assessed the surgical technique performed as a subgroup analysis, but not enough evidence exists on volume replacement techniques.
- The surgical techniques are not standardised in terminology nor methodology.
- This was a systematic review that used aggregated data (in which the subject of analysis was the study) and not a meta-analysis of individual data (in which the subject of analysis is the person or the participant).
- For patient-reported outcome measures and cosmetic evaluation, we used a narrative synthesis or vote counting synthesis. This provides no magnitude of effect nor does it account for the difference in relative study design.

Quality of the evidence

The overall certainty of the evidence was low due to most studies not accounting for confounding variables. There was inconsistency in the body of evidence and in comparisons 2 (O-BCS versus mastectomy) and 3 (O-BCS versus mastectomy with reconstruction), there was a lack of evidence resulting in imprecision. For patient-reported and cosmetic evaluation outcomes, studies did not always use validated or standardised tools, making the risk of bias due to measurement of these outcomes an issue.

Potential biases in the review process

There were several potential biases in the review process. We tried to limit bias in several ways - two or three review authors assessed the eligibility for inclusion and independently assessed the risks of bias. Although the review authors' views varied, we decided to accept the final conclusions after extensive discussion and reaching a consensus. We ensured an expert in oncoplastic surgery was involved at each of these steps.

We accept that carrying out reviews requires a number of subjective judgements, and it is possible that a different review team may have reached different decisions regarding the assessments of eligibility and risks of bias. We acknowledge that the comparisons and outcomes we have focused on are quite broad. Future reviews may be split into multiple reviews to allow narrower analysis. Feedback from readers will serve to improve the next review update.

Agreements and disagreements with other studies or reviews

We found a meta-analysis by Chen 2018 comparing S-BCS versus O-BCS. They found that O-BCS significantly reduced the number of re-excisions. They found that the local and distal recurrence rates were similar in both groups. Both disease-free survival (HR 1.19, 95% CI 0.96 to 1.49; P = 0.112) and overall survival (HR 1.14, 95% CI 0.76 to 1.69; P = 0.527) did not differ significantly between the two groups. These results are similar to our results. They noted clinicopathological differences between the two groups that could have confounded the results and suggested the need for randomising or matching patients in future studies.

De La Cruz 2016 conducted a comprehensive review but did not focus on comparative studies and only evaluated studies for T1-T2 cancers. They reported high rates of overall survival and disease-free survival with low local recurrence, distant recurrence, positive margin rate, re-excision rate, conversion to mastectomy rate and complication rates, thereby confirming the oncologic safety of this procedure in patients with T1–T2 invasive breast cancer. The oncoplastic techniques evaluated were mainly volume displacement (> 50%) but very few details on surgical technique were available.

Losken 2014 conducted a meta-analysis comparing O-BCS to S-BCS (called breast-conserving therapy (BCT) in the paper). They combined data from case series with more than 10 patients. They found that re-excision was more common in the S-BCS alone group (14.6% versus 4%, P < 0.0001), however, completion mastectomy was more common in the oncoplastic group (6.5% versus 3.79%, P <

0.0001). The average follow-up was longer in the S-BCS alone group (64 versus 37 months). Local recurrence was 4% in the oncoplastic group and 7% in the S-BCS alone group. Satisfaction with the aesthetic outcome was significantly higher in the oncoplastic group (89.5% versus 82.9%, P < 0.001). The conclusions are similar to what our review found, however combining case series from different studies is liable to very high risk of bias. Methodological conclusions drawn from this technique are uncertain.

Yiannakopoulou 2016 evaluated 40 studies of which 15 were on volume replacement. The majority of studies were observational studies. The length of follow-up was relatively short; long-term oncological outcome of oncoplastic surgery for breast cancer is not adequately investigated. They recommended further research efforts should focus on level 1 evidence on oncological outcome of oncoplastic surgery

Yoon 2016 conducted a comprehensive literature review but again did not focus on comparative studies and looked at radiotherapy with O-BCS. Haloua 2013 conducted a literature review but only included poorly designed and underpowered studies.

We acknowledge a recent publication by Rocco 2021, whereby a group of international breast specialists concluded there was low level evidence for outcomes after O-BCS, a lack of randomised data and absence of standardised tools for patient-reported outcome measures.

AUTHORS' CONCLUSIONS

Implications for practice

The evidence is very uncertain regarding oncological outcomes following O-BCS compared to S-BCS, though O-BCS has not been shown to be inferior. O-BCS may result in less need for a second re-excision surgery but may result in more complications and greater recall rate than S-BCS. It seems that O-BCS may give better patient satisfaction and surgeon rating for the look of the breast, but the evidence for this is of poor quality, and due to lack of numerical data, it was not possible to pool the results of different studies. It seems O-BCS results in fewer complications compared with surgeries involving mastectomy.

No firm conclusions can be made to inform policymakers, health professionals or patients based on this review. The surgical decision should be made jointly between clinician and patient after appropriate discussion about the risks and benefits of O-BCS personalised to the patient, taking into account clinicopathological factors.

Implications for research

This review highlighted the deficiency of well-conducted studies to evaluate efficacy, safety and patient-reported outcomes following O-BCS.

Well-designed cohort studies are still needed and randomised controlled trial (RCT) data should be sought. RCTs may not be feasible due to importance of patient choice in surgeries, especially when the motivation for choosing O-BCS may be patient satisfaction and cosmetic outcomes.

For planning and development of these studies, we suggest the following.

- Describe and adjust for all potential confounders (baseline patient characteristics, such as age and comorbidities and tumour characteristics).
- Define surgical techniques clearly and ensure surgeries are conducted by experienced surgeons and centres.
- Volume replacement and volume displacement techniques should be assessed separately - individual techniques should be noted.
- Use standardised criteria, defining endpoints and follow-up for objective outcomes.
- Use validated tools to assess patient-reported outcomes.
- Use objective tools or blinding large panels to assess aesthetic outcomes.
- Minimum 5-year follow-up is needed to allow conclusions on oncological safety to be made.
- Studies should adjust appropriately for follow-up time in the analysis of outcomes using survival analysis methods.
- A standardised categorisation of oncoplastic surgeries is needed to encompass the long list of techniques, often with overlapping but different terminology.
- Researching outcomes relevant to health economics, such as quality-adjusted life years.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Acea-Nebril 2005

Study characteristics	
Methods	Prospective single-centre cohort March 2003 to Dec 2004 Complejo Hospitalario Universitario Juan Canalejo. La Coruña. España 160 participants
Participants	**Inclusion**: women with invasive/in situ breast cancer with tumours less than 3 cm in diameter (T1-2) OR treated with neoadjuvant chemotherapy and reduced to a size less than 3 cm, axillary clinical stages N0-N1a-b **Exclusion**: women with breast cancer with T3-4 tumours, impossibility of postoperative radiotherapy (previous radiotherapy, scleroderma, collagen diseases, pregnant women etc.), small breast size, impossibility of disease-free margins or lack of compression technique by the patient or demand for a commitment to result.
Interventions	**Intervention**: volume displacement - vertical/lower pedicle/single limb vertical/horizontal/rotational/lateral mammoplasty, (n = 50) **Control**: 1) standard BCS, (n = 57); 2) mastectomy, (n = 53)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Re-excisions • Complications **Other outcomes**:

Acea-Nebril 2005 *(Continued)*

- Operative Time
- Length of Stay

Notes	No disclosures/funding declared

Acea-Nebril 2017

Study characteristics	
Methods	Retrospective single centre cohort Jan 2000 to June 2016 Complejo Hospitalario Universitario a Coruña, Spain 801 participants
Participants	**Inclusion**: women with invasive breast carcinoma/ductal carcinoma in situ (DCIS) undergoing breast conserving surgery **Exclusion**: patients who underwent mastectomy as the primary intervention, patients that did not give their consent to participate in the study
Interventions	**Intervention**: volume displacement - reduction mammoplasty, (n = 170) **Control:** BCS - wide local excision, (n = 631)
Outcomes	**Primary outcomes** (median 84 +/- 55.6 months): • Local recurrence • Disease-free survival • Overall survival **Secondary outcomes**: • Re-exicisions • Complications • PROMs (Breast-Q) • Time to adjuvant therapy **Other outcomes**: • Operative time
Notes	Some overlap with Acea-Nebril 2005 in patient group but different controls No funding/disclosures declared

Acosta-Marin 2014

Study characteristics	
Methods	Prospective single-centre cohort Jan 2011 to Oct 2012

Acosta-Marin 2014 *(Continued)*

	Breast Surgery Department, Centro Clinico de Estereotaxia—CECLINES, Caracas, Venezuela 107 participants
Participants	**Inclusion**: women with early breast cancer undergoing either standard BCS or level II OPS and with 12-month follow-up **Exclusion**: • Patients who had mastectomy • Patient who had a previous breast surgery due to breast cancer • Patients with insufficient information/did not reach at least 12 months of follow-up
Interventions	**Intervention**: volume displacement - round block (40.3%), inverted-T (26.8%), vertical scar (15.3%), racquet (7.6%), horizontal (5.7%), lower inner-quadrant mammoplasty (3.8%), (n = 52) **Control**: standard BCS, (n = 55)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Complications • PROMs (Self-designed) • Cosmetic assessment (4-person panel)
Notes	No disclosures/funding declared

Amitai 2018

Study characteristics	
Methods	Retrospective single=centre cohort 2009 to 2014 Tel Aviv University, Israel 335 participants
Participants	**Inclusion**: women with breast cancer undergoing either immediate OPS and those undergoing lumpectomy in the same week (the first 4 lumpectomies after an OPS that week) **Exclusion**: simple local tissue rearrangement. Women undergoing mastectomy eventually for positive lumpectomy margins
Interventions	**Intervention**: volume displacement - breast reduction (64%), mastopexy (30%) augmentation (6%), (n = 67) **Control**: BCS: lumpectomy, (n = 268)
Outcomes	**Primary outcomes**: • Local recurrence **Secondary outcomes**: • Re-excisions

Amitai 2018 *(Continued)*

	• Recall rates • Complications **Other outcomes**: • Follow-up imaging findings
Notes	No disclosures/funding disclosed Authors were contacted requesting full dataset for primary outcomes

Angarita 2020

Study characteristics	
Methods	Retrospective database review cohort 2005 to 2016 American College of Surgeons National Surgical Quality Improvement Program, USA 109,487 participants
Participants	**Inclusion**: adult women with an International Classification of Diseases Ninth Revision (ICD-9) code of in situ (ICD-9 code 233.0) or invasive breast cancer (ICD-9 code 174.0–9) who underwent a traditional lumpectomy or OPS (soft tissue transfer, mastopexy, or mammoplasty) **Exclusion**: male patients, metastatic tumours, and concurrent surgery (non-breast and bilateral procedures)
Interventions	**Intervention**: both VD and VR - adjacent tissue transfer < 10 cm (4.7%), 10 cm^2 to 30 cm^2 (16.2%), 30 cm^2 to60 cm^2 (34.9%), mastopexy (23.7%), reduction (20.5%), (n = 9126) **Control**: BCS: lumpectomy, (n = 100,361)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Complications **Other outcomes**: • Operative time • Length of Stay
Notes	No disclosures/funding declared

Atallah 2015

Study characteristics	
Methods	Retrospective single-centre cohort study Hotel-Diey de France, Beirut, France

Atallah 2015 *(Continued)*

	2005-2013 280 participants
Participants	**Inclusion**: women with early breast cancer who underwent breast conserving surgery
Interventions	**Intervention**: volume displacement - OPS stage 1 and 2, (n = 193) **Control**: wide local excision, (n = 87)
Outcomes	**Primary outcomes:** • Local recurrence (no follow-up time therefore excluded from analysis) **Secondary outcomes**: • Re-excisions **Other outcomes**: • Margins
Notes	Conference abstract No disclosures/funding declared

Bali 2018

Study characteristics	
Methods	Retrospective single-centre and surgeon cohort Apr 2014 to Sep 2016 University of Cambridge, England, UK 201 participants
Participants	**Inclusion**: women with breast cancer operated on by a single oncoplastic breast surgeon **Exclusion**: patients undergoing mastectomy
Interventions	**Intervention**: volume displacement and volume replacement (analysed separately) - mammoplasty (19), chest wall perforator flaps (16), (n = 35) **Control**: BCS: wide local excision, (n = 166)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Re-excisions **Other outcomes**: • Margins • Length of stay

Bali 2018 *(Continued)*

Notes	No disclosures/funding declared

Borm 2019

Study characteristics	
Methods	Retrospective single-centre cohort January 2000 to December 2005 Klinikum rechts der Isar, Munich, Germany 965 participants
Participants	**Inclusion**: women with breast cancer undergoing BCS with no distant metastases at the time of diagnosis **Exclusion**: patients with other malignancies in addition to breast cancer
Interventions	**Intervention**: volume displacement - rotation flap (265), reduction mammoplasty (23). 1 patient received a volume replacement flap (thoracoepigastric flap), (n = 288) **Control**: Standard BCS, (n = 677)
Outcomes	**Primary outcomes** (median 67 months (IQR 6 = 51-84)): • Local recurrence • Disease free survival • Overall survival **Secondary outcomes**: • Time to adjuvant therapy **Other outcomes**: • Distant and regional recurrence
Notes	No disclosures/funding declared

Carter 2016

Study characteristics	
Methods	Retrospective single-centre cohort January 2007 to December 2014 University of Texas MD Anderson Cancer Center, Houston, Texas, USA 10,407 participants
Participants	**Inclusion**: women who underwent operations for in situ or invasive breast cancer (Tis–T4)

Carter 2016 *(Continued)*

	Exclusion: male patients, surgeries performed for benign lesions or prophylaxis, lymph node only procedures, patients who did not consent to data collection
Interventions	**Intervention**: both VD and VR - adjacent tissue transfer/rearrangement < 10 cm2/10 to 30 cm2/30 to 60 cm2/other techniques, (n = 1177) **Control**: 1) standard BCS, (n = 3359) 2) mastectomy, (n = 3263) 3) mastectomy +reconstruction. (n = 2608)
Outcomes	**Primary outcomes** (median 40.8 months (range: 0 - 109.2): • Local recurrence free survival • Overall survival **Secondary outcomes**: • Complications **Other outcomes**: • Margins
Notes	Funded by the Cancer Center Support Grant No disclosures declared Authors were contacted for further outcomes - none available but authors confirmed 'recurrence free survival refers to local recurrence'

Cassi 2016

Study characteristics	
Methods	Retrospective single-centre cohort January 2012 to December 2014 University of Rome, Tor Vergata, Rome, Italy 215 participants
Participants	**Inclusion:** adult women with breast cancer undergoing breast conserving surgery
Interventions	**Intervention**: volume displacement - therapeutic mammoplasty and adjacent tissue transfer following lumpectomy, (n = 61) **Control**: BCS: lumpectomy, (n = 154)
Outcomes	**Primary outcomes** (median (I)44.8/(C)43.3 months): • Local recurrence **Secondary outcomes**: • Re-excisions • Complications • Time to adjuvant therapy
Notes	No disclosures/funding declared

Cassi 2016 *(Continued)*

	Authors declared they are employees of the University Hospital Authors were contacted requesting full dataset for primary outcomes

Chakravorty 2012

Study characteristics	
Methods	Retrospective single-centre and surgeon cohort June 2003 to February 2010 Royal Marsden Hospital, London, UK
Participants	**Inclusion:** women with breast cancer undergoing either OPS (consecutive patients of mainly one consultant) or standard BCS by the same surgeon
Interventions	**Intervention**: volume displacement - wise-pattern, comma & lateral (77), Grisotti (51) and Benelli (round block) (22) procedures, (n = 150) **Control**: standard BCS, (n = 440)
Outcomes	**Primary outcomes**: • Local recurrence (Median (I) 59 months (range 26-83), (C) 61 months (range 27-90) **Secondary outcomes**: • Re-excisions **Other outcomes**: • Distant recurrence
Notes	No disclosures/funding declared Authors were contacted requesting full dataset for primary outcomes

Chauhan 2016 (1)

Study characteristics	
Methods	Prospective single centre January 2012 to December 2014 Command Hospital, Lucknow (tertiary care teaching hospital), India 100 participants
Participants	**Inclusion**: women with locally advanced breast cancer (including stage III A, stage III B and stage IIB) and receiving doxorubicin based neoadjuvant chemotherapy, adjuvant chemotherapy and adjuvant radiotherapy **Exclusion**: patients with extensive peau d orange, extensive skin involvement(infiltration or ulceration), chest wall involvement or metastatic disease
Interventions	**Intervention**: volume displacement and replacement (analysed together) -

Chauhan 2016 (1) *(Continued)*

	VD: periareolar, superior and inferior pedicle techniques, quadrantectomy with glandular remodeling, and dermoglandular flaps, VR: (mini LD myofascial or myocutaneous flap) (n = 57) **Control**: BCS: lumpectomy or quadrantectomy, (n = 43)
Outcomes	**Primary outcomes**: • Local recurrence (Median: (I) 18 months (range 6-30) (C) 34 months (14-44)) **Secondary outcomes**: • Re-excisions • Complications **Other outcomes**: • Margins
Notes	No disclosures/funding declared Differs from Chauhan (2) in participant selection Authors were contacted requesting full dataset for primary outcomes

Chauhan 2016 (2)

Study characteristics	
Methods	Prospective single-centre cohort January 2012 to December 2014 Tertiary teaching hospital, India 79 participants
Participants	**Inclusion**: women with early breast cancer (T1/T2, N0/N1) undergoing breast conserving surgery **Exclusion**: • patients unwilling for BCS • patients of locally advanced breast cancers who had undergone neoadjuvant chemotherapy • patients unwilling to follow-up at this centre • patients who had undergone conventional BCS previously at outside centre and whose medical records were incomplete • patients with extensive peau d'orange or extensive skin involvement (infiltration or ulceration) or chest wall involvement/multicentric disease
Interventions	**Intervention**: volume displacement and replacement (analysed together) - lateral mammaplasty (9), medial mammaplasty (4), radial excision (5), grissotis flap (2) superior ped (5) inferior pedicl (4) donut (3) Mini LD (1), (n = 33) **Control**: BCS: margin or a formal quadrantectomy, (n = 46)
Outcomes	**Primary outcomes**:

Chauhan 2016 (2) *(Continued)*

	• Local recurrence (median: (I) 18 months (range 6-30) (C) 38 months (12-64))
	Secondary outcomes:
	• Re-excisions • Complications
	Other outcomes:
	• Margins
Notes	No disclosures/funding declared
	Differs from Chauhan (1) in participant selection
	Authors were contacted requesting full dataset for primary outcomes

Crown 2015

Study characteristics	
Methods	Retrospective single-centre cohort
	January 2009 to December 2010 for control
	January 2013 to September 2014 for intervention
	Virgina Mason Medical Center, Seattle, USA
Participants	**Inclusion**: women with invasive or non-invasive breast carcinoma undergoing breast conserving surgery
	Exclusion: patients who underwent breast surgery between January 2013 and September 2014 performed by surgeons who did not perform OPS
Interventions	**Intervention**: volume displacement - radial ellipse with adjacent tissue transfer (31%), racquet mammoplasty (22%), mastopexy (21%), reduction mammoplasty (15%), neoareolar reduction (3%), and other techniques (8%)
	Control: BCS
Outcomes	**Primary outcomes**:
	• No outcomes of interest
	Secondary outcomes:
	• Re-excisions
Notes	No disclosures
	Study supported by Benaroya Research Institute at VMC
	Same participant group as Crown 2019 but greater n as did not need patient follow-up data to be included in the study

Crown 2019

Study characteristics	
Methods	Retrospective single-centre cohort January 2009 to December 2010 for control January 2013 to July 2015 for intervention Virgina Mason Medical Center, Seattle, USA 561 participants
Participants	**Inclusion**: women with breast cancer undergoing breast conserving surgery with adequate follow up and information on complications **Exclusion**: patients treated with OPS between January 2011 and December 2012 were excluded from the study to allow for the learning period needed during the adoption of new surgical techniques.
Interventions	**Intervention**: volume displacement - mammoplasty (18%), mastopexy (23%), racquet mammoplasty (26%), (n = 288) **Control**: standard BCS, (n = 273)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Re-excisions - extracted from Crown 2015 as this had a greater number of patients therefore this is a duplicate patient group • Complications
Notes	No disclosures/funding declared Same as Crown 2015 but have had chart review for all patients, therefore, can extract complications from this study

DeLorenzi 2016 (1)

Study characteristics	
Methods	Retrospective matched multicentre database review cohort 2000 to 2008 European Institute of Oncology (IEO) Breast Cancer Institutional Database 1362 participants
Participants	**Inclusion**: patients with invasive breast cancer undergoing breast conserving surgery and radiotherapy **Exclusion**: patients presenting with secondary tumours or local relapses, bilateral tumours, patients that received neoadjuvant chemotherapy
Interventions	**Intervention**: volume displacement and volume replacement (analysed together) - (n = 454) VR: glandular flaps (33.8%), fasciocutaneous flap (3.3%), myocutaneous muscular flap (1.1%), implants (5.9%)

DeLorenzi 2016 (1) *(Continued)*

	VD: mastopexy (28.5%) round-block approach (14.5%), superior pedicled reduction mammoplasty (2.4%), inferior pedicled reduction mammoplasty (7.7%), other procedures (2.8%) **Control**: standard BCS, (n = 908)
Outcomes	**Primary outcomes** (median 84 months): • Local recurrence • Disease-free survival • Overall survival **Secondary outcomes**: • Re-excisions • Complications **Other outcomes**: • Distant recurrence
Notes	No disclosures/funding declared Different control to DeLorenzi 2016 (2)

DeLorenzi 2016 (2)

Study characteristics	
Methods	Retrospective matched multicentre database review cohort 2000 - 2008 European Institute of Oncology (IEO) Breast Cancer Institutional Database 579 participants
Participants	**Inclusion**: women with breast cancer with tumours larger than 2 cm (T2) undergoing OPS or mastectomy and reconstruction **Exclusion**: • Patients who have received intraoperative radiotherapy with electrons (ELIOT) to the tumour bed only or as a boost • Patients presenting with secondary tumours or local relapses, bilateral tumours, or those who have received neoadjuvant chemotherapy
Interventions	**Intervention**: volume displacement and replacement (analysed together): (n = 193) VR: glandular flaps (59.6 %), a fasciocutaneous flap (1.5 %) myocutaneous or muscular flap in 2 patients (1 %), implants (4.1 %) VD: mastopexy (18.1%), a round-block approach (1.5 %), a superior pedicled reduction mammoplasty (2.1 %), an inferior pedicled reduction mammoplasty (7.7 %), other procedures were performed in the remaining 4 patients (4.1 %) **Control**: nipple areola-sparing mastectomies (41.7 %), skin-sparing mastectomies, (58.3 %) 91% immediate postmastectomy reconstruction (definitive silicone implants (273 patients), temporary expanders (74 patients), and muscular flaps (4 cases)), (n = 386)
Outcomes	**Primary outcomes** (median 88.8 months):

DeLorenzi 2016 (2) *(Continued)*

- Local recurrence
- Disease-free survival
- Overall survival

Secondary outcomes:

- No outcomes of interest

Other outcomes:

- Distant recurrence

Notes	No disclosures/funding declared Different control to DeLorenzi 2016 (1)

DeLorenzi 2018

Study characteristics	
Methods	Retrospective multicentre database review cohort European Institute of Oncology (IEO) Breast Cancer Institutional Database 2000 to 2008 419 participants
Participants	**Inclusion**: patients with DCIS breast cancer who underwent breast conserving surgery (monolateral, bi-lateral procedures) followed by adjuvant radiation **Exclusion**: patients presenting with secondary tumours or local relapses, patients requiring re-excision or completion mastectomy for positive margins
Interventions	**Intervention**: both VD and VR: no breakdown given, (n = 44) **Control**: standard BCS (n = 375)
Outcomes	**Primary outcomes** (median follow-up (I) 92.4months (C) 110.4 months): • Local recurrence • Disease-free survival • Overall survival **Secondary outcomes**: • No outcomes of interest **Other outcomes**: • Distant recurrence • Margins
Notes	No disclosures/funding declared Different participants to DeLorenzi 2016 (1)

Di Micco 2017

Study characteristics	
Methods	Prospective single-centre cohort June 2009 to November 2014 Royal Marsden Hospital, London, UK 157 participants
Participants	**Inclusion**: large-breasted women with early breast cancer (tumours < 3 cm) undergoing bilateral reduction mammoplasty or unilateral BCS **Exclusion**: patients who did not undergo radiotherapy, patients who had bilateral or multicentric cancer, patients who went on to have a mastectomy for involved margins, developed distant disease or were lost to follow-up were excluded from the evaluation of patient satisfaction
Interventions	**Intervention**: volume displacement - bilateral reduction mammoplasty, (n = 70) **Control**: standard BCS, (n = 87)
Outcomes	**Primary outcomes:** • No outcomes of interest **Secondary outcomes:** • Re-excisions • Complications • PROMs (BREAST-Q) • Time to adjuvant therapy **Other outcomes:** • Margins • Length of stay
Notes	No disclosures/funding declared

Dolan 2015

Study characteristics	
Methods	Retrospective multicentre (2) cohort May 2009 to December 2011 Victoria Infirmary, Glasgow and Western Infirmary Glasgow, UK 187 participants
Participants	**Inclusion**: women with breast cancer undergoing breast conserving surgery **Exclusion**: patients requiring completion mastectomy for incomplete margins after breast conservation. 1 patient from the OBCS group who had a Grisotti flap for squamous cell carcinoma on her nipple requiring no follow-up imaging was also excluded. The data for 2 further patients who died within the 2-year follow-up period (1 with breast cancer-related death) were omitted from the WLE group.

Dolan 2015 *(Continued)*

Interventions	**Intervention**: volume displacement and replacement (analysed together) (n = 71) VD: benelli (12), wise pattern (44), melon slice (1), le-jour (1), tennis-racquet: (3) VR: TEF (6) , T-DAP (1), matrix rotation (3) **Contol**: BCS: wide local excision, (n = 116)
Outcomes	**Primary outcomes:** • No outcomes of interest **Secondary outcomes:** • Re-excisions • Complications • Recall rates **Other outcomes:** • Margins
Notes	No disclosures/funding declared

Down 2013

Study characteristics	
Methods	Retrospective single surgeon cohort July 2006 to April 2010 Norfolk and Norwich University Hospital, Norfolk, United Kingdom 158 participants
Participants	**Inclusion**: patients with early invasive breast cancer/DCIS requiring breast conserving surgery **Exclusion**: patients requiring mastectomy
Interventions	**Intervention**: volume displacement and replacement, (n = 37) - therapeutic mammoplasties (18), sub-axillary fat pad rotation mammoplasties (14), thoracoepigastric flaps (4), central flap (1) **Control**: BCS: wide local excision, (n = 121)
Outcomes	**Primary outcomes**: • Local recurrence (median (I) 29.3 months (C) 22.1 months) **Secondary outcomes**: • Re-excisions • Complications **Other outcomes**: • Margins
Notes	No disclosures/funding declared

Down 2013 *(Continued)*

	Authors were contacted requesting full dataset for primary outcomes

Eichler 2013

Study characteristics	
Methods	Retrospective single-centre study 2007 University of Cologne, Germany 143 participants
Participants	**Inclusion**: women with breast cancer undergoing breast conserving surgery
Interventions	**Intervention**: volume displacement - mastopexy (n = 72) Control: BCS: lumpectomy (n = 71)
Outcomes	**Primary outcomes:** • No outcomes of interest **Secondary outcomes:** • PROMs (self-designed questionnaire) **Other outcomes:** • Margins
Notes	No disclosures/funding declared

Fan 2019

Study characteristics	
Methods	Retrospective single-centre matched cohort May 2013 to December 2016 Yonsei University College of Medicine, Seoul, Korea
Participants	**Inclusion**: patients with breast cancer undergoing mini latissimus dorsi flap and a matched control group of breast conserving surgery
Interventions	**Intervention**: volume replacement - Mini-LD flap, (n = 29) Control: BCS: partial mastectomy, (n = 29)
Outcomes	**Primary outcomes**: • Local recurrence (median (I) 44.6 (13.1) months (C) 44.2 (10) months) **Secondary outcomes**: • Re-excisions

Fan 2019 *(Continued)*

	• Recall rates
Notes	No disclosures/funding declared Authors were contacted requesting full dataset for primary outcomes

Farooqi 2019

Study characteristics	
Methods	Retrospective single-centre cohort Aga Khan University Hospital, Karachi, Pakistan August 2016 to 2018 257 participants
Participants	**Inclusion**: women with early breast cancer (stages 1-3 and DCIS) who underwent breast conserving surgery
Interventions	**Intervention**: unclear whether volume displacement or replacement, (n = 146) **Control**: standard breast conserving surgery, (n = 111)
Outcomes	**Primary outcomes**: • No primary outcomes of interest **Secondary outcomes**: • Re-excisions **Other outcomes**: • Margins
Notes	Conference abstract No disclosures/funding declared

Gendy 2003

Study characteristics	
Methods	Prospective single-centre cohort Intervention: 1991 to 1999 Control: 1994 to 1999 Breast Unit, Royal Hampshire County Hospital, Winchester, UK 106 participants
Participants	**Inclusion**: all contactable disease-free patients who underwent latissimus dorsi mini-flap reconstruction (1991 to 1999) and standard segmental mastectomy (1994 to 1999)

Gendy 2003 *(Continued)*

	Exclusion: patients who did not consent and complete questionnaire
Interventions	**Intervention**: volume replacement - latissimus dorsi miniflap, (n = 49 out of 89 contacted) **Control**: skin sparing mastectomy, (n = 57)
Outcomes	**Primary outcomes**: • Local recurrence (median (I) 53 months (C) 34 months) **Secondary outcomes**: • Complications • PROMs (Hopwood Body Image score, Hospital anxiety and depression scale, Rosenberg self-esteem scale) • Cosmetic evaluation (self-designed, 5 person panel)
Notes	No disclosures/funding declared Authors were contacted requesting full dataset for primary outcomes Author RR

Gicalone 2007 (1)

Study characteristics	
Methods	Prospective single-centre cohort January 2004 to May 2005 University Hospital of Montpellier, France 74 participants
Participants	**Inclusion criteria**: women with breast cancer with tumours > 15 mm undergoing surgical treatment **Exclusion criteria**: • women with tumours < 15 mm (84) • insufficient breast ptosis or volume (114) • inflammatory carcinomas (46) • locally advanced tumours with gross lymph node involvement (15) • local failure of previous conservative treatment (15) • metastatic disease (12) • needed planned mastectomies (25)
Interventions	**Intervention**: volume displacement - inverted-T procedure (5), round-block technique (26), (n = 31) **Control**: BCS: quadrantectomy, (n = 43)
Outcomes	**Primary outcomes**: • No outcomes of interest • Secondary outcomes: • Re-excisions • Complications

Gicalone 2007 (1) *(Continued)*

	Other outcomes: • Margins • Operative time • Length of stay
Notes	No disclosures/funding declared Different to Giacalone 2007 (2) and Gicalone 2015 as has different intervention

Gicalone 2007 (2)

Study characteristics	
Methods	Prospective single centre January 2004 to May 2005 University Hospital of Montpellier, France 127 participants
Participants	**Inclusion**: women with breast cancer with tumours >2cm **Exclusion**: • Inflammatory carcinomas (4) • Locally advanced tumours with gross lymph node involvement (15) • Local failure of previous conservative treatment (15) • Metastatic disease (12)
Interventions	**Intervention**: VD-Donut Mastoplexy (n = 39) **Control**: BCS: standard lumpectomy without concomitant mammoplasty (n = 88)
Outcomes	**Primary outcomes**: • No outcomes of interest **Seondary outcomes**: • Re-excisions • Complications • PROMs • Cosmetic evaluation (self-designed, panel: 1 surgeon, 1 oncologist) **Other outcomes**: • Margins • Operative time • Length of stay
Notes	No disclosures/funding declared Different to Gicalone 2007 (1) and Gicalone 2015 as has different intervention

Gicalone 2015

Study characteristics	
Methods	Prospective single-centre cohort September 2003 to September 2004 University Hospital of Montpellier, France 99 participants
Participants	**Inclusion**: women with breast cancer whose breast size and/or ptosis, made it possible to consider either conventional surgical treatment or oncoplastic surgery as a first-line treatment **Exclusion**: • Inflammatory carcinomas (4) • Locally advanced tumours for which neoadjuvant chemotherapy was indicated (15) • Tumours requiring an immediate mastectomy (20) • Patients with local recurrence after conservative treatment (10) • Patients for whom the breast morphology did not allow oncoplastic surgery (9)
Interventions	**Intervention**: • VD-Upper 21 • Central 13 • Superomedial 7 • Inferior and central 1 **Control**: BCS - WLE
Outcomes	**Primary outcomes**: • No outcomes of interest **Seondary outcomes**: • Re-excisions • Complications **Other outcomes:** • Operative time • Length of stay
Notes	No disclosures/funding declared Different to Giacalone 2007 (1) and (2) as has different intervention Translated from French

Gulcelik 2013

Study characteristics	
Methods	Prospective single-centre cohort Ankara Oncology Training and Education Hospital, Ankara, Turkey 2003 to 2010

Gulcelik 2013 *(Continued)*

	268 participants
Participants	**Inclusion**: patients with breast cancer and macromastia undergoing breast cancer surgery. Patients with upper inner and upper outer-quadrant lesions were included in the study. **Exclusion**: patients who did not attain their follow-up and were excluded (n = 18)
Interventions	**Intervention**: volume displacement - bilateral reduction mammoplasty (n = 106) **Control**: quadrantectomy (n = 162)
Outcomes	**Primary outcomes** (median (I) 33 months (C) 37 months): • Local recurrence • Disease free survival • Overall survival **Secondary outcomes**: • Re-excisions **Other outcomes**: • Distant recurrence • Margins
Notes	No disclosures/funding declared

Hamdi 2008

Study characteristics	
Methods	Retrosepective single-centre cohort 2002 to 2003 Gent University Hospital, Belgium 152 participants
Participants	**Inclusion**: patients who received lumpectomies with or without reconstruction
Interventions	**Intervention**: volume displacement and replacement, (n = 26) • VR: T-dap, mini LD-flap • VD: therapeutic reduction mammoplasty **Control**: BCS: quadrantectomy (12), tumourectomy (114), (n = 126)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Re-excisions **Other outcomes**:

Hamdi 2008 *(Continued)*

	• Margins
Notes	No disclosures/funding declared

Hart 2015

Study characteristics	
Methods	Prospective single-centre and surgeon cohort 2009 to 2011 Division of Plastic and Reconstructive Surgery, Emory University, Atlanta, USA 70 participants
Participants	**Inclusion**: women with breast cancer treated with mastectomy and immediate BR (control) or lumpectomy with reduction mammoplasty (intervention)
Interventions	**Intervention**: oncoplastic reduction mammoplasty, (n = 10) **Control**: mastectomy + reconstruction: implant-based reconstruction (40.0%), latissimus dorsi flap (38.3%), and pedicled or free transverse rectus abdominis myocutaneous flaps (21.7%), (n = 60)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • PROMs (Self-designed questionnaire)
Notes	No disclosures/funding declared

Hashimoto 2019

Study characteristics	
Methods	Retrospective single-centre cohort April 2012 to November 2017 Osaka International Cancer Institute - Department of Breats and Endocrine Surgery, Osaka, Japan 1333 participants
Participants	**Inclusion**: women with breast cancer undergoing standard breast conserving surgery with or without latissimus dorsi flap reconstruction
Interventions	**Intervention**: volume replacement - Mini-latissimus dorsi flap (MLDF), (n = 183) **Control**: standard breast conserving surgery, (n = 1150)
Outcomes	**Primary outcomes**: • Local recurrence (median: 34 months)

Hashimoto 2019 *(Continued)*

	Secondary outcomes: • No outcomes of interest **Other outcomes**: • Margins
Notes	Conference abstract No disclosures/funding Authors were contacted requesting full dataset for primary outcomes

Hilli-Betz 2014

Study characteristics	
Methods	Retrospective single-centre cohort 2003 to 2011 Hannover Medical School, 30625 Hannover, Germany 230 participants
Participants	**Inclusion**: women with breast cancer with tumours in the upper inner, upper outer, and lower inner quadrants undergoing breast conserving surgery
Interventions	**Intervention**: volume displacement - dermoglandular rotation flap, (n = 69) **Control**: BCS: standard lumpectomy, (n = 161)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Complications • PROMs (self-designed questionnaire) • Cosmetic evaluation (BCCT.core and self-designed single surgeon evaluation)
Notes	No disclosures/funding declared

Hu 2019

Study characteristics	
Methods	Retrospective single-centre single surgeon cohort January 2013 to December 2014 Department of Breast Surgery, Oxford University Hospitals NHS Trust, Oxford, UK 36 participants

Hu 2019 *(Continued)*

Participants	**Inclusion**: Patients with breast cancer undergoing breast-conserving surgery by a single surgeon in a tertiary referral centre who received CWPF or WLE **Exclusion**: • Performed at a different institution and their mammograms were unavailable for qualitative assessment • Patients who went on to have completion mastectomy
Interventions	**Intervention**: Volume replacement - chest wall perforator flap, (n = 18) **Control**: BCS: wide local excision
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Recall rates **Other outcomes:** • Margins
Notes	Authors PG and JH No disclosures/funding declared

Jiang 2015

Study characteristics	
Methods	Prospective single-centre cohort Tangshan People's Hospital, China February 2011 to November 2013 60 participants
Participants	**Inclusion**: Women with breast cancer with: • Tumours < 3cm • Stages I & II • < 4 positive lymph nodes involved of < 2cm **Exclusion**: • Central cancer • T4 features • Major comorbidities • Lactating women • Psychiatric history
Interventions	**Intervention**: OPS surgery

Jiang 2015 *(Continued)*

	Control: BCS: lumpectomy
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Re-excisions • Complications • PROMs • Cosmatic evaluation **Other outcomes**: • Margins
Notes	No disclosures/funding declared Translated from Chinese

Kahn 2013

Study characteristics	
Methods	Retrospective single-centre cohort August 2008 to December 2011 Victoria and Western Infirmary Glasgow, UK 169 participants
Participants	**Inclusion**: • Patients with breast cancer treated with BCS or mastectomy with or without reconstruction followed by adjuvant chemotherapy • Patients in the study as well as the control groups were consecutive **Exclusion**: Patients with more than one of the following risk factors for wound healing problems were not offered OBCS: • BMI > 30 • Smoking • History of vasculitis • Immunosuppression
Interventions	**Intervention**: Volume displacement and replacement (analysed together), (n = 31) VD: wise pattern (16), benelli (6), lateral excision (3), matrix rotation (3) VR: TEPF (2), V-Y advancement flap (1) **Control**: (1) BCS: wide local excision, (n = 66) (2) Mastectomy, (n = 56) (3) Mastectomy + reconstruction, (n = 16)
Outcomes	**Primary outcomes**: • No outcomes of interest

Kahn 2013 *(Continued)*

	Secondary outcomes: • Time to adjuvant therapy **Other outcomes**: • Margins
Notes	No disclosures/funding declared

Keleman 2019

Study characteristics	
Methods	Retrospective single-centre cohort January 2010 to January 2017 National Institute of Oncology, Budapest, Hungary 700 participants
Participants	**Inclusion**: Patients with breast cancer undergoing breast-conserving surgery **Exclusion**: • Oncologic follow-up of the patients was performed at another institute • Patients that did not participate in the evaluation of the cosmetic and quality of life outcome measurements • Patients that had a history of BCS and/or radiation therapy (RT) • Patients that received immediate contralateral breast symmetrisation with therapeutic surgery
Interventions	**Intervention**: Volume displacement - therapeutic mammaplasty (superior, central, inferior pedicle Wise-pattern) (143), dermoglandular rotation (medial, lateral mammoplasty) (159), periareolar (round block, omega) (48), (n = 350) **Control**: BCS: Wide local excision/quadrantectomy, (n = 350)
Outcomes	**Primary outcomes**: • Local recurrence **Secondary outcomes**: • Re-excisions • Complications • Time to adjuvant therapy • PROMs (EORTC-QLQ C30 BR23) • Cosmetic evaluation (Self-designed - 3 surgeons panel) **Other outcomes:** • Regional recurrence • Distant recurrence
Notes	No disclosures/funding declared Authors were contacted requesting full dataset for primary outcomes

Kelsall 2017

Study characteristics	
Methods	Retrospective matched single-centre cohort 1999 to2014 Nottingham Breast Institute, Nottingham City Hospital, Nottingham, United Kingdom 567 participants
Participants	**Inclusion**: • Women with breast cancer undergoing either OPS or mastectomy and reconstruction AND the availability of PROMs data **Exclusion**: • Previous treatment for breast cancer • Delayed reconstruction • Unavailability of PROMS data • Surgery for prophylactic or benign disease • Previous breast radiotherapy
Interventions	**Intervention**: Volume displacement and replacement (analysed together), (n = 286) - bilateral therapeutic mammaplasty and a chest wall perforator flaps (LICAP [lateral intercostal artery perforator], LTAP [lateral thoracic artery perforator] (204) or TDAP [thoracodorsal artery perforator] (82)) **Control**: Mastectomy and reconstruction, (n = 281)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • PROMs (self-designed)
Notes	No disclosures/funding declared

Kimball 2018

Study characteristics	
Methods	Retrospective multi-centre database review cohort January 2010 to March 2017 Optum ClinformaticsTM DataMart, Eden Prairie, MN, USA) 18,251 participants
Participants	**Inclusion**: Women with breast cancer undergoing breast-conserving surgery

Kimball 2018 *(Continued)*

	Exclusion: Patients were excluded if they underwent: • lumpectomy • mastectomy • reconstruction procedure in the prior year
Interventions	**Intervention**: Volume displacement - lumpectomy & mammoplasty &/or mastopexy, (n = 709) **Control**: BCS: wide local excision, (n = 17,542)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Complications • Time to adjuvant treatment
Notes	Declarations: 2 of the authors were employees of Medtronic and one was a paid consultant, but for services unrelated to this present research Funding: Medtronic provided funds for professional medical writing but had no influence on study design and manuscript preparation

Klit 2017

Study characteristics	
Methods	Retrospective multi-centre database review cohort 2009 to 2013 Danish Breast Cancer Group (DBCG) registery 1798 participants
Participants	**Inclusion**: • Women with breast cancer undergoing mastectomy or breast-conserving surgery and receiving adjuvant chemotherapy **Exclusion**: • Women treated with neoadjuvant chemotherapy were excluded Patients with post-mastectomy breast reconstruction (39) • Patients treated with mastectomy secondary to lumpectomy or OBS due to insufficient resection margins (32) • Patients with incomplete data of onset of adjuvant chemotherapy (28) • Patients with a negative time interval from surgery to onset of chemotherapy, due to incorrect registration (5)
Interventions	**Intervention**: Both VD and VR, (n = 445) **Control**: (1) WLE, (n = 824) (2) Mastectomy, (n = 529)
Outcomes	**Primary outcomes**:

Klit 2017 *(Continued)*

	• No outcomes of interest **Secondary outcomes**: • Time to adjuvant therapy
Notes	No disclosures declared Funding: The Pink Tribute Foundation

Lansu 2014

Study characteristics	
Methods	Retrospective multi-centre cohort Regional hospitals referring to Institue Verbeeten, Netherlands July 2004 to May 2012 46 participants
Participants	**Inclusion**: • Women over 35 years with breast cancer with tumours of stage Tis, T1 or T2, irrespective of the N stage • All patients were disease-free and alive at the moment of inclusion • All patients had their last follow-up visit < 2 years ago • Patients had Karnofsky performance status 70 **Exclusion**: • Pregnant women • Poor performance status • Recurrence • Last follow-up > 2 years ago
Interventions	**Intervention**: Volume displacement - all patients had conventional RT fractionation scheme and simultaneous boost with OPS breast remodelling and careful closure by mobilising tissue, (n = 19) **Control**: BCS: wide local excision, all patients had conventional RT fractionation scheme and simultaneous boost, (n = 27) Other interventions not extracted: The following goups were investigated 1) The hypofractionated group (HF): hypofractionated RT fractionation scheme, sequential boost, and conventional BCS (lumpectomy). 2) The oncoplastic surgery hypofractionated group (OSHF): hypofractionated RT fractionation scheme, simultaneous boost and OPS
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Re-excisions • Complications

Lansu 2014 *(Continued)*

	• PROMs • Cosmetic evaluation **Other outcomes**: • Margins
Notes	No disclosures/funding declared

Lee 2018

Study characteristics	
Methods	Retrospective single-centre cohort January 2008 to December 2013 Kyungpook National University, Daegu, Korea
Participants	**Inclusion**: Women with breast cancer undergoing breast cancer surgery by a breast surgeon only or collaborative team of a breast and plastic surgeons
Interventions	**Intervention**: Volume displacement and replacement alone, (n = 260) VD: Volume displacement (11.2%), batwing mastopexy (0.3%), glandular reshaping (0.7%), round block technique (1.2%), purse-string suture technique (1.2%), tennis racket technique (3.3%), local flap (0.6%), rotating flap (2.5%), reduction mammoplasty (1.3%) VR: Volume replacement (24.3%), Intercostal artery perforator flap (1.6%), lateral thoracodorsal perforator flap (1.1%), thoracodorsal artery perforator flap (0.8%), latissimus dorsi myocutaneous flap (10.6%), latissimus dorsi myocutaneous flap with silicone implant (1.5%), transverse rectus abdominis myocutaneous flap (3.7%) **Control**: (1) BCS, (n = 582) (2) Mastecomy, (n=409) (3) Mastectomy and reconstruction, (n = 253)
Outcomes	**Primary outcomes** (median 72.4 (16.76) months): • Local recurrence • Overall survival **Other outcomes**: • Distant recurrence
Notes	No disclosures Funding: A national research foundation of Korea grant, funded by the Korean government and a grant from the national R&D programme for cancer control

Losken 2009

Study characteristics	
Methods	Retrospective single-centre and single surgeon cohort Before 2004

Losken 2009 *(Continued)*

	Emory University Hospital, Atlanta, GA, USA 34 patients
Participants	**Inclusion**: • Women with breast cancer undergoing breast-conserving surgery with or without reconstruction • All patients were diagnosed and followed postoperatively at the Emory Winship Cancer Center and the Emory Breast Imaging Center • All received adjuvant radiotherapy • The control group included women without reconstruction during the same time period by the same surgeon
Interventions	**Intervention**: Volume displacement - breast conservation with reduction, (n = 17) **Control**: standard BCS, (n = 17)
Outcomes	**Primary outcomes**: • Local recurrence **Secondary outcomes**: • Recall rates **Other outcomes**: • Distant recurrence
Notes	Different years and outcomes No disclosures/funding declared Authors were contacted requesting full dataset for primary outcomes

Losken 2014

Study characteristics	
Methods	Retrospective single-centre and single surgeon cohort 2009 to 2013 Emory University Hospital, Atlanta, GA, USA 222 participants
Participants	**Inclusion**: Patients with breast cancer undergoing breast-conserving surgery with sufficient follow-up (> 2 months after confirmed final margin status) **Exclusion**: If surgical pathology or clinical follow-up information was unavailable at the time of the review.
Interventions	**Intervention**: Volume displacement - tumour resection with oncoplastic reduction, (n = 83) **Control**: BCS: wide local excision, (n = 139)
Outcomes	**Primary outcomes**: • No outcomes of interest

Losken 2014 *(Continued)*

	Secondary outcomes: • Re-excisions **Other outcomes**: • Margins
Notes	No disclosures/funding declared

Malhaire 2015

Study characteristics	
Methods	Retrospective single-centre cohort May 2005 to September 2011 Institut Curie, 26 rue d'Ulm, France 113 participants
Participants	**Inclusion**: • Women with breast cancer undergoing bracketing wire localisation and breast-conserving surgery **Exclusion**: • Benign or atypical lesions (42) • Neoadjuvant chemotherapy (16) • Wire localisation performed for distinct lesions (17)
Interventions	**Intervention**: Volume displacement, (n = 73), lateral mammaplasty (37), inverted-T (superior pedicle) (15), omega (5), J-plasty (4), inverted-T (inferior pedicle) (4), peri-areolar (3), infra-mammary fold (1), medial mammaplasty (4) **Control**: BCS: wide local excision, (n = 40)
Outcomes	**Primary outcomes**: • Local recurrence (median 40 months) **Secondary outcomes**: • Re-excisions **Other outcomes**: • Margins • Findings on follow-up imaging
Notes	Authors were contacted requesting full dataset for primary outcomes No disclosures/funding declared

Mansell 2015

Study characteristics	
Methods	Retrospective multi-centre cohort 2009 to 2012 Glasgow Breast Units (Victoria & Western Infirmary), UK 1000 participants
Participants	**Inclusion**: • Women with breast cancer undergoing breast-conserving surgery or mastectomy and reconstruction • Patients presenting with bilateral breast cancers, the cancer side carrying the worse prognosis was included in the analysis only **Exclusion**: • Patients with previous ipsilateral or contralateral DCIS/invasive breast cancer
Interventions	**Intervention**: Volume displacement and replacement (analysed together) (n = 20) VD: (n = 103: Wise pattern reduction (81), Benelli-type “round-block” breast reduction (16), Racquet-type excision (6), Lejour (1), Grisotti (1), "Melon slice” reduction (1) VR (n=17): Thoracoepigastric flap (10), Breast matrix rotation (5), thoracodorsal artery perforator (TDAP) flap (1) **Control**: 1)WLE (n = 600) 2) Mastectomy with and without reconstruction (n = 281)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Re-excisions **Other outcomes**: • Margins
Notes	No disclosures/funding declared Duplicate with Mansell 2017, this study used for "re-excisions"

Mansell 2017

Study characteristics	
Methods	Retrospective multi-centre cohort June 2009 to August 2012 Glasgow Breast Units (Victoria & Western Infirmary), UK 1010 patients

Mansell 2017 *(Continued)*

Participants	**Inclusion**: Women with breast cancer undergoing breast-conserving surgery or mastectomy and reconstruction **Exclusion**: Patients with previous DCIS or breast cancer were excluded
Interventions	**Intervention**: Volume displacement and volume replacement (analysed together), (n = 104) VD: (n = 90); Wise pattern reduction (78), Benelli-type “roundblock” (6), "Racquettype” excision (3), Lejour (1), Grisotti (1) and “melon slice” reduction (1) VR: (n=14); Thoracoepigastric flap (9), breast matrix rotation (4) and thoracodorsal artery perforator (TDAP) flap (1) **Control**: (1) WLE (2) Mastectomy with and without reconstruction
Outcomes	**Primary outcomes** (median: (I) 56.8 months (C) 57.2 months/54.4 months • Local recurrence • Disease free survival • Overall survival **Secondary outcomes**: • Re-excisions (extracted from Mansell 2015) **Other outcomes**: • Distant recurrence • Margins
Notes	Different outcomes to Mansell 2015 No disclosures/funding declared

Matrai 2014

Study characteristics	
Methods	Retrospective single-centre matched cohort January 2010 to September 2013 Department of Breast and Soft Tissue Surgery of the National Institute of Oncology, Hungary
Participants	**Inclusion**: • Women with invasive early-stage breast cancer • Controls matched on clinicopathological parameters **Exclusion**: Distant metastases
Interventions	**Intervention**:

Matrai 2014 *(Continued)*

	Volume displacement, (n = 60); Inverse T (Wise pattern) (17) Regnault B (15) Round Block (dual plane) (8) Circum-vertical (5) Lateral matrix rotation (5) Batwing "bat wing" (3) Grisotti (2) Holmström's lobe (2) Medial matrix rotation (2) **Control**: WLE/quandrantectomy, (n = 60)
Outcomes	**Primary outcomes**: (median follow-up (I) 8.7 (3.05) (C) 32.2 (9.22)) • Local recurrence **Secondary outcomes**: • Time to adjuvant therapy • PROMs (EORTC QLQ C30 BR23) • Complications **Other outcomes**: • Margins • Operative time
Notes	Tranlated from Hungarian No disclosures/funding declared Authors were contacted requesting full dataset for primary outcomes

Mazouni 2013

Study characteristics	
Methods	Retrospective single-centre cohort January 2002 to November 2010 Institute Gustave Roussy, Villejuif, France 259 participants
Participants	**Inclusion**: Women with invasive breast cancer undergoing BCS after primary CT **Exclusion**: Patients with metastatic disease
Interventions	**Intervention**: Volume displacement, (n = 45): periareolar mammoplasty (the round block technique) (13), recentering of the nipple-areola complex (3), ablation of the nipple-areola complex (5), external radial mammaplasty (2), inferior pedicle mammaplasty (8), vertical mammaplasty (1), superior pedicle mammaplasty (11), cutaneous resection with a rotation flap (2)

Mazouni 2013 *(Continued)*

	Control: BCS: WLE, (n = 214)
Outcomes	**Primary outcomes** (median follow-up: 46 months): • Local recurrence • Disease-Free Survival • Overall Survival **Secondary outcomes**: • Re-excisions • PROMs (self-designed) **Other outcomes**: • Regional recurrence • Distant recurrence • Margins
Notes	No disclosures/funding declared

Morrow 2019

Study characteristics	
Methods	Retrospective multi-centre database review cohort January 2014 to December 2015 National Managed Clinical Networks/Cancer Networks of the 3 Scottish regions covering the whole of Scotland (WOSCAN: West of Scotland Cancer Network, SCAN: East of Scotland Cancer Network and NOSCAN: North of Scotland Cancer Network), UK
Participants	**Inclusion**: Patients with breast cancer undergoing surgical treatment **Exclusion**: Patients who had non-operative treatment only were excluded
Interventions	**Intervention**: Volume disaplacement - theraputic mammoplasty, (n=217) **Control**: (1) BCS, (n=5241) (2) Mastectomy, (n=1907) (3) Mastectomy and reconstruction, (n=710)
Outcomes	**Primary outcomes:** • No outcomes of interest **Secondary outcomes**: • Time to adjuvant therapy **Other outcomes**: • The main focus was on clinicopathological features of patients in each group
Notes	No disclosures/funding declared

Mukhtar 2018

Study characteristics	
Methods	Retrospective single-centre cohort 1992 to 2017 University of California, San Francisco, USA 326 participants
Participants	**Inclusion**: Women with breast cancer undergoing breast conserving surgery
Interventions	**Intervention**: • Volume displacement and replacement (analysed together) • Level 2 OPS techniques: mammoplasty OR parenchymal flaps, (n = 49) **Control**: • BCS: WLE, (n = 277)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Re-excisions **Other outcomes**: • Margins
Notes	No disclosures/funding declared

Mustonen 2004

Study characteristics	
Methods	Retrospective single-centre cohort January 1998 to June 2001 Kuopio University Hospital, Finland 66 participants
Participants	**Inclusion**: Patients with primary (invasive/in situ) breast cancer undergoing immediate breast reconstruction following mastectomy or breast-conserving surgery
Interventions	**Intervention**: Volume replacement: Latissimus-dorsi mini flap, (n = 12) **Control**: Mastectomy plus reconstruction, (n = 54)
Outcomes	**Primary outcomes**: (medican follow-up: (I) > 24 months (C) 45.6 months) • Local recurrence **Secondary outcomes**:

Mustonen 2004 *(Continued)*

	• Complications **Other outcomes**: • Regional recurrence • Distant recurrence
Notes	No disclosures/funding declared Authors were contacted requesting full dataset for primary outcomes

Nakada 2019

Study characteristics	
Methods	Retrospective single-centre cohort January 2000 to December 2012 University of Yamanashi, Yamanashi, Japan 1043 participants
Participants	**Inclusion**: Patients with breast cancer undergoing breast-conserving surgery and were followed for more than 5 years after surgery
Interventions	**Intervention**: Volume replacement, (n = 417): Pedicled fat flaps: lateral epidermal fat flap (276), Inframammary adipofascial flap (25), rotation of surrounding tissue (116) **Control**: BCS; Quadrantectomy, (n=626)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Complications - fat necrosis only
Notes	No disclosures/funding declared

Nakagomi 2019

Study characteristics	
Methods	Retrospective single-centre cohort January 2000 to December 2017 University of Yamanashi, Yamanashi, Japan

Nakagomi 2019 *(Continued)*

	1193 participants
Participants	**Inclusion**: Patients with breast cancer undergoing surgery with either lateral thoracoaxillar dermal-fat flap (ltdf) or mastectomy or BCS
Interventions	**Intervention**: Volume replacement: lateral thoracoaxillar dermal fat flap, (n = 487) **Control**: Mastectomy, (n = 706) **Other study groups:** BCS without lateral thoracoaxillar dermal fat flap (includes some OPS rechniques)
Outcomes	**Primary outcomes** (120 months): • Local recurrence • Disease-free survival **Secondary outcomes**: • No outcomes of interest **Other outcomes**: • Distant recurrence
Notes	Same patient database as Nakada (different outcomes) No disclosures/funding declared Authors were contacted requesting full dataset for primary outcomes

Niinikoski 2019 (2)

Study characteristics	
Methods	Retrospective single-centre cohort Breast Surgery Unit, Helsinki University Hospital, Helsinki, Finland January 2010 to December 2012 1800 participants
Participants	**Inclusion**: • Patients with primary invasive breast cancer or DCIS who underwent BCS • None of the patients had received neoadjuvant treatment **Exclusion**: • Patients who underwent merely a tumorectomy with neither adjuvant treatment nor axillary surgery due to comorbidities (29) • Patients who had been diagnosed by surgical biopsy (45) • Patients whose breast cancer was found unexpectedly in reduction mammoplasty specimen (2)

Niinikoski 2019 (2) *(Continued)*

Interventions	**Intervention**: Volume displacement, (n = 611): Racket (184) Round block (171) Upper rotation (67) Lower rotation (50) Superior pedicle (37) inferior pedicle (10) Mastopexy (26) S-plasty (21) J-plasty (20) Batwing (17) Wise-amputation (8) **Control**: Standard BCS, (n = 1189)
Outcomes	**Primary outcomes** (median follow-up 75 months): • Local recurrence • Disease-free survival • Overall survival **Secondary outcomes**: • Re-excisions **Other outcomes**: • Margins • Regional recurrence • Distant recurrence
Notes	No disclosures/funding declared Authors were contacted requesting full dataset for primary outcomes

Ojala 2017

Study characteristics	
Methods	Retrospective multi-centre cohort Helsinki and Uusimaa Hospital District, Finland 2010 379 participants
Participants	**Inclusion**: Patients with invasive breast cancer undergoing breast-conserving surgery **Exclusion**: Bilateral disease or previous breast cancer
Interventions	**Intervention**:

Ojala 2017 *(Continued)*

	Volume displacement, (n = 86): Racket mammoplasty (22%) Reduction mammoplasty techniques (22%) Round block (19%) Rotation plasty techniques (19%) Extensive dual plane undermining (14%) Other oncoplastic techniques (5%) **Control**: Standard BCS, (n = 293)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Re-excisions • Complications • PROMs (Breast cancer treatment outcome scale (BCTOS)/self-designed)
Notes	No disclosures declared Funding: Kurt and Doris Palander Foundation Grant

Ozmen 2016

Study characteristics	
Methods	Prospective single-centre cohort Turkey 2005 to 2015 309 participants
Participants	**Inclusion**: • Women with early-stage breast cancer (T1-3, N0-1, M0) • Control group comprised from patients who underwent BCS before clinic started performing mini latissimus dorsi flap (MLDF)
Interventions	**Intervention**: Volume replacement- BCS+MLDF (after 2010) **Control**: Standard BCS (before 2010)
Outcomes	**Primary outcomes:** • No outcomes of interest

Ozmen 2016 *(Continued)*

	Secondary outcomes: • Complications **Other outcomes**: • Margins
Notes	Poster No funding/disclosures

Ozmen 2020

Study characteristics	
Methods	Retrospective single-centre cohort Department of Surgery, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey January 2010 to January 2018 317 participants
Participants	**Inclusion**: • Patients with early breast cancer (Stage I, IIA) **Exclusion**: Contraindications for intervention: • Diffuse microcalcifications and extensive multicentric cancer requiring mastectomy • Patients' desire • Locally advanced BC • Inflammatory BC. • Last two contraindications were also valid for the control group. • There was no bilateral breast cancer in the two groups.
Interventions	**Intervention**: Volume replacement - partial mastectomy plus mini-latissimus dorsi flap, (n = 242) **Control**: Mastectomy plus reconstruction (with implant), (n = 75)
Outcomes	**Primary outcomes** (median follow-up 54 months): • Local recurrence • Disease-free survival • Overall survival **Secondary outcomes**: • Re-excisions • Complications • Patient questionnaire (EORTC-QLQ C30 & BR23) • Cosmetic evaluation (Japanese Breast Cancer Society Cosmetic Evaluation Scale)

Ozmen 2020 *(Continued)*

Notes	No disclosures/funding declared

Palsodittlir 2018

Study characteristics	
Methods	Retrospective single-centre cohort January 2008 to Dec 2014 University of Iceland, Reykjavík, Iceland 750 participants
Participants	**Inclusion**: Women with breast cancer undergoing breast-conserving surgery **Exclusion**: • Mastectomy • No tumour seen in the removed breast • Bilateral surgery and males
Interventions	**Intervention**: Volume displacement and replacement (analysed together), (n = 85); Volume displacement (89.4%) - glandular rotational flaps or the use of secondary or extended dermoglandular flaps within the breast and may often involve the use of breast reduction techniques Volume replacement (10.6%) - chest wall perforator flaps (lateral intercostal artery perforator (LICAP); intercostal perforator (ICAP) or pedicled flaps (thoracodorsal artery perforator (T-DAP) or latissimus dorsi (LD-miniflap) **Control**: standard BCS, (n = 665)
Outcomes	**Primary outcomes:** • No outcomes of interest **Secondary outcomes:** • Re-excisions • Complications • Time to adjuvant therapy • PROMs (self-designed) **Other outcomes:** • Length of stay • Margins
Notes	No disclosures declared Funding: Visindasjoour Landspitalans (Landspitali Uni Hosp reserch fund)

Peled 2014

Study characteristics	
Methods	Retrospective single-centre cohort 2001 to 2010 Department of Surgery, University of California, San Francisco, USA 101 participants
Participants	**Inclusion**: Patients with breast cancer undergoing partial or complete mastectomy with immediate reconstruction and neo-adjuvant CT and adjuvant RT
Interventions	**Intervention**: Volume displacement: wise pattern incision for all, (n = 37) **Control:** Mastectomy plus reconstruction, (n = 64)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Complications
Notes	No disclosures/funding declared

Piper 2016

Study characteristics	
Methods	Retrospective single-centre matched cohort 2001 to 2009 University of California, San Francisco, USA 98 participants
Participants	**Inclusion**: Patients with breast cancer undergoing breast-conserving surgery **Exclusion**: Patients without negative margins at the time of initial surgery
Interventions	**Intervention**: Volume displacement - simultaneous partial mastectomy and bilateral reduction mammoplasty, (n = 49) **Control**: standard BCS: WLE, (n = 49)

Piper 2016 *(Continued)*

Outcomes	**Primary outcomes** (median follow-up 60 months): • Local recurrence • Overall survival **Secondary outcomes** • Re-excisions • Recall rates **Other outcomes**: • Findings on follow-up imaging • Margins
Notes	No disclosures/funding declared Authors were contacted requesting full dataset for primary outcomes

PlaFarnos 2018

Study characteristics	
Methods	Prospective single-centre cohort June 2014 to June 2016 Hospital de llobregat, Barcelona, Spain 180 participants
Participants	**Inclusion**: Women undergoing breast-conserving surgery for breast cancer
Interventions	**Intervention**: Volume displacement - oncological reduction pattern, (n = 60) **Control**: Standard BCS, (n = 120)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • PROMs - Breast Q **Other outcomes**: • Margins
Notes	Conference abstract No funding/disclosures declared Abstract refers to study as case-control trial - according to Cochrane Handbook classified as Cohort

Potter 2020

Study characteristics	
Methods	Prospective multi-centre cohort July to December 2016 (iBRA), September 2016 to June 2017 (TeaM) Centres invovled in iBRA-2 and TeaM trials, UK 2916 participants
Participants	**Inclusion**: • Patients with invasive/in situ breast cancer undergoing therapeutic mammoplasty in participating centres of the TeaM study • Only the subgroup of patients offered TM to avoid mastectomy was included in the present study • Patients with invasive/in situ breast cancer undergoing mastectomy with or without breast reconstruction in participating centres of the iBRA
Interventions	**Intervention**: Volume displacement - theraputic mammoplasty, (n = 376) **Control**: 1) Mastectomy, (n = 1532) 2) Mastectomy plus reconstruction, (n = 1008)
Outcomes	**Primary outcomes:** • No outcomes of interest **Secondary outcomes:** • Complications • Time to adjuvant therapy **Other outcomes:** • Margins and re-excision only mentioned for the intervention group therefore not extracted
Notes	S.P. is a National Institute for Health Research (NIHR) Clinician Scientist (CS-2016-16-019). T.R. has received support from the NIHR through a Doctoral Research Fellowship (DRF-2014-07-079) and Academic Clinical Lectureship The TeaM study was funded by an Association of Breast Surgery research grant. This work was undertaken with the support of the NIHR Biomedical Research Centre at University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed in this publication are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

Ren 2014

Study characteristics	
Methods	Retrospective single-centre matched cohort

Ren 2014 *(Continued)*

	2003 to 2013 Department of Surgery, Jiangsu Cancer Hospital, China 273 participants
Participants	**Inclusion**: Patients with breast cancer undergoing breast surgery with either MLDF or mastectomy with resection-free margins (> 1mm) **Exclusion**: Patients with multifocal diseases
Interventions	**Intervention**: Volume replacement - mini-LD flaps, (n = 91) **Control**: Mastectomy, (n = 182)
Outcomes	**Primary outcomes** (median follow-up: (I) 83 months (C) 81 months): • Local recurrence • Overall survival **Secondary outcomes**: • No outcomes of interest **Other outcomes**: • Distant recurrence
Notes	No disclosures/funding declared Authors were contacted requesting full dataset for primary outcomes

Rose 2019

Study characteristics	
Methods	Retrospective multi-centre matched cohort 2008 to 2013 Hospitals in the southern region of Denmark and northern region of Denmark 1596 participants
Participants	**Inclusion**: Patients with breast cancer undergoing breast-conserving surgery in the Region of Northern Denmark and Southern Denmark, (n = 197) **Exclusion**: Patients who had bilateral cancers at the time of surgery (24)
Interventions	**Intervention**:

Rose 2019 *(Continued)*

	Volume displacement and replacement (analysed together) **Control**: BCS: WLE
Outcomes	**Primary outcomes** (median follow-up (I) 49.2 months (C) 67.2 months): • Disease-free survival • Overall survival **Secondary outcomes**: • Time to adjuvant therapy
Notes	No disclosures/funding declared

Rose 2020

Study characteristics	
Methods	Retrospective multi-centre cohort January 2008 to December 2013 Danish Breast Cancer Group (DBCG) registry 727 participants
Participants	**Inclusion**: Patients who received BCS for primary breast cancer **Exclusion**: • Patients at the time of the survey had had a recurrence of the disease • A secondary mastectomy • Registered with bilateral cancer • Did not have surgery in the period 2008 to 2013 • Patients were not registered in the DBCG registry
Interventions	**Intervention**: Volume displacement and volume replacement (analysed together) - mammoplasty, perforator flaps and muscle sparing LD, (n = 96) **Control**: BCS: WLE, (n = 631)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • PROMs (BREAST-Q)
Notes	No disclosures declared

Rose 2020 *(Continued)*

	Funding: The Malmö University Hospital Cancer Research Fund, The Einar and Inga Nilsson Foundation, Skåne University Hospital Funds and Donations and The Hospital of Southwest Jutland. Same patient database as Rose 2019 (different outcomes)

Santos 2015

Study characteristics	
Methods	Retrospective single-centre cohort 2007 to 2012 Hospital Nossa Senhora das Grac ¸as (HNSG) Breast Unit, Curitiba, Brazil 122 participants
Participants	**Inclusion**: • Women with invasive/in situ breast cancer with T1-T2 tumours undergoing breast-conserving surgery • In order to be included in this study, all patients had to be finished their treatments, and be at least 6 months after the conclusion of radiotherapy • All participants agreed to take part in the study and have signed an informed consent form
Interventions	**Intervention**: Volume displacement - mammoplasty, (n = 57) Inferior pedicle techniques (38), superior pedicle (17), central quadrantectomy (1) and round block (1) **Control**: BCS: WLE, (n = 65)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • PROMs • Cosmetic evaluation
Notes	No disclosure/funding declared

Scheter 2019

Study characteristics	
Methods	Retrospecting single-centre matched cohort January 2011 to December 2016 Tel-Aviv Sourasky Medical Center, Tel Aviv, Israel 24 participants

Scheter 2019 *(Continued)*

Participants	**Inclusion**: Patient with breast cancer with central tumours undergoing breast-conserving surgery **Exclusion**: Patients who had subsequently proceeded to total mastectomy
Interventions	**Intervention**: Volume displacement - mammoplasty, (n = 12) **Control**: BCS: WLE, (n = 12)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Complications • PROMs - (self-designed/Breast-Q) • Cosmetic evaluation - self-designed 13 person panel **Other outcomes:** • Margins • Further aesthetic procedures • Length of stay
Notes	Declaration: One author is a speaker for Johnson Medical, no financial or personal declarations No funding declared

Sherwell-Cabello 2006

Study characteristics	
Methods	Prospective single-centre January 2010 to July 2013 Instituto de Enfermedades de la Mama, FUCAM A.C, Coyoacán D.F, México 170 participants
Participants	**Inclusion**: Women with breast cancer with a complete clinical history and had answered a questionnaire of aesthetic satisfaction in person or by phone were included **Exclusion**: Those who did not continue their follow-up at the institution were eliminated from the study
Interventions	**Intervention**:

Sherwell-Cabello 2006 *(Continued)*

	VD, (n = 75) - OPS level 1 (15), lateral (21), internal rotation (1), circular (13), grisotti (8), vertical (13), double (3) **Control**: Standard BCS, (n = 95)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Complications • PROMs (self-designed) **Other outcomes**: • Margins
Notes	No disclosures/funding declared

Tang 2016

Study characteristics	
Methods	Retrospective single-centre cohort Affiliated Cancer Hospital of Guangxi Medical University, China January 2011 to December 2013 184 participants
Participants	**Inclusion**: Women with breast cancer undergoing breast cancer surgery **Exclusion**: Women who underwent mastectomy
Interventions	**Intervention**: Volume displacement and replacment (analysed together), (n = 67); Including round block, omega-plasty, teniis racket mammoplasty, inverted T-mammoplasty, inferior pedicle mammoplasty, local pedicled skin flap, partial LD flap **Control**: BCS - WLE, (n = 117)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Re-excisions • Complications

Tang 2016 *(Continued)*

	• PROMs (self-designed) **Other outcomes**: • Margins
Notes	No disclosures/funding declared

Tenofsky 2014

Study characteristics	
Methods	Retrospective single-centre cohort December 2006 to April 2011 University of Kansas School of Medicine - Wichita, USA 142 participants
Participants	**Inclusion**: • 18 years of age or older • female • Had been treated with lumpectomy, either oncoplastic or non-oncoplastic surgery **Exclusion**: • Patients were excluded if they received a mastectomy within 6 months of the lumpectomy
Interventions	**Intervention**: Volume displacement - mammoplasty & adjacent tissue transfer, (n = 58) **Control**: BCS - WLE, (n = 84)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Re-excisions • Complications • Recall rates • Time to adjuvant therapy • PROMs (self-designed)
Notes	No disclosures/funding declared

Tong 2016

Study characteristics	
Methods	Retrospective single-centre cohort

Tong 2016 *(Continued)*

	January 2005 to April 2013 The University of Texas M. D. Anderson Cancer Center, Texas, USA 408 participants
Participants	**Inclusion**: • Obese patients (body mass index ≥ 30 kg/m2) with breast cancer undergoing oncoplastic breast reconstruction or implant-based or abdominally based free flap immediate breast reconstruction **Exclusion**: • BMI < 30 • Reconstructions performed with a technique other than oncoplastic breast reconstruction, implant-only reconstruction, or abdomen based free flap reconstruction • Standard delayed, "delayed-delayed," or "delayed-immediate" breast reconstruction • Latissimus dorsi–, gluteus-, or thigh-based flap reconstructions
Interventions	**Intervention**: Volume displacement - mammoplasty, (n = 131) **Control**: Mastectomy plus reconstruction, (n = 277)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Complications • Time to adjuvant therapy **Other outcomes**: • Length of stay • Further aesthetic procedures
Notes	No disclosures/funding declared

Viega 2010

Study characteristics	
Methods	Prospective single-centre matched cohort Hospital das Clinicas Samuel Libanio - Universidade do Vale do Sapucai, Brazil August 2005 to August 2008 87 participants
Participants	**Inclusion**: Patients with breast cancer undergoing breast-conserving surgery by the mastology team **Exclusion**:

Viega 2010 *(Continued)*

	• Patients older than 75 years • Patients receiving neo-adjuvant chemotherapy • Metastatic disease • Previous breast surgery
Interventions	**Intervention**: Both VD and VR - 11 reduction & 34 local flaps, (n = 45) **Control**: BCS: Quandrantectomy, (n = 42)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • PROMs (Short form-36, Rosenberg EPM self-esteem)
Notes	Some crossover in study group as Veiga 2011 but different outcomes No disclosures/funding declared

Viega 2011

Study characteristics	
Methods	Prospective single-centre matched cohort study Hospital das Clinicas Samuel Libanio - Universidade do Vale do Sapucai, Brazil December 2005 to March 2009 90 participants
Participants	**Inclusion**: • Patients with breast cancer, undergoing breast-conserving surgery **Exclusion**: • Patients older than 75 years • Patients receiving neoadjuvant chemotherapy • Metastatic disease • Previous breast surgery
Interventions	**Intervention**: Both VD and VR - 11 reduction & 34 local flaps, (n = 45) **Control**: BCS: Quandrantectomy, (n = 45)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**:

Viega 2011 *(Continued)*

	• Cosmetic evaluation (Self-designed - 2 breast surgeons, 2 plastic surgeons (1 male and 1 female of each)
Notes	Some crossover in study group as Veiga 2010 but different outcomes No disclosures/funding declared

Vieira 2016

Study characteristics	
Methods	Retrospective single-centre cohort October 2005 to December 2011 Barretos Cancer Hospital, Brazil 78 participants
Participants	**Inclusion**: Patients with locally advanced breast cancer undergoing neoadjuvant CT and breast-conserving surgery **Exclusion**: • Metastatic breast cancer • Inflammatory breast cancer
Interventions	**Intervention:** Volume displacement, (n = 26); central quadrectomy (8), dermoglandular rotation flap (7), periareolar quad (5), inferior pedicle (4), superior pedicle (2) **Control:** BCS: Quandrantectomy, (n = 52)
Outcomes	**Primary outcomes** (median follow-up: (I) 60.01 (18.19) months (C) 64.88 (24.53) months): • Local recurrence • Disease-free survival • Overall survival **Secondary outcomes**: • Re-excisions **Other outcomes**: • Margins
Notes	

Wijgman 2017

Study characteristics	
Methods	Retrospective multi-centre database review cohort Netherlands Cancer Registry, The Netherlands January 2010 to December 2014 842 breasts
Participants	**Inclusion**: Patients with breast cancer undergoing breast-conserving surgery **Exclusion**: • Patients with primary mastectomy • Diagnostic microdochectomy or benign histology • Patients having recurrent or metastatic breast cancer
Interventions	**Intervention**: Volume displacement, mammoplasty, (n = 314) **Control**: BCS: WLE, (n = 528)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Re-excisions • Complications **Other outcomes**: • Margins
Notes	No disclosures/funding declared

Wong 2017

Study characteristics	
Methods	Retrospective single-centre cohort University of California San Francisco, USA 1992 to April 2017 167 participants
Participants	**Inclusion**: Women with invasive lobular carcinoma
Interventions	**Intervention**: Volume displacement - oncoplastic reduction mammoplasty, (n = 30) **Contol**:

Wong 2017 *(Continued)*

	BCS - lumpectomy, (n = 137)
Outcomes	**Primary outcomes**: • No outcomes of interest reported **Secondary outcomes**: • Re-excisions **Other outcomes**: • Surgical margins
Notes	No funding/disclosures declared Conference abstract

Zhou 2019

Study characteristics	
Methods	Retrospective single-centre cohort Sun Yat-sen University Cancer Center, Guangzhou, China October 2015 to March 2017 60 participants
Participants	**Inclusion**: • Women with early breast cancer (T1-2 tumor) with clinically axillary lymph nodes positive (cA+) undergoing breast-conserving surgery **Exclusion**: • Previous history of surgery, trauma or any diseases influencing the shoulder function • Inability to complete the questionnaire • Failure to complete the follow-up
Interventions	**Intervention**: Volume replacement - all mini latissimus dorsi flap (MLDF) (n = 32) **Control**: BCS: WLE (n = 28)
Outcomes	**Primary outcomes**: • No outcomes of interest **Secondary outcomes**: • Complications • PROMs (self-designed)
Notes	No disclosures/funding declared

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Adimulam 2014	Ineligible study design
Angarita 2019	Conference abstract - published in full journal form Angarita 2020 (same participants)
Ayoub 2019	Ineligible outcomes
Bogusevicius 2014	Ineligible study design
Chapa 2019	Ineligible study design
Cil 2016	Dataset with additions published as Angarita 2020 (duplicate participants)
Emiroglu 2016	Ineligible study design
Flanagan 2019	Ineligible intervention
Freitas 2019	Ineligible intervention
Fung 2001	Ineligible intervention
Geluk 2020	Ineligible study design
Hamilton 2019	Ineligible intervention
Han 2010	Ineligible intervention
Hashem 2017	Ineligible comparator
IRCT20111207008316N4	No longer registered
Jonczyk 2019	Ineligible study design
Kabir 2015	No outcomes of interest
Kabir 2015a	Ineligible outcomes
Kaur 2005	No outcomes of interest
Kawanaka 2019	Ineligible study design
Kelemen 2016	Duplicate dataset
Khan 2018	Ineligible comparator
Lima 2012	No outcomes of interest
Mondani 2019	Ineligible study design
Moustafa 2016	Ineligible comparator
Nano 2005	Ineligible study design

Study	Reason for exclusion
NCT00870415	Ineligible intervention
NCT02376413	Withdrawn (unavailable to recruit participants)
NCT03273348	Ineligible study design
NCT03900299	Ineligible study design
NCT04349527	Ineligible comparator
Niinikoski 2019 (1)	Conference abstract - published in full journal from Niinikoski 2019 (2) (same participants)
Nisiri 2018	Too few participants n = 16 in O-BCS intervention group
Pearce 2020	Ineligible study design
Pukancsik 2017	Ineligible study design
Pukancsik 2019	Ineligible study design
Rietjens 2007	Ineligible study design
Romics 2017	Ineligible study design
Sun 2014	Ineligible intervention
Tang 2013	Ineligible study design
van Paridon 2017	Ineligible study design
Youssef 2017	Ineligible study design
Youssef 2018	Ineligible comparator
Zucca 2012	Ineligible study design

Characteristics of studies awaiting classification *[ordered by study ID]*

Srivastava 2018

Methods	Prospective single-centre cohort All India Institute of Medical Sciences, Surgical Disciplines, New Delhi, India April 2015 to October 2016 64 participants
Participants	**Inclusion**: women with early breast cancer (T1-T2) undergoing breast conserving surgery
Interventions	**Intervention**: volume displacement - O-BCS (oncoplastic breast conserving surgery), (n = 32) **Control**: standard BCS (breast conserving surgery), (n = 32)
Outcomes	**Primary outcomes**:

Srivastava 2018 *(Continued)*

	• No outcomes of interest **Secondary outcomes**: • Patient-reported outcome measures (PROMs) - European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-BR23)
Notes	No disclosures/funding declared Conference abstract Abstract refers to study as randomised controlled trial - according to *Cochrane Handbook* classified as Cohort (Higgins 2021)

Characteristics of ongoing studies *[ordered by study ID]*

ACTRN12612000638831

Study name	Effect of breast oncoplastic reshaping on the long term cosmetic outcome after breast conservation surgery: a prospective randomised trial
Methods	Prospective randomised controlled trial (RCT) Norfolk and Norwich University Hospital, Norwich, England, UK 316 participants
Participants	**Inclusion** • Female patients selected for breast conservation surgery for breast cancer after multidisciplinary decision and informed consent **Exclusion** • Not requiring breast conservation surgery
Interventions	**Intervention**: breast reshaping - the breast tissue is mobilised superficially and deep from the skin and the pectoral muscles in order to close the defect **Control**: wide local excision
Outcomes	**Primary outcomes** • Subjective assessment of cosmesis on a scale of 0 to 10 by a panel (consists of 2 trained observers) and by the patient • Objective assessment of cosmesis • Skin changes after radiotherapy **Secondary outcomes** • Demographics: patient's age, weight, height, BMI and side of the surgery • Bra and cup size • Grade of breast ptosis • Preoperative measurements (mm) • The clinical tumour size (using callipers measured in mm) and tumour location • Distance from the closest edge of the tumour to nipple (mm) • Mammographic assessment • Neoadjuvant treatment, either chemotherapy or hormonal therapy (all measurements will be assessed again after neoadjuvant treatment and prior to surgery)

ACTRN12612000638831 *(Continued)*	• Postoperative complications • Details of re-excision of margins • Details of radiotherapy • Details of chemotherapy • Patient satisfaction questionnaire using the body image scale.
Starting date	April 2012
Contact information	Maged Hussien MD, FRCS (Gen. Surg) maged.hussien@nnuh.nhs.uk
Notes	Recruitment status: no update since 2012

Catsman 2018

Study name	The COSMAM TRIAL a prospective cohort study of quality of life and cosmetic outcome in patients undergoing breast conserving surgery
Methods	Single-centre prospective cohort The Amphia Hospital, Breda, Netherlands
Participants	**Inclusion criteria** • All female patients referred to our outpatient clinic from June 2015, eligible for BCS and BCS with O-BCS that are older than 18 years **Exclusion criteria** • Patients who are not familiar with Dutch language • Patients with a history of breast cancer and/or radiation therapy in the head/neck/axillary or breast region in the past
Interventions	**Intervention arm 1**: level 1 oncoplastic surgery **Intervention arm 2**: level 2 oncoplastic surgery **Control**: standard lumpectomy with/without minor volume replacement Aim at least 75 patients per group
Outcomes	• The cosmetic score at 4 weeks is considered the primary outcome variable • Photographs of the breast will be used to score cosmetic result both by the patient, an independent expert panel and BCCT.Core software • Patient satisfaction will be scored preceding surgery, and at 1 month and 1 year follow up • Quality of life will be measured by using the BREAST-Q BCT, EORTC-QLQ and EQ-5D-5 L questionnaires
Starting date	July 2015, protocol published 2018
Contact information	cjlmcatsman@gmail.com
Notes	Funding: Amphia Hospital Breda, the Netherlands

NCT01396993

Study name	Prospective non-randomized evaluation of oncoplastic surgery (iTOP)
Methods	Prospective cohort study Medical University of Vienna, Vienna, Austria 150 participants
Participants	**Inclusion** • Ages eligible for study: 18 years to 65 years (adult, older adult) • Sexes eligible for study: female • Patients scheduled for unilateral breast conserving surgery due to cancer or a suspicious lesion, in whom >10%* of breast volume (measured by mammograms using a defined formula 37) has to be removed or breast cancer patients scheduled for mastectomy and immediate reconstruction (immediate or delayed contralateral correction is allowed) • Breast Imaging Reporting and Database System score IV, V or VI are eligible • Psychological and physical capable of understanding and performing the trial • Signed written informed consent * if oncologic safety necessitates to resect more than half of one breast quadrant **Exclusion** • Inflammatory breast cancer • Progression after neoadjuvant therapy • Pregnant women • Patients unable to perform surgery under general anaesthesia • Bilateral breast lesions
Interventions	**Intervention**: Immediate techniques for Oncoplastic surgery (iTOP) - patients undergoing immediate techniques for oncoplastic surgery (level I only parenchymal rotation and breast undermining as well as level II using complex reduction plastics for nipple-areola-complex movings) and patients with mastectomy and immediate reconstruction. Breast conserving surgery and immediate defect filling using local flaps (level I) or reduction plastics (level II) as well as mastectomy and immediate reconstruction using free flaps **Control**: patients undergoing conservative breast surgery. Breast-conserving therapy without defect correction
Outcomes	**Primary outcome measures** • Breast image scale (time frame: 2 years) • Self-esteem measured by the breast image scale will be assessed before and every 6 months after surgery as primary endpoint **Secondary outcome measures** • Quality of life (time frame: 2 years) • BREAST Q, non-validated questionnaires • Morbidity (time frame: 6 months) - necrosis, infection, reoperations and bleedings as well as haematoma and seroma formation will be clinically assessed after surgery • Breast symmetry index (time frame: 2 years) - using the breast analysing tool software we will analyse breast symmetry before and every 6 months after surgery • Oncologic parameters (time frame: 2-5 years) - local, distant and overall survival 2 as well as 5 years after surgery will be assessed
Starting date	July 2011 (estimated completion August 2016)

NCT01396993 *(Continued)*

Contact information	Florian Fitzal, Professor of Surgery, Medical University of Vienna
Notes	Recruitment status: unknown - no update since 2015

NCT02159274

Study name	Shoulder disability and late symptoms following oncoplastic breast surgery
Methods	Observational Cohort Study University of Aarhus, Aarhus, Denmark 408 participants
Participants	**Inclusion** • 18 Years to 75 Years • Female • Invasive breast cancer or carcinoma in situ • Breast-conserving surgery including or without oncoplastic surgical techniques **Exclusion** • Patients who are unable to sign an informed consent form • Patients above the age of 75 and under the age of 18 • Patients who have previously been operated in the same or the contralateral breast, shoulder or arm
Interventions	**Intervention**: Breast conserving surgery (BCS) with oncoplastic techniques **Control**: BCS without oncoplastic techniques
Outcomes	Primary outcome measures: • Shoulder function (time frame: before and 18 months after surgery) Secondary outcome measures: • Quality of life [Time Frame: 18 months] • EORTC QLQ-c30 and Br23 before and 18 months after surgery Other outcome measures: • Lymphoedema of the breast and arm (time frame: 18 months) • Cosmetic results (time frame: 18 months)
Starting date	March 2014 to October 2018
Contact information	Katrine R Hauerslev, MD
Notes	Recruitment status: completed - not published

NCT02901223

Study name	The impact of oncoplastic breast surgery on the oncological safety and patient satisfaction

NCT02901223 *(Continued)*

Methods	Prospective Cohort Ain Shams University, Egypt, Cairo 70 participants
Participants	Inclusion: • Up to 60 Years • Female • Stage 1, 2 breast cancer • Non-metastatic breast caner • Signed informed consent Exclusion: • Metastatic breast cancer • Stage 3, 4 breast cancer • Inflammatory breast cancer • Multicentric/multifocal disease • Ductal carcinoma in situ • Patients older than 60 years • History of breast surgery in oncoplastic group • Comorbidity in oncoplastic group • Patients more than 60 years old
Interventions	**Intervention**: oncoplastic group 35 female patients with non-metastatic breast cancer who had oncoplastic techniques for tumour resection by well-trained oncoplastic breast surgeons **Control**: quadrantectomy group 35 female patients with non-metastatic breast cancer who had standard conservative breast surgery with no use of any plastic techniques by general breast surgeons
Outcomes	**Primary outcome measures** • Margins in all specimens measured in mm (time frame: 2 years) • Patient satisfaction assessed using questionnaire (time frame: 2 years)
Starting date	September 2012 to September 2013
Contact information	Yasser Mohamed abdel-samii El Ghamrini - Cairo, Egypt
Notes	Recruitment: Completed - not published Study published on clinicaltrials.gov October 2016 Similar to NCT02923635 and NCT03012152

NCT02923635

Study name	A prospective comparative study between oncoplastic breast surgery and standard wide local excision
Methods	Prospective Cohort

NCT02923635 *(Continued)*

	Ain Shams University, Egypt, Cairo 70 participants
Participants	**Inclusion** • Ages eligible for study: up to 60 years (child, adult) • Sexes eligible for study: female • Patients with macromastia in oncoplastic group • Tumors > 20% of breast volume in oncoplastic group • Tumors in medial or central quadrants **Exclusion** • Patients > 60 years • Patients with comorbidities in oncoplastic group • Tumours > 20% of breast volume in standard group • Tumours in medial or central quadrants in standard group
Interventions	**Intervention**: oncoplastic group - (35 patients) have curative oncoplastic surgery in which plastic techniques integrated with oncological procedures **Control**: standard wide - (35 patients) have standard curative conservative breast surgery without integration of plastic techniques
Outcomes	**Primary outcome measures** • Margins in all specimens measured in mm (time frame: 2 years) **Secondary outcome Measures** • Patient satisfaction assessed using questionnaire (time frame: 2 years)
Starting date	August 2013 to June 2016 (uploaded to clinicaltrials.gov October 2016)
Contact information	Yasser Mohamed Abdel-samii, Ain Shams University
Notes	Recruitment status: completed - not published Similar to NCT02901223 and NCT03012152

NCT03012152

Study name	A comparative study between oncoplastic breast surgery and standard conservative surgery: margin status and patient satisfaction
Methods	Prospective cohort Ain Shams University, Egypt, Cairo 70 participants
Participants	**Inclusion** • Female patients with stage 1, 2 breast cancer **Exclusion** • Patients > 60 years

NCT03012152 *(Continued)*

	• Patients with previous breast surgery • Patients candidate for mastectomy or palliative excision • Patients with collagen disease
Interventions	**Intervention:** O-BCS oncoplastic breast conserving surgery(35 patients) have curative oncoplastic surgery in which plastic techniques integrated with oncological procedures **Control:** standard breast conserving surgery- (35 patients) have standard curative conservative breast surgery without integration of plastic techniques
Outcomes	**Primary outcome measures** • Margins in all specimens measured in mm (time frame: 2 years)
Starting date	May 2013 to September 2016 uploaded onto clinicaltrials.gov January 2017
Contact information	Yasser Mohamed Abdel-samii, Ain Shams University
Notes	Recruitment status: completed - not published SImilar to NCT02901223 and NCT02923635

NCT04030845

Study name	Patient reported outcome - reconstruction and oncoplastic cohort (PRO-ROC)
Methods	Prospective cohort study 10000 patients
Participants	**Inclusion** • Breast cancer patients • Adult (> 18 years old) • Female • Must undergo breast reconstruction or oncoplastic breast-conserving surgery **Exclusion** • Younger (< 18 years old) • Male • Stage IV breast cancer patients • Refuse to undergo breast reconstruction or oncoplastic breast-conserving surgery
Interventions	**Intervention**: oncoplastic breast-conserving surgery. The oncoplastic breast-conserving surgery were mainly those surgeries using volume displacement or volume replacement techniques. **Control**: breast reconstruction - mainly included autologous tissue flaps (latissimus dorsi myocutaneous flaps, pedicled transverse rectus abdominis myocutaneous flaps, free transverse rectus abdominis musculocutaneous flaps, deep inferior epigastric artery perforator flaps, etc.), implant based breast reconstruction, autologous flaps combined with implant reconstruction, fat graft, etc.
Outcomes	**Primary outcome measures** • Change from baseline in BREAST-Q score (time frame: change from baseline at 1 year and 2 years post-operatively)

NCT04030845 *(Continued)*

- Change from baseline in health-related quality of life measured by What does Eortc QLQ-C30 mean?European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) (time frame: change from baseline at 1 year and 2 years post-operatively)
- Change from baseline in health-related quality of life measured by EORTC QLQ-BR23 (time frame: change from baseline at 1 year and 2 years post-operatively)

Secondary outcome measures

- Rates of complications (time frame: up to 24 months)
- Change from baseline in cosmetic scores rated by patients (time frame: change from baseline at 1 year and 2 years post-operatively)
- Breast aesthetics (time frame: up to 24 months)
- Overall survival (time frame: up to 24 months)
- Recurrence-free survival (time frame: up to 24 months)

Other outcome measures

- Change from baseline in Visual Analog Score for pain (time frame: change from baseline at 1 day, 3 days, 7 days, 3 months, 1 year and 2 years post-operatively)

Starting date	July 2019 (estimated finish date December 2024)
Contact information	
Notes	Recruitment status: recruiting

NTR6901

Study name	Patient satisfaction after oncoplastic breast surgery in the context of breast conserving therapy
Methods	Observational Cohort Zuyderland Medical Centre, Netherlands 110 participants
Participants	**Inclusion** • Female • Age at least 18 years • Patient will undergo a curative breast-conserving surgery due to breast cancer in the affected breast • Mastery of the Dutch language in word and writing • Informed consent for participation in the research **Exclusion** • Intellectual limitation to such an extent that it can be expected that the interpretation and/or completion of the questionnaires is a problem • Previous radiotherapy on the affected chest
Interventions	
Outcomes	**Primary outcome** • Satisfaction of the breast after breast-conserving therapy with reconstruction **Secondary outcomes**

NTR6901 *(Continued)*	• Difference regarding the satisfaction between the 2 groups (with and without reconstruction) • Difference regarding the satisfaction between before and after the adjuvant radiotherapy • Postoperative complications
Starting date	February 2018 to May 2019
Contact information	Nadine Hillbergm, n.hillberg@zuyderland.nl, 0031648531220
Notes	Funding: Zuyderland-Maastro Grant

DATA AND ANALYSES

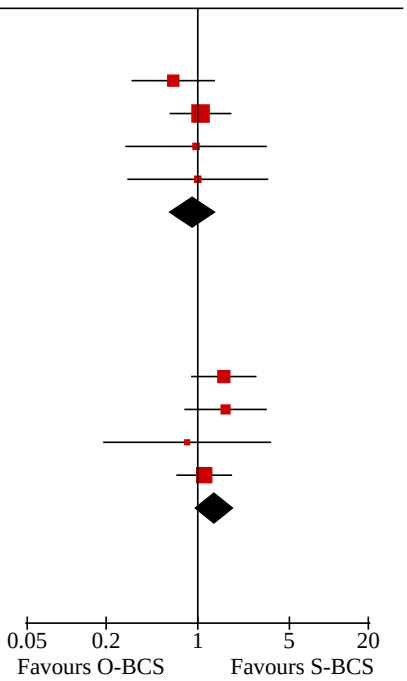
Comparison 1. Any O-BCS versus S-BCS

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Local recurrence-free survival (time to recurrence)	8		Hazard Ratio (IV, Fixed, 95% CI)	Subtotals only
1.1.1 Local recurrence-free survival	4		Hazard Ratio (IV, Fixed, 95% CI)	0.90 [0.61, 1.34]
1.1.2 Local Recurrence Rates	4		Hazard Ratio (IV, Fixed, 95% CI)	1.33 [0.96, 1.83]
1.2 Local recurrence	24		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.2.1 1 year	3	637	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.25, 2.10]
1.2.2 1 to 5 years	15	9014	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.66, 1.04]
1.2.3 5 years	10	6672	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.82, 1.39]
1.3 Disease-free survival (HR)	7		Hazard Ratio (IV, Fixed, 95% CI)	1.06 [0.89, 1.26]
1.4 Disease-free survival (RR)	9		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.4.1 1 to 5 years	3	946	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.74, 1.34]
1.4.2 5 years	6	5054	Risk Ratio (M-H, Fixed, 95% CI)	1.19 [0.99, 1.44]
1.4.3 10 years	2	2163	Risk Ratio (M-H, Fixed, 95% CI)	1.21 [1.04, 1.40]
1.5 Overall survival (HR)	8		Hazard Ratio (IV, Fixed, 95% CI)	1.02 [0.82, 1.28]
1.6 Overall survival (RR)	13		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.6.1 1 to 5 years	3	4970	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.60, 1.09]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.6.2 5 years	12	8730	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.65, 0.96]
1.7 Re-excision rates	38		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.7.1 Total re-excisions	38	13341	Risk Ratio (M-H, Fixed, 95% CI)	0.76 [0.69, 0.85]
1.7.2 Mastectomies	23	10756	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.85, 1.18]
1.8 Complications	20	118005	Risk Ratio (M-H, Fixed, 95% CI)	1.19 [1.10, 1.27]
1.9 Recall rates	6	715	Risk Ratio (M-H, Fixed, 95% CI)	2.39 [1.67, 3.42]
1.10 Time to therapy	7		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.10.1 Any adjuvant therapy	1	120	Mean Difference (IV, Fixed, 95% CI)	2.60 [-5.48, 10.68]
1.10.2 Chemotherapy	4	4566	Mean Difference (IV, Fixed, 95% CI)	-1.13 [-2.55, 0.29]
1.10.3 Radiotherapy	5	3720	Mean Difference (IV, Fixed, 95% CI)	9.67 [7.21, 12.14]
1.11 Patient-reported outcomes (BREAST-Q)	5		Other data	No numeric data
1.12 Aesthetic outcome BCCT.core	3		Other data	No numeric data

Analysis 1.1. Comparison 1: Any O-BCS versus S-BCS, Outcome 1: Local recurrence-free survival (time to recurrence)

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
1.1.1 Local recurrence-free survival				
Borm 2019	-0.4308	0.3739	28.4%	0.65 [0.31 , 1.35]
Carter 2016 (1)	0.0488	0.2766	51.8%	1.05 [0.61 , 1.81]
Niinikoski 2019 (2) (2)	-0.0305	0.6339	9.9%	0.97 [0.28 , 3.36]
Piper 2016 (2)	0	0.6316	9.9%	1.00 [0.29 , 3.45]
Subtotal (95% CI)			**100.0%**	**0.90 [0.61 , 1.34]**
Heterogeneity: Chi² = 1.11, df = 3 (P = 0.77); I² = 0%				
Test for overall effect: Z = 0.50 (P = 0.62)				
1.1.2 Local Recurrence Rates				
DeLorenzi 2016 (1)	0.4574	0.2928	31.7%	1.58 [0.89 , 2.80]
DeLorenzi 2018	0.4886	0.3695	19.9%	1.63 [0.79 , 3.36]
Mansell 2017	-0.1863	0.7523	4.8%	0.83 [0.19 , 3.63]
Vieira 2016 (2)	0.1133	0.2498	43.6%	1.12 [0.69 , 1.83]
Subtotal (95% CI)			**100.0%**	**1.33 [0.96 , 1.83]**
Heterogeneity: Chi² = 1.52, df = 3 (P = 0.68); I² = 0%				
Test for overall effect: Z = 1.71 (P = 0.09)				



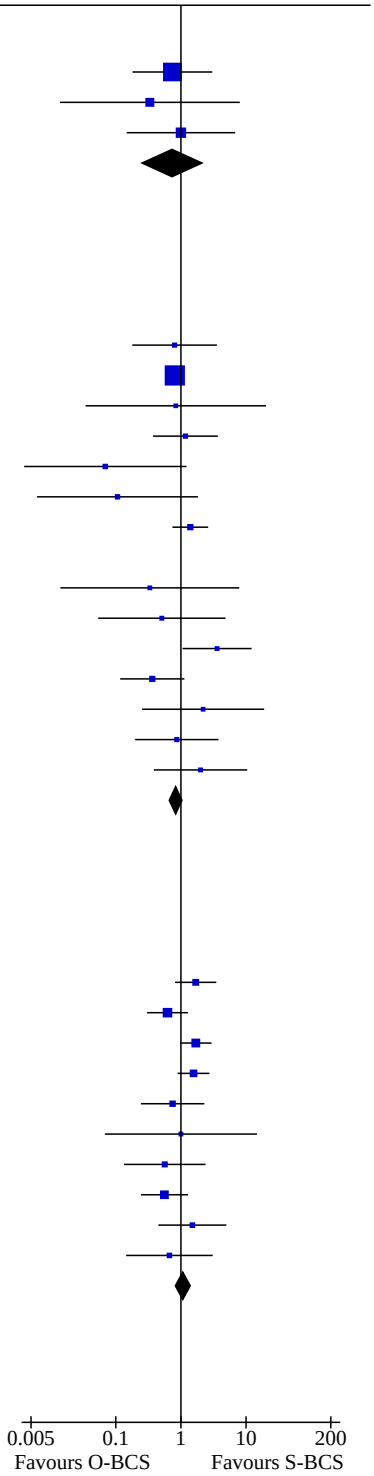
Footnotes

(1) follow up not 5 years median (months): 40.8 (range 0-109.2)

(2) Estimated from Kaplan Meier graph

Analysis 1.2. Comparison 1: Any O-BCS versus S-BCS, Outcome 2: Local recurrence

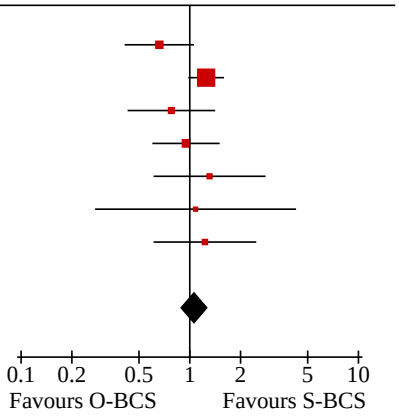
Study or Subgroup	O-BCS Events	O-BCS Total	S-BCS Events	S-BCS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 1 year						
DeLorenzi 2018	2	44	23	375	58.0%	0.74 [0.18 , 3.04]
Matrai 2014	0	60	1	60	18.0%	0.33 [0.01 , 8.02]
Piper 2016	2	49	2	49	24.0%	1.00 [0.15 , 6.82]
Subtotal (95% CI)		**153**		**484**	**100.0%**	**0.73 [0.25 , 2.10]**
Total events:	4		26			
Heterogeneity: Chi² = 0.34, df = 2 (P = 0.84); I² = 0%						
Test for overall effect: Z = 0.58 (P = 0.56)						
1.2.2 1 to 5 years						
Amitai 2018	2	67	10	268	2.5%	0.80 [0.18 , 3.57]
Carter 2016	56	1078	207	3211	64.6%	0.81 [0.60 , 1.07]
Cassi 2016	0	61	1	154	0.5%	0.83 [0.03 , 20.18]
Chakravorty 2012	4	150	10	440	3.2%	1.17 [0.37 , 3.69]
Chauhan 2016 (1)	0	57	5	43	3.9%	0.07 [0.00 , 1.21]
Chauhan 2016 (2)	0	33	6	46	3.4%	0.11 [0.01 , 1.82]
DeLorenzi 2018	9	44	55	375	7.2%	1.39 [0.74 , 2.62]
Down 2013	0	37	0	121		Not estimable
Fan 2019	0	29	1	29	0.9%	0.33 [0.01 , 7.86]
Gulcelik 2013	1	106	3	162	1.5%	0.51 [0.05 , 4.83]
Hashimoto 2019	4	183	7	1150	1.2%	3.59 [1.06 , 12.15]
Keleman 2019	4	350	11	350	6.8%	0.36 [0.12 , 1.13]
Malhaire 2015	4	73	1	40	0.8%	2.19 [0.25 , 18.95]
Mazouni 2013	2	45	11	214	2.4%	0.86 [0.20 , 3.77]
Piper 2016	4	49	2	49	1.2%	2.00 [0.38 , 10.42]
Subtotal (95% CI)		**2362**		**6652**	**100.0%**	**0.83 [0.66 , 1.04]**
Total events:	90		330			
Heterogeneity: Chi² = 17.85, df = 13 (P = 0.16); I² = 27%						
Test for overall effect: Z = 1.64 (P = 0.10)						
1.2.3 5 years						
Acea-Nebril 2017	10	170	22	631	9.5%	1.69 [0.81 , 3.49]
Borm 2019	9	288	34	677	20.6%	0.62 [0.30 , 1.28]
DeLorenzi 2016 (1)	22	454	26	908	17.6%	1.69 [0.97 , 2.95]
DeLorenzi 2018	11	44	60	375	12.8%	1.56 [0.89 , 2.74]
Lee 2018	4	260	12	582	7.5%	0.75 [0.24 , 2.29]
Losken 2009	1	17	1	17	1.0%	1.00 [0.07 , 14.72]
Mansell 2017	2	104	19	558	6.1%	0.56 [0.13 , 2.39]
Niinikoski 2019 (2)	7	471	25	940	16.9%	0.56 [0.24 , 1.28]
Piper 2016	6	49	4	49	4.1%	1.50 [0.45 , 4.99]
Vieira 2016	2	26	6	52	4.1%	0.67 [0.14 , 3.08]
Subtotal (95% CI)		**1883**		**4789**	**100.0%**	**1.07 [0.82 , 1.39]**
Total events:	74		209			
Heterogeneity: Chi² = 12.21, df = 9 (P = 0.20); I² = 26%						
Test for overall effect: Z = 0.49 (P = 0.63)						



Analysis 1.3. Comparison 1: Any O-BCS versus S-BCS, Outcome 3: Disease-free survival (HR)

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
Borm 2019	-0.4155	0.2417	13.4%	0.66 [0.41 , 1.06]
DeLorenzi 2016 (1)	0.2231	0.1242	50.9%	1.25 [0.98 , 1.59]
DeLorenzi 2018 (1)	-0.2513	0.305	8.4%	0.78 [0.43 , 1.41]
Gulcelik 2013 (2)	-0.0513	0.2345	14.3%	0.95 [0.60 , 1.50]
Mansell 2017	0.27	0.39	5.2%	1.31 [0.61 , 2.81]
Mazouni 2013 (3)	0.0791	0.7	1.6%	1.08 [0.27 , 4.27]
Rose 2019	0.207	0.3578	6.1%	1.23 [0.61 , 2.48]
Total (95% CI)			**100.0%**	**1.06 [0.89 , 1.26]**

Heterogeneity: Chi² = 7.32, df = 6 (P = 0.29); I² = 18%
Test for overall effect: Z = 0.64 (P = 0.52)
Test for subgroup differences: Not applicable

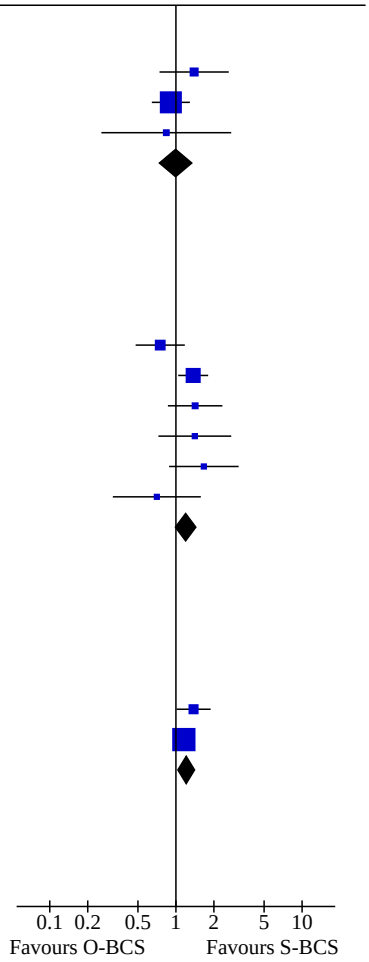


Footnotes

(1) Estimated from Kaplan Meier graph
(2) Estimated from Kaplan Meier graph, follow up not 5 years median (months): 33 (range; 9-41)
(3) Estimated from Kaplan Meier graph, follow up not 5 years median (months): 46

Analysis 1.4. Comparison 1: Any O-BCS versus S-BCS, Outcome 4: Disease-free survival (RR)

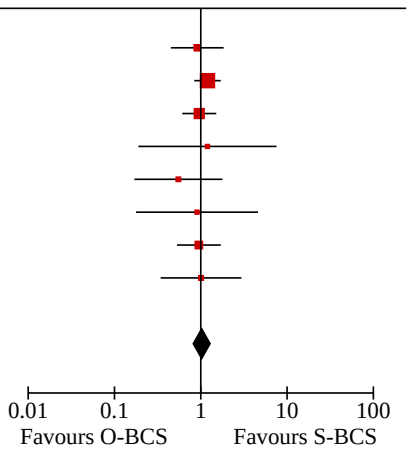
Study or Subgroup	O-BCS Events	O-BCS Total	S-BCS Events	S-BCS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 1 to 5 years						
DeLorenzi 2018	9	44	55	375	18.5%	1.39 [0.74 , 2.62]
Gulcelik 2013	34	106	57	162	72.1%	0.91 [0.64 , 1.29]
Mazouni 2013	3	45	17	214	9.4%	0.84 [0.26 , 2.74]
Subtotal (95% CI)		**195**		**751**	**100.0%**	**0.99 [0.74 , 1.34]**
Total events:	46		129			
Heterogeneity: Chi² = 1.42, df = 2 (P = 0.49); I² = 0%						
Test for overall effect: Z = 0.04 (P = 0.97)						
1.4.2 5 years						
Borm 2019	23	288	72	677	25.8%	0.75 [0.48 , 1.18]
DeLorenzi 2016 (1)	74	454	108	908	43.3%	1.37 [1.04 , 1.80]
DeLorenzi 2018	13	44	78	375	9.9%	1.42 [0.86 , 2.34]
Mansell 2017	10	104	38	558	7.2%	1.41 [0.73 , 2.74]
Rose 2019	11	183	50	1385	7.0%	1.67 [0.88 , 3.14]
Vieira 2016	6	26	17	52	6.8%	0.71 [0.32 , 1.58]
Subtotal (95% CI)		**1099**		**3955**	**100.0%**	**1.19 [0.99 , 1.44]**
Total events:	137		363			
Heterogeneity: Chi² = 8.50, df = 5 (P = 0.13); I² = 41%						
Test for overall effect: Z = 1.86 (P = 0.06)						
1.4.3 10 years						
Acea-Nebril 2017	42	170	113	631	22.8%	1.38 [1.01 , 1.88]
DeLorenzi 2016 (1)	141	454	244	908	77.2%	1.16 [0.97 , 1.38]
Subtotal (95% CI)		**624**		**1539**	**100.0%**	**1.21 [1.04 , 1.40]**
Total events:	183		357			
Heterogeneity: Chi² = 0.95, df = 1 (P = 0.33); I² = 0%						
Test for overall effect: Z = 2.43 (P = 0.02)						



Analysis 1.5. Comparison 1: Any O-BCS versus S-BCS, Outcome 5: Overall survival (HR)

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
Borm 2019	-0.0943	0.3593	10.0%	0.91 [0.45 , 1.84]
Carter 2016 (1)	0.179	0.1803	39.9%	1.20 [0.84 , 1.70]
DeLorenzi 2016 (1)	-0.0408	0.2314	24.2%	0.96 [0.61 , 1.51]
DeLorenzi 2018 (2)	0.1778	0.94	1.5%	1.19 [0.19 , 7.54]
Mansell 2017	-0.5978	0.5991	3.6%	0.55 [0.17 , 1.78]
Mazouni 2013 (2)	-0.1	0.83	1.9%	0.90 [0.18 , 4.60]
Rose 2019	-0.0513	0.2978	14.6%	0.95 [0.53 , 1.70]
Vieira 2016 (2)	0.0069	0.55	4.3%	1.01 [0.34 , 2.96]
Total (95% CI)			**100.0%**	**1.02 [0.82 , 1.28]**

Heterogeneity: Chi² = 2.12, df = 7 (P = 0.95); I² = 0%
Test for overall effect: Z = 0.21 (P = 0.83)
Test for subgroup differences: Not applicable

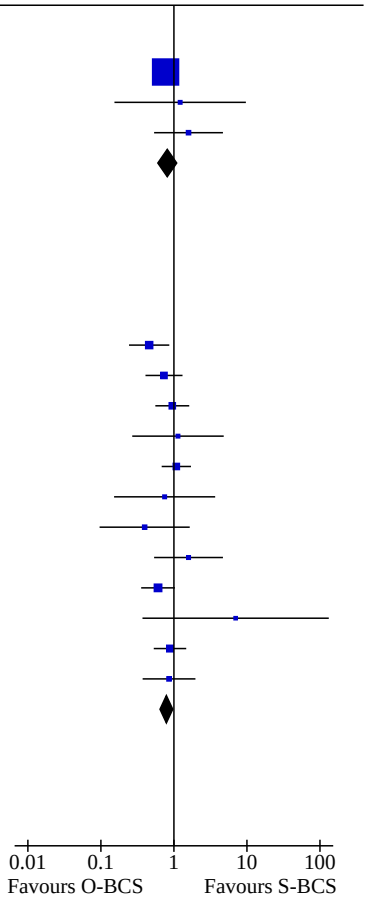


Footnotes

(1) follow up not 5 years median (months): 40.8 (range 0-109.2)
(2) Estimated from Kaplan Meier graph

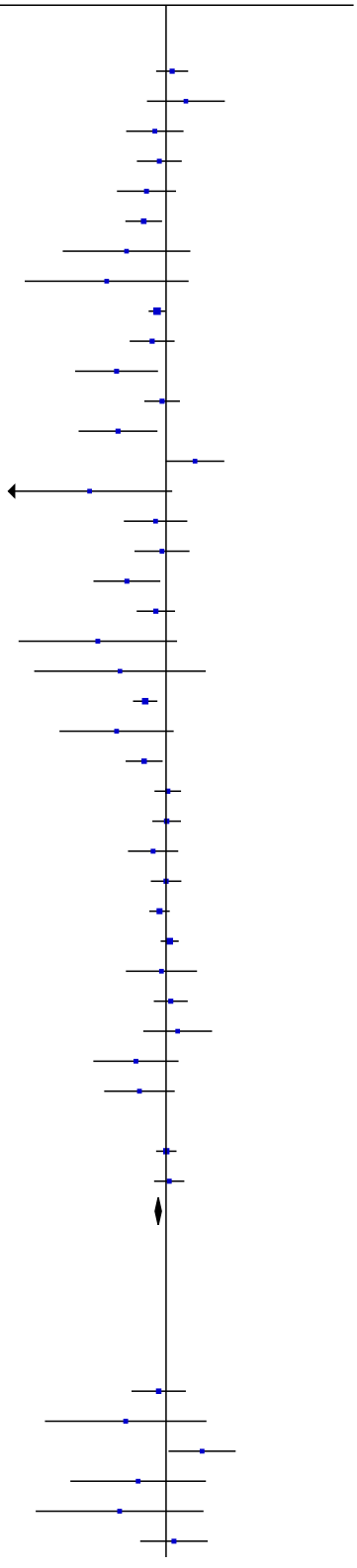
Analysis 1.6. Comparison 1: Any O-BCS versus S-BCS, Outcome 6: Overall survival (RR)

Study or Subgroup	O-BCS Events	O-BCS Total	S-BCS Events	S-BCS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.6.1 1 to 5 years						
Carter 2016	47	1079	182	3213	94.2%	0.77 [0.56 , 1.05]
DeLorenzi 2018	1	44	7	375	1.5%	1.22 [0.15 , 9.67]
Mazouni 2013	4	45	12	214	4.3%	1.59 [0.54 , 4.69]
Subtotal (95% CI)		**1168**		**3802**	**100.0%**	**0.81 [0.60 , 1.09]**
Total events:	52		201			
Heterogeneity: Chi² = 1.72, df = 2 (P = 0.42); I² = 0%						
Test for overall effect: Z = 1.38 (P = 0.17)						
1.6.2 5 years						
Acea-Nebril 2017	10	170	81	631	16.3%	0.46 [0.24 , 0.86]
Borm 2019	14	288	45	677	12.7%	0.73 [0.41 , 1.31]
DeLorenzi 2016 (1)	19	454	40	908	12.6%	0.95 [0.56 , 1.62]
DeLorenzi 2018	2	44	15	375	1.5%	1.14 [0.27 , 4.81]
Gulcelik 2013	24	106	34	162	12.7%	1.08 [0.68 , 1.71]
Lee 2018	2	260	6	582	1.8%	0.75 [0.15 , 3.67]
Mansell 2017	2	104	27	558	4.0%	0.40 [0.10 , 1.65]
Mazouni 2013	4	45	12	214	2.0%	1.59 [0.54 , 4.69]
Niinikoski 2019 (2)	17	471	56	940	17.7%	0.61 [0.36 , 1.03]
Piper 2016	3	49	0	49	0.2%	7.00 [0.37 , 132.03]
Rose 2019	15	182	129	1383	14.2%	0.88 [0.53 , 1.47]
Vieira 2016	6	26	14	52	4.4%	0.86 [0.37 , 1.97]
Subtotal (95% CI)		**2199**		**6531**	**100.0%**	**0.79 [0.65 , 0.96]**
Total events:	118		459			
Heterogeneity: Chi² = 11.15, df = 11 (P = 0.43); I² = 1%						
Test for overall effect: Z = 2.33 (P = 0.02)						



Analysis 1.7. Comparison 1: Any O-BCS versus S-BCS, Outcome 7: Re-excision rates

Study or Subgroup	O-BCS Events	O-BCS Total	S-BCS Events	S-BCS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.7.1 Total re-excisions						
Acea-Nebril 2017	15	170	45	631	2.7%	1.24 [0.71 , 2.16]
Amitai 2018	3	67	6	268	0.3%	2.00 [0.51 , 7.79]
Atallah 2015	9	193	6	87	1.2%	0.68 [0.25 , 1.84]
Bali 2018	6	35	36	166	1.8%	0.79 [0.36 , 1.73]
Cassi 2016	4	61	20	154	1.6%	0.50 [0.18 , 1.42]
Chakravorty 2012	10	150	64	440	4.6%	0.46 [0.24 , 0.87]
Chauhan 2016 (1)	1	57	3	43	0.5%	0.25 [0.03 , 2.33]
Chauhan 2016 (2)	0	33	5	46	0.7%	0.13 [0.01 , 2.20]
Crown 2015	60	387	90	425	12.2%	0.73 [0.54 , 0.98]
DeLorenzi 2016 (1)	8	454	26	908	2.5%	0.62 [0.28 , 1.35]
Di Micco 2017	2	70	14	87	1.8%	0.18 [0.04 , 0.76]
Dolan 2015	13	83	23	128	2.6%	0.87 [0.47 , 1.62]
Down 2013	2	37	35	121	2.3%	0.19 [0.05 , 0.74]
Fan 2019	11	29	4	29	0.6%	2.75 [0.99 , 7.64]
Farooqi 2019	0	146	5	111	0.9%	0.07 [0.00 , 1.24]
Gicalone 2007 (1)	4	31	8	43	1.0%	0.69 [0.23 , 2.10]
Gicalone 2007 (2)	5	39	13	88	1.1%	0.87 [0.33 , 2.27]
Gicalone 2015	3	42	16	57	1.9%	0.25 [0.08 , 0.82]
Gulcelik 2013	11	106	24	162	2.7%	0.70 [0.36 , 1.37]
Hamdi 2008	0	26	25	126	1.3%	0.09 [0.01 , 1.47]
Jiang 2015	0	30	2	30	0.4%	0.20 [0.01 , 4.00]
Keleman 2019	28	350	58	350	8.3%	0.48 [0.32 , 0.74]
Lansu 2014	1	19	8	27	0.9%	0.18 [0.02 , 1.31]
Losken 2014	10	83	36	139	3.8%	0.47 [0.24 , 0.89]
Malhaire 2015	31	73	16	40	2.9%	1.06 [0.67 , 1.69]
Mansell 2015	16	119	79	600	3.7%	1.02 [0.62 , 1.68]
Matrai 2014	7	60	11	60	1.6%	0.64 [0.26 , 1.53]
Mazouni 2013	12	45	57	214	2.8%	1.00 [0.59 , 1.71]
Mukhtar 2018	20	49	142	277	6.1%	0.80 [0.56 , 1.14]
Niinikoski 2019 (2)	56	611	96	1189	9.3%	1.14 [0.83 , 1.56]
Ojala 2017	3	86	12	293	0.8%	0.85 [0.25 , 2.95]
Palsodittlir 2018	11	85	73	665	2.4%	1.18 [0.65 , 2.13]
Piper 2016	6	49	4	49	0.6%	1.50 [0.45 , 4.99]
Tang 2016	2	67	10	117	1.0%	0.35 [0.08 , 1.55]
Tenofsky 2014	3	58	11	84	1.3%	0.39 [0.12 , 1.35]
Vieira 2016	0	26	0	52		Not estimable
Wijgman 2017	42	314	70	528	7.4%	1.01 [0.71 , 1.44]
Wong 2017	11	30	45	137	2.3%	1.12 [0.66 , 1.89]
Subtotal (95% CI)		**4370**		**8971**	**100.0%**	**0.76 [0.69 , 0.85]**
Total events:	426		1198			
Heterogeneity: Chi² = 63.37, df = 36 (P = 0.003); I² = 43%						
Test for overall effect: Z = 5.09 (P < 0.00001)						
1.7.2 Mastectomies						
Acea-Nebril 2017	5	170	24	631	4.1%	0.77 [0.30 , 2.00]
Bali 2018	0	35	9	166	1.3%	0.24 [0.01 , 4.10]
Chakravorty 2012	6	150	5	440	1.0%	3.52 [1.09 , 11.37]
Chauhan 2016 (1)	1	57	2	43	0.9%	0.38 [0.04 , 4.03]
Chauhan 2016 (2)	0	33	3	46	1.2%	0.20 [0.01 , 3.70]
Crown 2015	6	387	5	425	1.9%	1.32 [0.41 , 4.28]



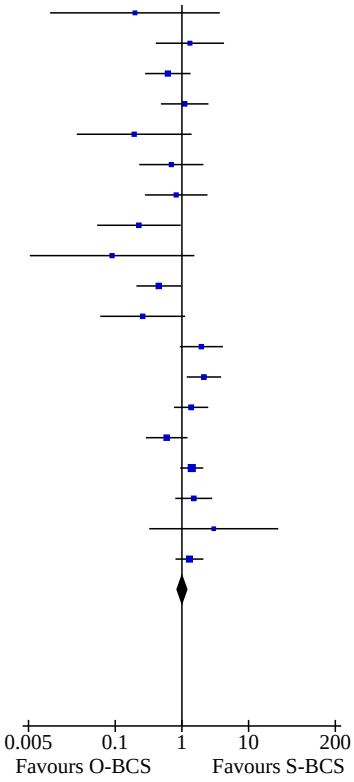
Analysis 1.7. (Continued)

Chaunan 2016 (2)	0	33	3	46	1.2%	0.20 [0.01 , 3.70]
Crown 2015	6	387	5	425	1.9%	1.32 [0.41 , 4.28]
DeLorenzi 2016 (1)	8	454	26	908	6.9%	0.62 [0.28 , 1.35]
Dolan 2015	11	128	10	128	4.0%	1.10 [0.48 , 2.50]
Down 2013	1	37	17	121	3.2%	0.19 [0.03 , 1.40]
Gicalone 2007 (1)	4	31	8	43	2.7%	0.69 [0.23 , 2.10]
Gicalone 2007 (2)	4	39	11	88	2.7%	0.82 [0.28 , 2.42]
Gicalone 2015	2	42	12	57	4.1%	0.23 [0.05 , 0.96]
Gulcelik 2013	0	106	8	162	2.7%	0.09 [0.01 , 1.54]
Keleman 2019	9	350	20	350	8.0%	0.45 [0.21 , 0.97]
Losken 2014	2	83	13	139	3.9%	0.26 [0.06 , 1.11]
Malhaire 2015	25	73	7	40	3.6%	1.96 [0.93 , 4.12]
Mansell 2015	14	119	33	600	4.4%	2.14 [1.18 , 3.87]
Mazouni 2013	11	45	38	214	5.3%	1.38 [0.76 , 2.48]
Mukhtar 2018	7	49	67	277	8.0%	0.59 [0.29 , 1.21]
Niinikoski 2019 (2)	39	611	54	1189	14.6%	1.41 [0.94 , 2.10]
Palsodittlir 2018	10	85	52	665	4.7%	1.50 [0.79 , 2.85]
Piper 2016	3	49	1	49	0.4%	3.00 [0.32 , 27.85]
Wijgman 2017	27	314	35	528	10.4%	1.30 [0.80 , 2.10]
Subtotal (95% CI)		**3447**		**7309**	**100.0%**	**1.00 [0.85 , 1.18]**
Total events:	195		460			

Heterogeneity: Chi² = 45.71, df = 22 (P = 0.002); I² = 52%

Test for overall effect: Z = 0.00 (P = 1.00)

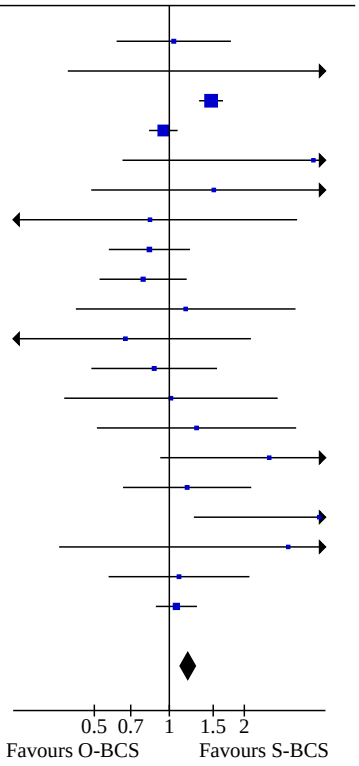
Test for subgroup differences: Chi² = 7.36, df = 1 (P = 0.007), I² = 86.4%



Analysis 1.8. Comparison 1: Any O-BCS versus S-BCS, Outcome 8: Complications

Study or Subgroup	O-BCS Events	O-BCS Total	S-BCS Events	S-BCS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Acea-Nebril 2017	16	170	57	631	2.2%	1.04 [0.61 , 1.77]
Acosta-Marin 2014	3	52	0	55	0.0%	7.40 [0.39 , 139.81]
Angarita 2020	346	9126	2587	100361	38.7%	1.47 [1.32 , 1.64]
Carter 2016	231	939	587	2258	30.9%	0.95 [0.83 , 1.08]
Cassi 2016	3	61	2	154	0.1%	3.79 [0.65 , 22.11]
Chauhan 2016 (1)	8	57	4	43	0.4%	1.51 [0.49 , 4.68]
Chauhan 2016 (2)	3	33	5	46	0.4%	0.84 [0.21 , 3.26]
Crown 2015	43	288	49	273	4.5%	0.83 [0.57 , 1.21]
Di Micco 2017	24	70	38	87	3.0%	0.78 [0.52 , 1.17]
Gicalone 2015	6	42	7	57	0.5%	1.16 [0.42 , 3.21]
Jiang 2015	4	30	6	30	0.5%	0.67 [0.21 , 2.13]
Keleman 2019	20	350	23	350	2.1%	0.87 [0.49 , 1.55]
Lansu 2014	5	19	7	27	0.5%	1.02 [0.38 , 2.72]
Matrai 2014	9	60	7	60	0.6%	1.29 [0.51 , 3.23]
Ozmen 2016	13	157	5	152	0.5%	2.52 [0.92 , 6.89]
Palsodittlir 2018	11	85	73	665	1.5%	1.18 [0.65 , 2.13]
PlaFarnos 2018	8	60	4	120	0.2%	4.00 [1.25 , 12.75]
Scheter 2019	3	12	1	12	0.1%	3.00 [0.36 , 24.92]
Sherwell-Cabello 2006	14	76	16	95	1.3%	1.09 [0.57 , 2.10]
Wijgman 2017	113	314	178	528	11.9%	1.07 [0.88 , 1.29]
Total (95% CI)		**12001**		**106004**	**100.0%**	**1.19 [1.10 , 1.27]**
Total events:	883		3656			

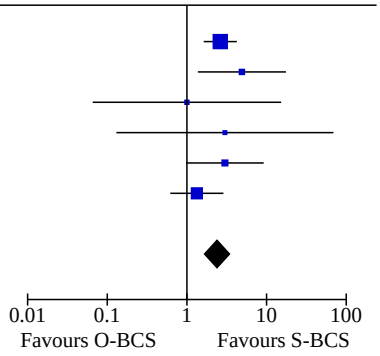
Heterogeneity: Chi² = 47.74, df = 19 (P = 0.0003); I² = 60%
Test for overall effect: Z = 4.74 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.9. Comparison 1: Any O-BCS versus S-BCS, Outcome 9: Recall rates

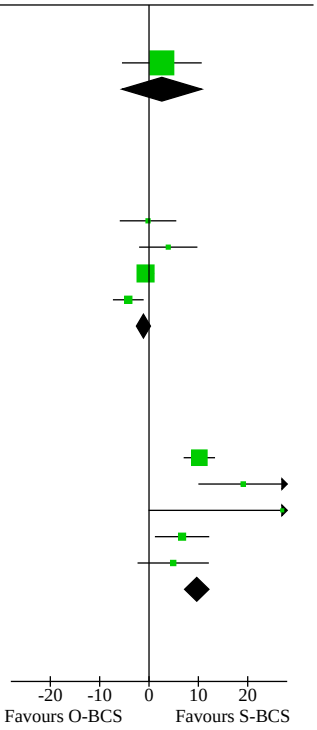
Study or Subgroup	O-BCS Events	O-BCS Total	S-BCS Events	S-BCS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Amitai 2018	21	62	31	240	44.7%	2.62 [1.63 , 4.23]
Dolan 2015	9	71	3	116	8.0%	4.90 [1.37 , 17.50]
Fan 2019	1	29	1	29	3.5%	1.00 [0.07 , 15.24]
Hu 2019	1	18	0	18	1.8%	3.00 [0.13 , 69.09]
Losken 2009	9	17	3	17	10.5%	3.00 [0.98 , 9.20]
Piper 2016	12	49	9	49	31.6%	1.33 [0.62 , 2.87]
Total (95% CI)		**246**		**469**	**100.0%**	**2.39 [1.67 , 3.42]**
Total events:	53		47			

Heterogeneity: Chi² = 4.16, df = 5 (P = 0.53); I² = 0%
Test for overall effect: Z = 4.74 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.10. Comparison 1: Any O-BCS versus S-BCS, Outcome 10: Time to therapy

Study or Subgroup	O-BCS Mean	O-BCS SD	O-BCS Total	S-BCS Mean	S-BCS SD	S-BCS Total	Weight	Mean Difference IV, Fixed, 95% CI
1.10.1 Any adjuvant therapy								
Matrai 2014	39.8	20.13	60	37.2	24.79	60	100.0%	2.60 [-5.48 , 10.68]
Subtotal (95% CI)			**60**			**60**	**100.0%**	**2.60 [-5.48 , 10.68]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.63 (P = 0.53)								
1.10.2 Chemotherapy								
Acea-Nebril 2017	57.9	31.6	170	58.1	41	631	6.2%	-0.20 [-5.93 , 5.53]
Borm 2019	68.4	41.9	289	64.5	42.8	611	5.8%	3.90 [-2.00 , 9.80]
Klit 2017	34.2	13.9537	445	34.9	16.8754	824	67.2%	-0.70 [-2.43 , 1.03]
Rose 2019	36.7	21.7	197	40.9	13.6	1399	20.9%	-4.20 [-7.31 , -1.09]
Subtotal (95% CI)			**1101**			**3465**	**100.0%**	**-1.13 [-2.55 , 0.29]**
Heterogeneity: Chi² = 6.86, df = 3 (P = 0.08); I² = 56%								
Test for overall effect: Z = 1.56 (P = 0.12)								
1.10.3 Radiotherapy								
Acea-Nebril 2017	77.5	16.6	170	67.3	25.2	631	60.2%	10.20 [7.02 , 13.38]
Borm 2019	105	68	289	85.9	61.2	677	7.3%	19.10 [10.01 , 28.19]
Cassi 2016	153	93	61	126	87	154	0.8%	27.00 [-0.08 , 54.08]
Rose 2019	60.6	38	197	53.9	28	1399	20.0%	6.70 [1.19 , 12.21]
Tenofsky 2014	56	20.4	58	51.1	23.2	84	11.6%	4.90 [-2.32 , 12.12]
Subtotal (95% CI)			**775**			**2945**	**100.0%**	**9.67 [7.21 , 12.14]**
Heterogeneity: Chi² = 8.60, df = 4 (P = 0.07); I² = 54%								
Test for overall effect: Z = 7.70 (P < 0.00001)								
Test for subgroup differences: Chi² = 55.50, df = 2 (P < 0.00001), I² = 96.4%								



Analysis 1.11. Comparison 1: Any O-BCS versus S-BCS, Outcome 11: Patient-reported outcomes (BREAST-Q)

Patient-reported outcomes (BREAST-Q)

Study	Intervention details (type - n)	Intervention BREAST-Q (n/100)	Control	Statistics	Conclusion
Acea-Nebril 2017	VD - 60	> 80 in all domains	-	-	No comparison
Di Micco 2017	VD -170	Median: psychological = 83; satisfaction with breast = 82 evolution = 73, sexual = 70	-	-	No comparison
PlaFarnos 2018	VD - 70	Median (IQR): satisfaction with breast: 80 (0-100); psychosocial well-being: 76 (0-100); sexual well being: 46 (26-100); physical well-being: 81 (37-100)	Median (IQR): satisfaction with breast: 68 (IQR 29-100); psychosocial well-being: 82 (0-100); sexual well-being: 57 (0-100); physical well-being: 75 (17-100) P = 0.32/0.71/0.08/0.422	P value: 0.32/0.705/0.079/0.422	No significant difference (SD) in any domain
Rose 2020	Both - 96	No. of patients above median score psychosocial: 2.15 (1.25-3.69); physical: 0.83 (0.5-1.39); satisfaction with breast: 0.95 (0.57-1.59); sexual well-being 1.42 (0.78-2.58)	No. of patients above median score: psychosocial: 2.15 (1.25-3.69); physical: 0.83 (0.5-1.39); satisfaction with breast 0.95 (0.57-1.59); sexual well-being; 1.42 (0.78-2.58)	Odds ratio psychosocial: 2.15 (1.25-3.69); physical: 0.83 (0.5-1.39); satisfaction with breast 0.95 (0.57-1.59); sexual well-being: 1.42 (0.78-2.58)	Better psychosocial well-being in O-BCS. No SD in any other domain
Scheter 2019	VD - 12	Mean score per domains: satisfaction with breast: 75.18; psychosocial well-being: 76.09; sexual well-being: 78	Satisfaction with breast: 39.64; psychosocial well-being: 43.18; sexual well-being: 41	0.001/0.025/0.021	O-BCS better in satisfaction of breast, psychosocial wellbeing and sexual well-being

Analysis 1.12. Comparison 1: Any O-BCS versus S-BCS, Outcome 12: Aesthetic outcome BCCT.core

Aesthetic outcome BCCT.core

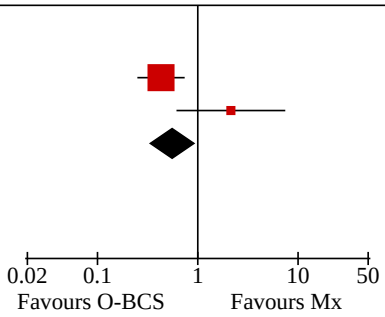
Study	Intervention type	BCCT.core - Intervention	BCCT.core - Control	P value	Conclusion
Hilli-Betz 2014	VD	Excellent: 4.3%, good: 75.4%, moderate: 18.8%	BCCT.core Excellent: 10.6%, good: 77.0%, moderate in 5.6%, poor in 0.6%	< 0.001	OPS significantly worse in expert panel cosmetic than standard segnentectomy
Lansu 2014	VD	Mean (SD) 2.45 (0.52)	Mean (SD) 2.11 (0.6)	0.02	OPS significantly better than control
Santos 2015	VD	BCCT.core: Excellent: 22.8%, good: 54.4%, moderate: 21.1%, bad:1.8%, poor in 1.8%	BCCT.core Excellent: 6.2%, good: 73.8%, moderate: 15.4%, poor: 4.6%	0.004	OPS significantly better than control

Comparison 2. Any O-BCS versus mastectomy (Mx)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Local recurrence (HR)	2		Hazard Ratio (IV, Fixed, 95% CI)	Subtotals only
2.1.1 Local recurrence-free survival	2		Hazard Ratio (IV, Fixed, 95% CI)	0.55 [0.34, 0.91]
2.2 Local recurrence (RR)	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.2.1 1 to 5 years	2	4025	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.24, 0.41]
2.2.2 5 years	2	942	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.41, 1.75]
2.2.3 10 years	1	1193	Risk Ratio (M-H, Fixed, 95% CI)	6.52 [1.42, 30.06]
2.3 Disease-free survival	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.3.1 10 years	1	1193	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.41, 0.82]
2.4 Overall survival (HR)	2		Hazard Ratio (IV, Fixed, 95% CI)	0.39 [0.30, 0.51]
2.5 Overall survival (RR)	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.5.1 1 to 5 years	1	3924	Risk Ratio (M-H, Fixed, 95% CI)	0.30 [0.22, 0.40]
2.5.2 5 years	2	932	Risk Ratio (M-H, Fixed, 95% CI)	1.71 [0.79, 3.69]
2.6 Complications	4	4839	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.67, 0.83]
2.7 Time to therapy	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.7.1 Chemotherapy	1	974	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-2.23, 2.03]

Analysis 2.1. Comparison 2: Any O-BCS versus mastectomy (Mx), Outcome 1: Local recurrence (HR)

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
2.1.1 Local recurrence-free survival				
Carter 2016 (1)	-0.844	0.277	84.1%	0.43 [0.25 , 0.74]
Ren 2014 (2)	0.76	0.6372	15.9%	2.14 [0.61 , 7.46]
Subtotal (95% CI)			**100.0%**	**0.55 [0.34 , 0.91]**
Heterogeneity: Chi² = 5.33, df = 1 (P = 0.02); I² = 81%				
Test for overall effect: Z = 2.32 (P = 0.02)				
Test for subgroup differences: Not applicable				



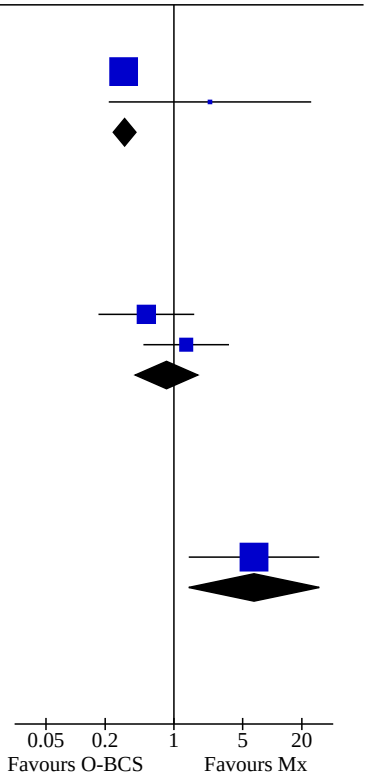
Footnotes

(1) follow up not 5 years median (months): 40.8 (range 0-109.2)

(2) Estimated from Kaplan Meier graph

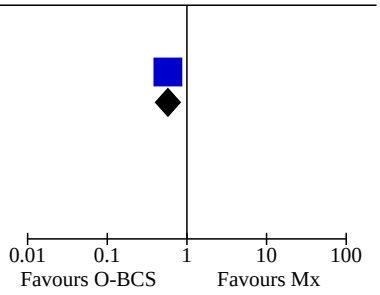
Analysis 2.2. Comparison 2: Any O-BCS versus mastectomy (Mx), Outcome 2: Local recurrence (RR)

Study or Subgroup	OPS Events	OPS Total	Mx Events	Mx Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.1 1 to 5 years						
Carter 2016	56	1078	479	2841	99.7%	0.31 [0.24 , 0.40]
Gendy 2003	2	49	1	57	0.3%	2.33 [0.22 , 24.89]
Subtotal (95% CI)		**1127**		**2898**	**100.0%**	**0.32 [0.24 , 0.41]**
Total events:	58		480			
Heterogeneity: Chi² = 2.76, df = 1 (P = 0.10); I² = 64%						
Test for overall effect: Z = 8.55 (P < 0.00001)						
2.2.2 5 years						
Lee 2018	4	260	12	409	60.9%	0.52 [0.17 , 1.61]
Ren 2014	6	91	9	182	39.1%	1.33 [0.49 , 3.63]
Subtotal (95% CI)		**351**		**591**	**100.0%**	**0.84 [0.41 , 1.75]**
Total events:	10		21			
Heterogeneity: Chi² = 1.50, df = 1 (P = 0.22); I² = 33%						
Test for overall effect: Z = 0.46 (P = 0.64)						
2.2.3 10 years						
Nakagomi 2019	9	487	2	706	100.0%	6.52 [1.42 , 30.06]
Subtotal (95% CI)		**487**		**706**	**100.0%**	**6.52 [1.42 , 30.06]**
Total events:	9		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.41 (P = 0.02)						



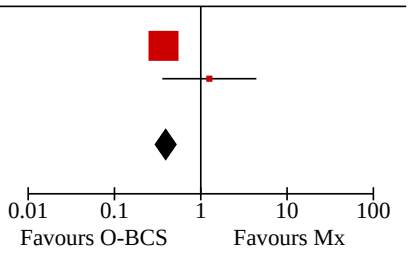
Analysis 2.3. Comparison 2: Any O-BCS versus mastectomy (Mx), Outcome 3: Disease-free survival

Study or Subgroup	O-BCS Events	O-BCS Total	Mx Events	Mx Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.3.1 10 years						
Nakagomi 2019	39	487	98	706	100.0%	0.58 [0.41 , 0.82]
Subtotal (95% CI)		**487**		**706**	**100.0%**	**0.58 [0.41 , 0.82]**
Total events:	39		98			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.06 (P = 0.002)						



Analysis 2.4. Comparison 2: Any O-BCS versus mastectomy (Mx), Outcome 4: Overall survival (HR)

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
Carter 2016 (1)	-0.9943	0.1422	95.3%	0.37 [0.28 , 0.49]
Ren 2014 (2)	0.2287	0.6403	4.7%	1.26 [0.36 , 4.41]
Total (95% CI)			**100.0%**	**0.39 [0.30 , 0.51]**
Heterogeneity: Chi² = 3.48, df = 1 (P = 0.06); I² = 71%				
Test for overall effect: Z = 6.75 (P < 0.00001)				
Test for subgroup differences: Not applicable				



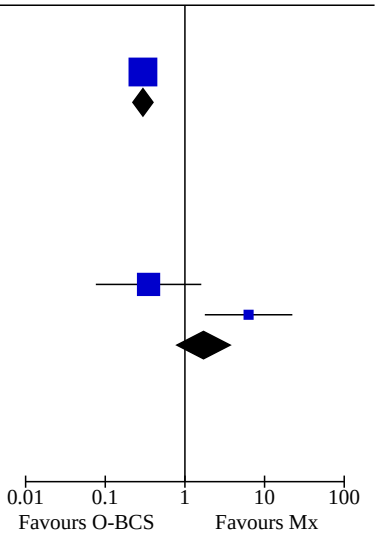
Footnotes

(1) follow up not 5 years median (months): 40.8 (range 0-109.2)

(2) Estimated from Kaplan Meier graph

Analysis 2.5. Comparison 2: Any O-BCS versus mastectomy (Mx), Outcome 5: Overall survival (RR)

Study or Subgroup	O-BCS Events	O-BCS Total	Mx Events	Mx Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.5.1 1 to 5 years						
Carter 2016 (1)	48	1079	426	2845	100.0%	0.30 [0.22 , 0.40]
Subtotal (95% CI)		**1079**		**2845**	**100.0%**	**0.30 [0.22 , 0.40]**
Total events:	48		426			
Heterogeneity: Not applicable						
Test for overall effect: Z = 8.20 (P < 0.00001)						
2.5.2 5 years						
Lee 2018	2	260	9	409	77.1%	0.35 [0.08 , 1.61]
Ren 2014	10	91	3	172	22.9%	6.30 [1.78 , 22.32]
Subtotal (95% CI)		**351**		**581**	**100.0%**	**1.71 [0.79 , 3.69]**
Total events:	12		12			
Heterogeneity: Chi² = 8.25, df = 1 (P = 0.004); I² = 88%						
Test for overall effect: Z = 1.37 (P = 0.17)						

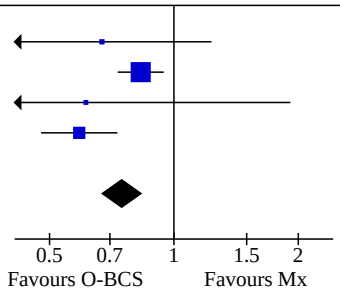


Footnotes

(1) follow up not 5 years median (months): 40.8 (range 0-109.2)

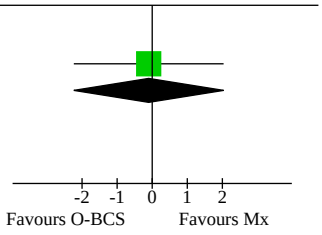
Analysis 2.6. Comparison 2: Any O-BCS versus mastectomy (Mx), Outcome 6: Complications

Study or Subgroup	O-BCS Events	O-BCS Total	Mx Events	Mx Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Acea-Nebril 2005	12	50	19	53	3.0%	0.67 [0.36 , 1.23]
Carter 2016	231	939	682	2304	64.2%	0.83 [0.73 , 0.95]
Gendy 2003	4	49	8	60	1.2%	0.61 [0.20 , 1.91]
Potter 2020	79	376	359	1008	31.7%	0.59 [0.48 , 0.73]
Total (95% CI)		**1414**		**3425**	**100.0%**	**0.75 [0.67 , 0.83]**
Total events:	326		1068			
Heterogeneity: Chi² = 7.61, df = 3 (P = 0.05); I² = 61%						
Test for overall effect: Z = 5.30 (P < 0.00001)						
Test for subgroup differences: Not applicable						



Analysis 2.7. Comparison 2: Any O-BCS versus mastectomy (Mx), Outcome 7: Time to therapy

Study or Subgroup	O-BCS Mean	O-BCS SD	O-BCS Total	Mx Mean	Mx SD	Mx Total	Weight	Mean Difference IV, Fixed, 95% CI
2.7.1 Chemotherapy								
Klit 2017	34.2	13.9537	445	34.3	19.9036	529	100.0%	-0.10 [-2.23 , 2.03]
Subtotal (95% CI)			**445**			**529**	**100.0%**	**-0.10 [-2.23 , 2.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.09 (P = 0.93)								
Test for subgroup differences: Not applicable								

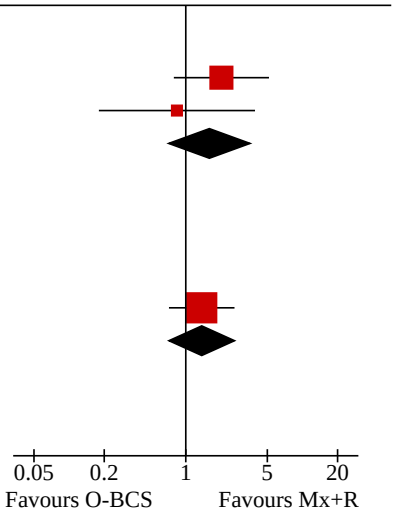


Comparison 3. Any O-BCS versus mastectomy plus reconstruction (Mx+R)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Local recurrence-free survival	3		Hazard Ratio (IV, Fixed, 95% CI)	Subtotals only
3.1.1 Local recurrence rate: Mx+/-R	2		Hazard Ratio (IV, Fixed, 95% CI)	1.59 [0.71, 3.55]
3.1.2 Local recurrence-free survival: Mx+R only	1		Hazard Ratio (IV, Fixed, 95% CI)	1.37 [0.72, 2.62]
3.2 Local recurrence	6		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.2.1 1 to 5 years	2	3449	Risk Ratio (M-H, Fixed, 95% CI)	1.19 [0.87, 1.64]
3.2.2 5 years: Mx+R only	2	830	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.19, 1.44]
3.2.3 5 years: Mx+/-R	2	1001	Risk Ratio (M-H, Fixed, 95% CI)	1.54 [0.74, 3.21]
3.3 Disease-free survival (HR): Mx+R	3		Hazard Ratio (IV, Fixed, 95% CI)	Subtotals only
3.3.1 Mx+/-R	2		Hazard Ratio (IV, Fixed, 95% CI)	1.03 [0.75, 1.42]
3.3.2 Mx+R only	1		Hazard Ratio (IV, Fixed, 95% CI)	0.45 [0.09, 2.22]
3.4 Disease-free survival (RR): Mx+R	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.4.1 5 years: Mx+R only	1	317	Risk Ratio (M-H, Fixed, 95% CI)	0.74 [0.27, 2.04]
3.4.2 5 years: Mx+/-R	2	1001	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.66, 1.18]
3.5 Overall survival (HR): Mx+R	4		Hazard Ratio (IV, Fixed, 95% CI)	Subtotals only
3.5.1 Mx+R only	2		Hazard Ratio (IV, Fixed, 95% CI)	1.74 [1.23, 2.47]
3.5.2 Mx+/-R	2		Hazard Ratio (IV, Fixed, 95% CI)	0.65 [0.40, 1.07]
3.6 Overall survival (RR): Mx+R	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.6.1 1 to 5 years	1	3387	Risk Ratio (M-H, Fixed, 95% CI)	1.39 [0.97, 1.98]
3.6.2 5 years: Mx only	2	830	Risk Ratio (M-H, Fixed, 95% CI)	0.74 [0.24, 2.28]
3.6.3 5 years: Mx+/-R	2	1001	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.33, 0.84]
3.7 Complications: Mx+R only	5	4973	Risk Ratio (M-H, Fixed, 95% CI)	0.49 [0.45, 0.54]

Analysis 3.1. Comparison 3: Any O-BCS versus mastectomy plus reconstruction (Mx+R), Outcome 1: Local recurrence-free survival

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
3.1.1 Local recurrence rate: Mx+/-R				
DeLorenzi 2016 (2)	0.7031	0.479	72.9%	2.02 [0.79 , 5.17]
Mansell 2017	-0.1744	0.786	27.1%	0.84 [0.18 , 3.92]
Subtotal (95% CI)			**100.0%**	**1.59 [0.71 , 3.55]**
Heterogeneity: Chi² = 0.91, df = 1 (P = 0.34); I² = 0%				
Test for overall effect: Z = 1.14 (P = 0.26)				
3.1.2 Local recurrence-free survival: Mx+R only				
Carter 2016 (1)	0.3148	0.3299	100.0%	1.37 [0.72 , 2.62]
Subtotal (95% CI)			**100.0%**	**1.37 [0.72 , 2.62]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.95 (P = 0.34)				
Test for subgroup differences: Chi² = 0.08, df = 1 (P = 0.77), I² = 0%				

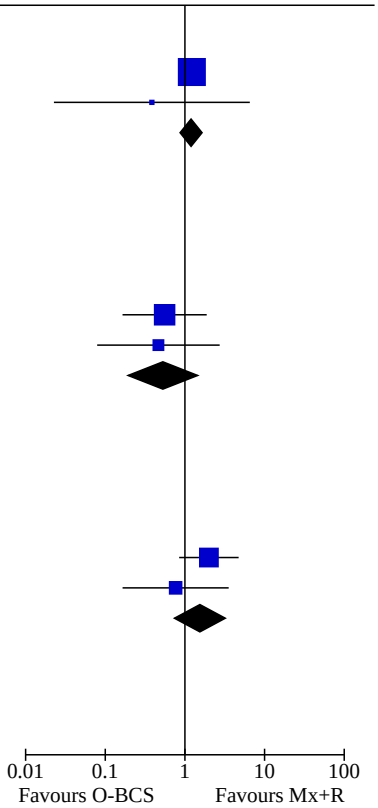


Footnotes

(1) follow up not 5 years median (months): 40.8 (range 0-109.2)

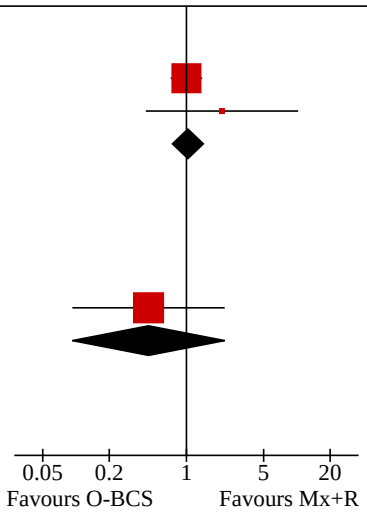
Analysis 3.2. Comparison 3: Any O-BCS versus mastectomy plus reconstruction (Mx+R), Outcome 2: Local recurrence

Study or Subgroup	O-BCS Events	O-BCS Total	Mx+R Events	Mx+R Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.2.1 1 to 5 years						
Carter 2016	56	1078	98	2305	96.7%	1.22 [0.89 , 1.68]
Mustonen 2004	0	12	5	54	3.3%	0.38 [0.02 , 6.53]
Subtotal (95% CI)		**1090**		**2359**	**100.0%**	**1.19 [0.87 , 1.64]**
Total events:	56		103			
Heterogeneity: Chi² = 0.63, df = 1 (P = 0.43); I² = 0%						
Test for overall effect: Z = 1.10 (P = 0.27)						
3.2.2 5 years: Mx+R only						
Lee 2018	4	260	7	253	69.9%	0.56 [0.16 , 1.88]
Ozmen 2020	3	242	2	75	30.1%	0.46 [0.08 , 2.73]
Subtotal (95% CI)		**502**		**328**	**100.0%**	**0.53 [0.19 , 1.44]**
Total events:	7		9			
Heterogeneity: Chi² = 0.03, df = 1 (P = 0.87); I² = 0%						
Test for overall effect: Z = 1.24 (P = 0.21)						
3.2.3 5 years: Mx+/-R						
DeLorenzi 2016 (1)	10	193	10	386	62.8%	2.00 [0.85 , 4.72]
Mansell 2017	2	104	8	318	37.2%	0.76 [0.16 , 3.54]
Subtotal (95% CI)		**297**		**704**	**100.0%**	**1.54 [0.74 , 3.21]**
Total events:	12		18			
Heterogeneity: Chi² = 1.16, df = 1 (P = 0.28); I² = 14%						
Test for overall effect: Z = 1.15 (P = 0.25)						
Test for subgroup differences: Chi² = 2.96, df = 2 (P = 0.23), I² = 32.3%						



Analysis 3.3. Comparison 3: Any O-BCS versus mastectomy plus reconstruction (Mx+R), Outcome 3: Disease-free survival (HR): Mx+R

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
3.3.1 Mx+/-R				
DeLorenzi 2016 (2)	0	0.1676	95.9%	1.00 [0.72 , 1.39]
Mansell 2017	0.7414	0.81	4.1%	2.10 [0.43 , 10.27]
Subtotal (95% CI)			**100.0%**	**1.03 [0.75 , 1.42]**
Heterogeneity: Chi² = 0.80, df = 1 (P = 0.37); I² = 0%				
Test for overall effect: Z = 0.19 (P = 0.85)				
3.3.2 Mx+R only				
Ozmen 2020 (1)	-0.79	0.81	100.0%	0.45 [0.09 , 2.22]
Subtotal (95% CI)			**100.0%**	**0.45 [0.09 , 2.22]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.98 (P = 0.33)				
Test for subgroup differences: Chi² = 0.99, df = 1 (P = 0.32), I² = 0%				

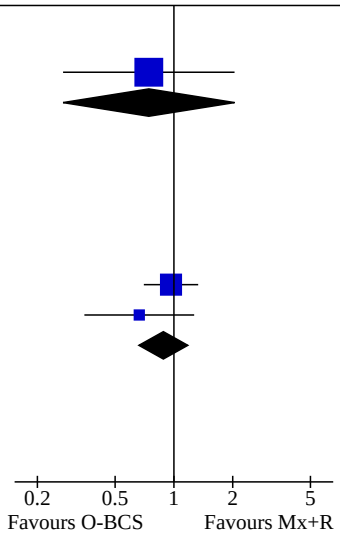


Footnotes

(1) Estimated from Kaplan Meier graph

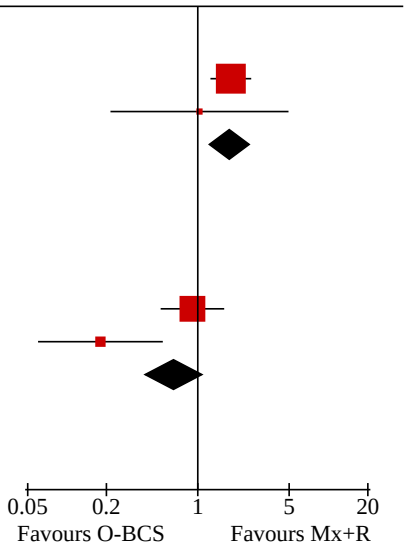
Analysis 3.4. Comparison 3: Any O-BCS versus mastectomy plus reconstruction (Mx+R), Outcome 4: Disease-free survival (RR): Mx+R

Study or Subgroup	O-BCS Events	O-BCS Total	Mx+R Events	Mx+R Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.4.1 5 years: Mx+R only						
Ozmen 2020	12	242	5	75	100.0%	0.74 [0.27 , 2.04]
Subtotal (95% CI)		**242**		**75**	**100.0%**	**0.74 [0.27 , 2.04]**
Total events:	12		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.57 (P = 0.57)						
3.4.2 5 years: Mx+/-R						
DeLorenzi 2016 (2)	43	193	89	386	72.4%	0.97 [0.70 , 1.33]
Mansell 2017	10	104	46	318	27.6%	0.66 [0.35 , 1.27]
Subtotal (95% CI)		**297**		**704**	**100.0%**	**0.88 [0.66 , 1.18]**
Total events:	53		135			
Heterogeneity: Chi² = 1.04, df = 1 (P = 0.31); I² = 4%						
Test for overall effect: Z = 0.85 (P = 0.40)						



Analysis 3.5. Comparison 3: Any O-BCS versus mastectomy plus reconstruction (Mx+R), Outcome 5: Overall survival (HR): Mx+R

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
3.5.1 Mx+R only				
Carter 2016 (1)	0.5822	0.1832	95.0%	1.79 [1.25 , 2.56]
Ozmen 2020 (2)	0.0301	0.8	5.0%	1.03 [0.21 , 4.94]
Subtotal (95% CI)			**100.0%**	**1.74 [1.23 , 2.47]**
Heterogeneity: Chi² = 0.45, df = 1 (P = 0.50); I² = 0%				
Test for overall effect: Z = 3.11 (P = 0.002)				
3.5.2 Mx+/-R				
DeLorenzi 2016 (2)	-0.0943	0.2855	79.4%	0.91 [0.52 , 1.59]
Mansell 2017	-1.7148	0.5605	20.6%	0.18 [0.06 , 0.54]
Subtotal (95% CI)			**100.0%**	**0.65 [0.40 , 1.07]**
Heterogeneity: Chi² = 6.64, df = 1 (P = 0.010); I² = 85%				
Test for overall effect: Z = 1.68 (P = 0.09)				



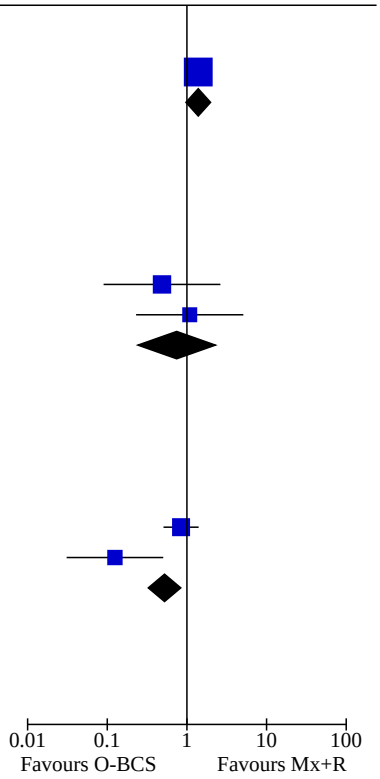
Footnotes

(1) follow up not 5 years median (months): 40.8 (range 0-109.2)

(2) Estimated from Kaplan Meier graph

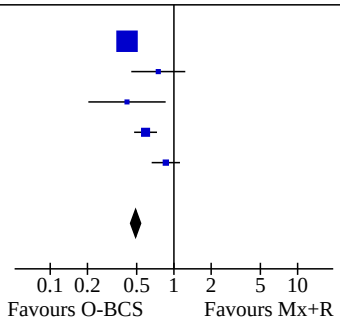
Analysis 3.6. Comparison 3: Any O-BCS versus mastectomy plus reconstruction (Mx+R), Outcome 6: Overall survival (RR): Mx+R

Study or Subgroup	O-BCS Events	O-BCS Total	Mx+R Events	Mx+R Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.6.1 1 to 5 years						
Carter 2016	48	1079	74	2308	100.0%	1.39 [0.97 , 1.98]
Subtotal (95% CI)		**1079**		**2308**	**100.0%**	**1.39 [0.97 , 1.98]**
Total events:	48		74			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.80 (P = 0.07)						
3.6.2 5 years: Mx only						
Lee 2018	2	260	4	253	57.0%	0.49 [0.09 , 2.63]
Ozmen 2020	7	242	2	75	43.0%	1.08 [0.23 , 5.11]
Subtotal (95% CI)		**502**		**328**	**100.0%**	**0.74 [0.24 , 2.28]**
Total events:	9		6			
Heterogeneity: Chi² = 0.47, df = 1 (P = 0.49); I² = 0%						
Test for overall effect: Z = 0.52 (P = 0.60)						
3.6.3 5 years: Mx+/-R						
DeLorenzi 2016 (2)	19	193	45	386	55.4%	0.84 [0.51 , 1.40]
Mansell 2017	2	104	49	318	44.6%	0.12 [0.03 , 0.50]
Subtotal (95% CI)		**297**		**704**	**100.0%**	**0.52 [0.33 , 0.84]**
Total events:	21		94			
Heterogeneity: Chi² = 7.46, df = 1 (P = 0.006); I² = 87%						
Test for overall effect: Z = 2.70 (P = 0.007)						



Analysis 3.7. Comparison 3: Any O-BCS versus mastectomy plus reconstruction (Mx+R), Outcome 7: Complications: Mx+R only

Study or Subgroup	O-BCS Events	O-BCS Total	Mx+R Events	Mx+R Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Carter 2016	231	939	1074	1824	69.7%	0.42 [0.37 , 0.47]
Ozmen 2020	41	242	17	75	2.5%	0.75 [0.45 , 1.24]
Peled 2014	7	37	29	64	2.0%	0.42 [0.20 , 0.86]
Potter 2020	79	376	359	1008	18.6%	0.59 [0.48 , 0.73]
Tong 2016	48	131	118	277	7.2%	0.86 [0.66 , 1.12]
Total (95% CI)		**1725**		**3248**	**100.0%**	**0.49 [0.45 , 0.54]**
Total events:	406		1597			
Heterogeneity: Chi² = 30.32, df = 4 (P < 0.00001); I² = 87%						
Test for overall effect: Z = 14.96 (P < 0.00001)						
Test for subgroup differences: Not applicable						

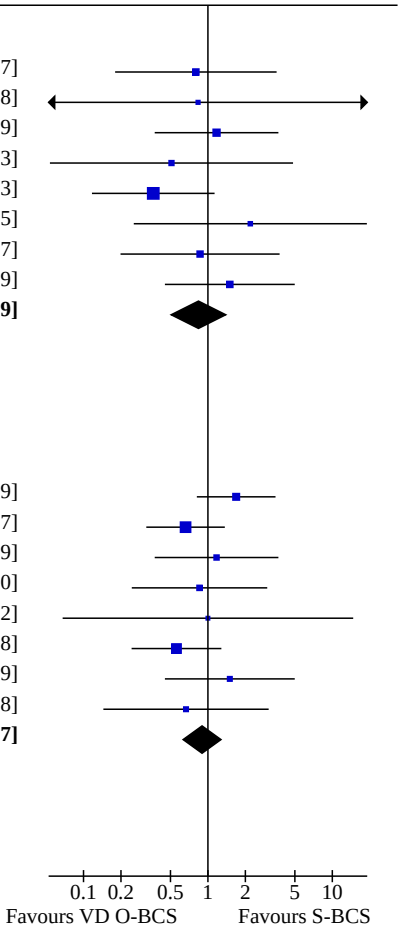


Comparison 4. Volume displacement versus S-BCS

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Local recurrence	14		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1.1 1 to 5 years	8	2578	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.51, 1.39]
4.1.2 5 years	8	4729	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.63, 1.27]
4.2 Overall survival	7		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.2.1 5 years	7	4373	Risk Ratio (M-H, Fixed, 95% CI)	0.76 [0.59, 0.98]
4.3 Re-excision rates	27		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.3.1 Total re-excisions	27	9076	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.69, 0.87]
4.3.2 Mastectomies	16	7097	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.86, 1.28]
4.4 Complications	14	4083	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.90, 1.18]

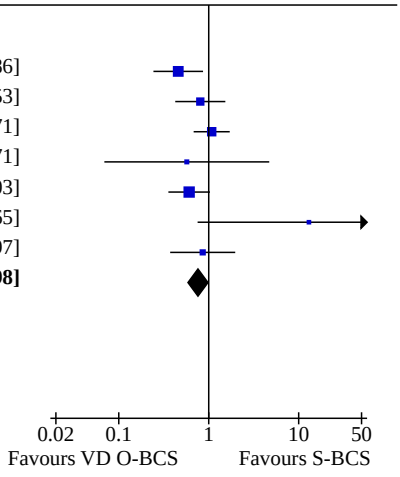
Analysis 4.1. Comparison 4: Volume displacement versus S-BCS, Outcome 1: Local recurrence

Study or Subgroup	VD O-BCS Events	VD O-BCS Total	S-BCS Events	S-BCS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.1.1 1 to 5 years						
Amitai 2018	2	67	10	268	12.3%	0.80 [0.18 , 3.57]
Cassi 2016	0	61	1	154	2.6%	0.83 [0.03 , 20.18]
Chakravorty 2012	4	150	10	440	15.7%	1.17 [0.37 , 3.69]
Gulcelik 2013	1	106	3	162	7.3%	0.51 [0.05 , 4.83]
Keleman 2019	4	350	11	350	33.9%	0.36 [0.12 , 1.13]
Malhaire 2015	4	73	1	40	4.0%	2.19 [0.25 , 18.95]
Mazouni 2013	2	45	11	214	11.8%	0.86 [0.20 , 3.77]
Piper 2016	6	49	4	49	12.3%	1.50 [0.45 , 4.99]
Subtotal (95% CI)		**901**		**1677**	**100.0%**	**0.84 [0.51 , 1.39]**
Total events:	23		51			
Heterogeneity: Chi² = 4.27, df = 7 (P = 0.75); I² = 0%						
Test for overall effect: Z = 0.68 (P = 0.50)						
4.1.2 5 years						
Acea-Nebril 2017	10	170	22	631	14.4%	1.69 [0.81 , 3.49]
Borm 2019	9	288	32	677	29.5%	0.66 [0.32 , 1.37]
Chakravorty 2012	4	150	10	440	7.9%	1.17 [0.37 , 3.69]
Lee 2018	3	170	12	582	8.4%	0.86 [0.24 , 3.00]
Losken 2009	1	17	1	17	1.5%	1.00 [0.07 , 14.72]
Niinikoski 2019 (2)	7	471	25	940	25.8%	0.56 [0.24 , 1.28]
Piper 2016	6	49	4	49	6.2%	1.50 [0.45 , 4.99]
Vieira 2016	2	26	6	52	6.2%	0.67 [0.14 , 3.08]
Subtotal (95% CI)		**1341**		**3388**	**100.0%**	**0.90 [0.63 , 1.27]**
Total events:	42		112			
Heterogeneity: Chi² = 5.89, df = 7 (P = 0.55); I² = 0%						
Test for overall effect: Z = 0.61 (P = 0.54)						
Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.83), I² = 0%						



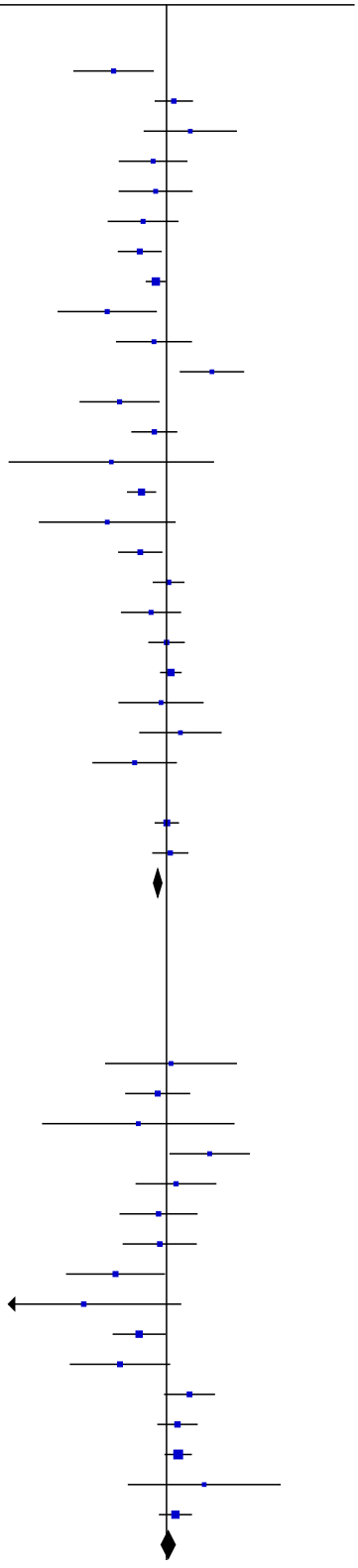
Analysis 4.2. Comparison 4: Volume displacement versus S-BCS, Outcome 2: Overall survival

Study or Subgroup	VD O-BCS Events	VD O-BCS Total	S-BCS Events	S-BCS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.2.1 5 years						
Acea-Nebril 2017	10	170	81	631	26.0%	0.46 [0.24 , 0.86]
Borm 2019	12	288	35	677	15.8%	0.81 [0.42 , 1.53]
Gulcelik 2013	24	106	34	162	20.4%	1.08 [0.68 , 1.71]
Lee 2018	1	170	6	582	2.1%	0.57 [0.07 , 4.71]
Niinikoski 2019 (2)	17	471	56	940	28.3%	0.61 [0.36 , 1.03]
Piper 2016	6	49	0	49	0.4%	13.00 [0.75 , 224.65]
Vieira 2016	6	26	14	52	7.1%	0.86 [0.37 , 1.97]
Subtotal (95% CI)		**1280**		**3093**	**100.0%**	**0.76 [0.59 , 0.98]**
Total events:	76		226			
Heterogeneity: Chi² = 9.35, df = 6 (P = 0.15); I² = 36%						
Test for overall effect: Z = 2.11 (P = 0.03)						



Analysis 4.3. Comparison 4: Volume displacement versus S-BCS, Outcome 3: Re-excision rates

Study or Subgroup	VD O-BCS Events	VD O-BCS Total	S-BCS Events	S-BCS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.3.1 Total re-excisions						
Acea-Nebril 2005	3	50	16	57	2.8%	0.21 [0.07 , 0.69]
Acea-Nebril 2017	15	170	45	631	3.6%	1.24 [0.71 , 2.16]
Amitai 2018	3	67	6	268	0.4%	2.00 [0.51 , 7.79]
Atallah 2015	9	193	6	87	1.5%	0.68 [0.25 , 1.84]
Bali 2018	3	19	36	166	1.4%	0.73 [0.25 , 2.14]
Cassi 2016	4	61	20	154	2.1%	0.50 [0.18 , 1.42]
Chakravorty 2012	10	150	64	440	6.1%	0.46 [0.24 , 0.87]
Crown 2015	60	387	90	425	16.0%	0.73 [0.54 , 0.98]
Di Micco 2017	2	70	14	87	2.3%	0.18 [0.04 , 0.76]
Gicalone 2007 (1)	4	31	8	43	1.3%	0.69 [0.23 , 2.10]
Gicalone 2007 (2)	10	39	6	88	0.7%	3.76 [1.47 , 9.62]
Gicalone 2015	3	42	16	57	2.5%	0.25 [0.08 , 0.82]
Gulcelik 2013	11	106	24	162	3.6%	0.70 [0.36 , 1.37]
Jiang 2015	0	30	2	30	0.5%	0.20 [0.01 , 4.00]
Keleman 2019	28	350	58	350	10.8%	0.48 [0.32 , 0.74]
Lansu 2014	1	19	8	27	1.2%	0.18 [0.02 , 1.31]
Losken 2014	10	83	36	139	5.0%	0.47 [0.24 , 0.89]
Malhaire 2015	31	73	16	40	3.9%	1.06 [0.67 , 1.69]
Matrai 2014	7	60	11	60	2.1%	0.64 [0.26 , 1.53]
Mazouni 2013	12	45	57	214	3.7%	1.00 [0.59 , 1.71]
Niinikoski 2019 (2)	56	611	96	1189	12.2%	1.14 [0.83 , 1.56]
Ojala 2017	3	86	12	293	1.0%	0.85 [0.25 , 2.95]
Piper 2016	6	49	4	49	0.7%	1.50 [0.45 , 4.99]
Tenofsky 2014	3	58	11	84	1.7%	0.39 [0.12 , 1.35]
Vieira 2016	0	26	0	52		Not estimable
Wijgman 2017	42	314	70	528	9.8%	1.01 [0.71 , 1.44]
Wong 2017	11	30	45	137	3.0%	1.12 [0.66 , 1.89]
Subtotal (95% CI)		**3219**		**5857**	**100.0%**	**0.77 [0.69 , 0.87]**
Total events:	347		777			
Heterogeneity: Chi² = 55.99, df = 25 (P = 0.0004); I² = 55%						
Test for overall effect: Z = 4.22 (P < 0.0001)						
4.3.2 Mastectomies						
Acea-Nebril 2005	2	50	2	57	1.1%	1.14 [0.17 , 7.80]
Acea-Nebril 2017	5	170	24	631	6.1%	0.77 [0.30 , 2.00]
Bali 2018	0	19	9	166	1.2%	0.44 [0.03 , 7.27]
Chakravorty 2012	6	150	5	440	1.5%	3.52 [1.09 , 11.37]
Crown 2015	6	387	5	425	2.9%	1.32 [0.41 , 4.28]
Gicalone 2007 (1)	4	31	7	43	3.5%	0.79 [0.25 , 2.47]
Gicalone 2007 (2)	4	39	11	88	4.1%	0.82 [0.28 , 2.42]
Gicalone 2015	2	42	12	57	6.1%	0.23 [0.05 , 0.96]
Gulcelik 2013	0	106	8	162	4.0%	0.09 [0.01 , 1.54]
Keleman 2019	9	350	20	350	12.0%	0.45 [0.21 , 0.97]
Losken 2014	2	83	13	139	5.8%	0.26 [0.06 , 1.11]
Malhaire 2015	25	73	7	40	5.4%	1.96 [0.93 , 4.12]
Mazouni 2013	11	45	38	214	7.9%	1.38 [0.76 , 2.48]
Niinikoski 2019 (2)	39	611	54	1189	22.0%	1.41 [0.94 , 2.10]
Piper 2016	3	49	1	49	0.6%	3.00 [0.32 , 27.85]
Wijgman 2017	27	314	35	528	15.7%	1.30 [0.80 , 2.10]
Subtotal (95% CI)		**2519**		**4578**	**100.0%**	**1.05 [0.86 , 1.28]**



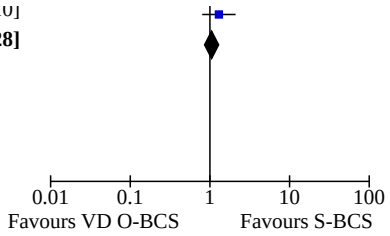
Analysis 4.3. (Continued)

Wijgman 2017	27	314	35	528	15.7%	1.30 [0.80 , 2.10]
Subtotal (95% CI)		**2519**		**4578**	**100.0%**	**1.05 [0.86 , 1.28]**
Total events:	145		251			

Heterogeneity: Chi² = 27.97, df = 15 (P = 0.02); I² = 46%

Test for overall effect: Z = 0.47 (P = 0.64)

Test for subgroup differences: Chi² = 6.54, df = 1 (P = 0.01), I² = 84.7%



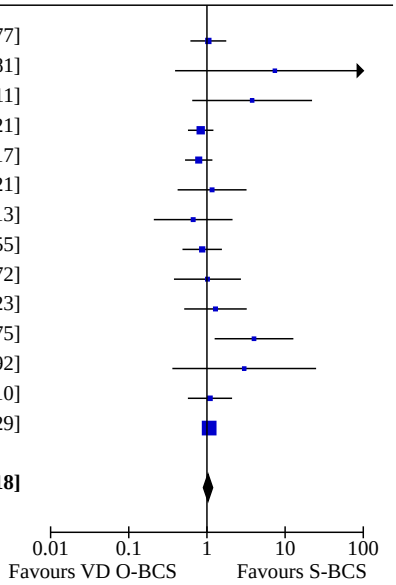
Analysis 4.4. Comparison 4: Volume displacement versus S-BCS, Outcome 4: Complications

Study or Subgroup	VD O-BCS Events	VD O-BCS Total	S-BCS Events	S-BCS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Acea-Nebril 2017	16	170	57	631	7.8%	1.04 [0.61 , 1.77]
Acosta-Marin 2014	3	52	0	55	0.2%	7.40 [0.39 , 139.81]
Cassi 2016	3	61	2	154	0.4%	3.79 [0.65 , 22.11]
Crown 2015	43	288	49	273	16.3%	0.83 [0.57 , 1.21]
Di Micco 2017	24	70	38	87	11.0%	0.78 [0.52 , 1.17]
Gicalone 2015	6	42	7	57	1.9%	1.16 [0.42 , 3.21]
Jiang 2015	4	30	6	30	1.9%	0.67 [0.21 , 2.13]
Keleman 2019	20	350	23	350	7.5%	0.87 [0.49 , 1.55]
Lansu 2014	5	19	7	27	1.9%	1.02 [0.38 , 2.72]
Matrai 2014	9	60	7	60	2.3%	1.29 [0.51 , 3.23]
PlaFarnos 2018	8	60	4	120	0.9%	4.00 [1.25 , 12.75]
Scheter 2019	3	12	1	12	0.3%	3.00 [0.36 , 24.92]
Sherwell-Cabello 2006	14	76	16	95	4.6%	1.09 [0.57 , 2.10]
Wijgman 2017	113	314	178	528	43.1%	1.07 [0.88 , 1.29]
Total (95% CI)		**1604**		**2479**	**100.0%**	**1.03 [0.90 , 1.18]**
Total events:	271		395			

Heterogeneity: Chi² = 14.38, df = 13 (P = 0.35); I² = 10%

Test for overall effect: Z = 0.46 (P = 0.65)

Test for subgroup differences: Not applicable



ADDITIONAL TABLES

Table 1. Confounding variables

Study name	Clinicopathological variables: significantly different	Clinicopathological variables: demonstrated balance	Clinicopathological variables: matched	Clinicopathological variables: statistical adjustment	Co-interventions: significantly different	Co-interventions: demonstrated balance	Co-interventions: matched	Co-interventions: statistical adjustment
Acea-Nebril 2005	Size (BCS)	Age (BCS, Mx), size (Mx)	-	-	-	-	-	-
Acea-Nebril 2017	Age, menopausal status, tumour size, tumour stage, axillary lymph node status, location of tumour, multifocality	BMI, histological type, immunohistochemical receptors	-	-	Neoadjuvant CT, axillary management	-	-	-
Acosta-Marin 2014	Preoperative bra size, tumour size,	Age, BMI	-	-	-	-	-	-
Amitai 2018	Age, axillary node status, immunohistochemical receptors,	Smoking status, BMI, histological type, tumour size	-	-	-	Adjuvant RT	-	-
Angarita 2020	Age, BMI, race, smoking status, alcohol consumption, COPD, PCI, HTN, bleeding disorder, steroid use, previous vascular disease, previous cardiac surgery, dialysis,hemiplegia, TIA, CVA, ASA status, histological type	Weight loss, transfusion, diabetes mellitus	-	-	Axillary management, neoadjuvant chemotherapy, anaesthetic technique	-	-	-
Atallah 2015		Age, BMI, menopausal status, tumour size, location, histological type, immunohistochemical receptors	-	-	-	-	-	-

Table 1. Confounding variables *(Continued)*

Bali 2018	Tumour size	Age, histological type, immunohistochemical receptors, tumour locations	-	-	Neoadjuvant CT, adjuvant CT	Adjuvant RT	-	-
Borm 2019	Age, tumour size, tumour grade, axillary node status, immunohistochemical receptors (ER status),	Immunohistochemical receptors (PR, HER2)	-	-	Adjuvant CT, adjuvant ET	Neo-adjuvant CT, adjuvant RT	-	-
Carter 2016	Age (BCS, Mx, Mx+R), BMI (BCS), tumour size (BCS, Mx, Mx+R), tumour stage (BCS, Mx, Mx+R), tumour grade (BCS), axillary node status (BCS), immunohistochemical receptors (HER2), multifocality (BCS, Mx, Mx+R).	BMI (Mx, Mx+R), Tumour grade (Mx, Mx+R), axillary node status (Mx, Mx+R), immunohistochemical receptors (ER, PR- Mx), lymphovascular invasion	In LR calculation multivariate analysis	-	Neoadjuvant CT (BCS, Mx, Mx+R), adjuvant RT (Mx/MxR), adjuvant CT (BCS, Mx, Mx +R)	Adjuvant RT (BCS)	-	-
Cassi 2016	-	Age, BMI, tumour size	-	-	-	Adjuvant RT	-	-
Chakravorty 2012	Histological type, tumour size, grade, sample weight	Age, axillary node status	-	-	Neoadjuvant CT	Adjuvant RT, adjuvant CT	-	-
Chauhan 2016 (1)	Age, tumour size, tumour location	Histological type, grade, axillary node status, immunohistochemical receptors	-	-	-	-	-	-
Chauhan 2016 (2)	Age, tumour size, tumour location	Axillary node status	-	-	-	-	-	-
Crown 2015	Tumour size, immunohistochemical receptors	Age, histological type	-	-	-	Adjuvant RT	-	-
Crown 2019	Tumour size, immunohistochemical receptors	Age, smoking, BMI, histological type	-	-	Neoadjuvant CT	Adjuvant CT	-	-
DeLorenzi 2016 (1)	Tumour size and multifocality	Menopausal, histological type, grade, axillary node status, immunohistochemical receptors, lymphovascular invasion	Age (within 5 years), year of surgery (within 2			Adjuvant CT, Adjuvant RT, Adjuvant ET	-	-

Table 1. Confounding variables *(Continued)*

			years), tumour size (T) and multifocality					
DeLorenzi 2016 (2)	Multifocality	Grade, immunohistochemical receptors	Age (within 5 years), year of surgery (within 2 years), number of positive axillary lymph nodes, tumour subtype, multifocality		Adjuvant RT	Adjuvant CT, Adjuvant ET	-	-
DeLorenzi 2018	Menopausal, grade	Age, BMI, tumour size, immunohistochemical receptors, multifocality	-	-	-	Adjuvant RT, any adjuvant therapy	-	-
Di Micco 2017	Age, axillary node status	Smoking status, BMI, histological type, tumour size, immunohistochemical receptor, tumour location			Radiation boost, adjuvant CT	Neoadjuvant CT, adjuvant ET, axillary management, adjuvant RT		
Dolan 2015	Age, tumour size, axillary node status	Histological type, grade, immunohistochemical receptor	-	-	Adjuvant CT	Adjuvant RT, adjuvant ET, axillary management	-	-
Down 2013	Tumour size	Age, histological type, grade	-	-	-	Adjuvant RT	-	-
Eichler 2013	Tumour size	Age, histological type, grade	-	-	Neoadjuvant CT	Adjuvant CT	-	-
Fan 2019	-	Histological type	Age, BMI, stage	-	-	Neoadjuvant CT, adjuvant RT, adjuvant CT, adjuvant ET		-

Table 1. Confounding variables *(Continued)*

Farooqi 2019	Tumour size,	Age, histological type	-	-	-	Neoadjuvant CT	-	-
Gendy 2003	Histological type, tumour size	Age, grade, axillary node status	-	-	Adjuvant RT	-	-	-
Gicalone 2007 (1)	Age	BMI, histological type, tumour size, grade, axillary node status, immunohistochemical receptor	-	-	-	-	-	-
Gicalone 2007 (2)	Age	BMI, tumour size, tumour location		-	-	-	-	-
Gicalone 2015	-	Age, smoking status, diabetes, BMI, other medical comorbidities, histological type, tumour size		-	-	-	-	-
Gulcelik 2013	-	Age, tumour size, immunohistochemical receptor	-	-	-	Adjuvant CT, Adjuvant ET, axillary management, adjuvant RT		
Hamdi 2008	Age, histological type, tumour size,	-	-	-	-	Axillary management	-	-
Hart 2015	Age, BMI	Stage	-	-	Adjuvant RT	-	-	-
Hashimoto 2019	-	-	-	-	-	-	-	-
Hilli-Betz 2014	Tumour size, preoperative bra size	Axillary node status	-	-	-	Axillary management	-	-
Hu 2019	-	Age, tumour size, immunohistochemical receptor	-	-	-	Neoadjuvant CT, axillary management	-	-
Jiang 2015	-	Age, weight, histology type,tumour size, grade, stage, tumour location	-	-	-	-	-	-

Table 1. Confounding variables *(Continued)*

Kahn 2013	-	-	-	-	-	Adjuvant CT (BCS, Mx, Mx +R)	-	-
Keleman 2019	Preoperative bra size, axillary node status	Age, smoking status, diabetes, BMI, type of cancer, tumour size, grade, stage, immunohistochemical receptor	-	-	Neoadjuvant CT, adjuvant CT, adjuvant ET, axillary management	Adjuvant RT	-	-
Kelsall 2017	-	Axillary node status	Age, tumour size, date of surgery, breast size	-	Adjuvant RT	Neoadjuvant CT	Adjuvant CT, adjuvant ET	-
Kimball 2018	Age, medical comorbidities, histological type	BMI	-	-	Adjuvant RT, adjuvant CT, axillary management		-	-
Klit 2017	Age (BCS, Mx), BMI (BCS, Mx), tumour size (BCS, Mx), axillary node status (BCS, Mx)	-	-	-	Axillary management, Adjuvant RT (BCS)	Adjuvant CT (BCS, Mx), Adjuvant RT (Mx)	-	-
Lansu 2014	-	Age, tumour size, tumour location	-	-	Neoadjuvant CT	Adjuvant CT, Adjuvant ET, axillary management, adjuvant RT		-
Lee 2018	Tumour size (BCS, Mx, Mx+R), stage (BCS, Mx, Mx+R)	Age (BCS, Mx, Mx+R), BMI (BCS, Mx, Mx+R)	-	-	-	-	-	-
Losken 2009	Age, histological type, stage	BMI	-	-	Adjuvant CT, axillary surgery	Adjuvant RT	-	-

Table 1. Confounding variables *(Continued)*

Losken 2014	Age, BMI	Histological type, tumour size, stage, immunohistochemical receptor	-	-	Neoadjuvant CT		-	-
Malhaire 2015	-	-	-	-	-	-	-	-
Mansell 2015	Age (both), histological type (BCS), tumour size (BCS), grade (BCS), axillary node status (BCS), immunohistochemical receptor (ER, PR)	Histological type (Mx), tumour size (Mx), grade (Mx), axillary node status (Mx), immunohistochemical receptor (HER2)	-	-	Adjuvant RT (MxR), adjuvant CT (BCS), adjuvant ET (BCS)	Adjuvant RT (BCS), adjuvant CT (MxR), adjuvant ET (MxR)	-	-
Mansell 2017	Age (both), histological type (BCS), tumour size (BCS), grade (BCS), axillary node status (BCS), immunohistochemical receptor (ER)	Histological type (Mx), tumour size (Mx), grade (Mx), axillary node status (Mx), immunohistochemical receptor (HER2)	-	-	Adjuvant RT (MxR), adjuvant CT (BCS), adjuvant ET (BCS)	Adjuvant RT (BCS), adjuvant CT (MxR), adjuvant ET (MxR)	-	-
Matrai 2014	Tumour size	Age, histological type, grade, tumour location, bra size, immunohistochemical receptor, axillary lymph node status	Matched of clinicopathological factors - details not given	-	Adjuvant CT	Axillary surgery, adjuvant RT, adjuvant ET	-	-
Mazouni 2013	Immunohistochemical receptor (ER), tumour location	Histological type, tumour size, grade, axillary node status, immunohistochemical receptor (PR)	-	-	-	Axillary surgery, neoadjuvant CT, adjuvant RT	-	-
Morrow 2019	Age (all), histological type (BCS, Mx), tumour size (BCS, Mx), grade (BCS, Mx), axillary node status (Mx, MxIR)	Histological type (MxIR), tumour size (MxIR), grade (MxIR), axillary node status (BCS), immunohistochemical receptors	-	-	Adjuvant CT (BCS), Adjuvant RT (all)	Adjuvant CT (Mx, MxIR), adjuvant ET (Mx, MxIR)	-	-
Mukhtar 2018	Tumour size	"No significant difference in patient or tumour characteristics"	-	-	-	-	-	-

Table 1. Confounding variables *(Continued)*

Mustonen 2004	Tumour size	Age	-	-	Adjuvant, RT	Adjuvant CT	-	-
Nakada 2019	-	-	-	-	-	-	-	-
Nakagomi 2019	Age, tumour size, stage	Histological type, axillary node status, immunohistochemical receptor status	-	-	Neoadjuvant CT	-	-	-
Niinikoski 2019 (2)	Age, tumour size, grade, axillary node status, immunohistochemical status (ER, TN), multifocality,	Histological type, immunohistochemical receptor status (PR, HER2)	-	-	Adjuvant CT, adjuvant ET	Adjuvant RT, axillary management	-	-
Ojala 2017	Tumour size, tumour location, axillary node status, multifocality, histological type,	Age, grade	-	-	Axillary management	Adjuvant RT	-	-
Ozmen 2016	Age, BMI, multifocality	-	-	-	-	Adjuvant RT	-	-
Ozmen 2020	Age, menopausal status, BMI, tumour size, grade, axillary node status, immunohistochemical receptor status (ER), multifocality	histological type, immunohistochemical receptor status (PR, HER2, TN)	-	-	Adjuvant RT, axillary management	-	-	-
Palsodittlir 2018	Age, smoking status, tumour size	Histological type, axillary node status	-	-	Adjuvant ET	-	-	-
Peled 2014	Age, BMI	Smoking status, diabetes	-	-	-	Neoadjuvant CT	-	-
Piper 2016	Tumour stage	BMI, histological type	Age	-	-	-	-	-
PlaFarnos 2018	Multifocality	-	-	-	Previous breast surgery	-	-	-
Potter 2020	Age (Mx, Mx+R), diabetes (Mx, Mx+R), BMI (Mx, Mx	Smoking status (Mx, Mx+R)	-	-	Neoadjuvant CT (Mx,	-	-	-

Table 1. Confounding variables *(Continued)*

	+R), other medical comorbidities (Mx, Mx+R), histological type (Mx, Mx+R), grade (Mx, Mx +R), axillary node status (Mx, Mx+R), immunohistochemical receptors (BCS, Mx, Mx+R), multifocality (BCS, Mx, Mx+R)				Mx+R), adjuvant RT (Mx, Mx+R), adjuvant CT (Mx, Mx+R), axillary surgery (Mx, Mx+R)			
Ren 2014	-	Histological type, tumour location	Age, tumour size, axillary lymph node status, immunohistochemical receptor, (ER, HER2)	-	-	-	-	-
Rose 2019	Menopausal status, axillary node status	-	-	Age, lymphovascular invasion, grade, tumour size, multifocality, immunohistochemical receptor (ER, HER2)	Axillary surgery	Adjuvant RT, adjuvant CT, adjuvant ET	-	-
Rose 2020	-	-	-	Age, follow-up time, menopausal status, tumour size, bra size, tumour location, bra size, BMI, smoking status, marital status, living arrange-	-	-	-	Adjuvant RT, adjuvant CT, adjuvant ET, immunotherapy, axillary surgery

Table 1. Confounding variables *(Continued)*

				ment and education				
Santos 2015	BMI, histological type, axillary node status,	Age, menopausal status, tumour size, grade, immunohistochemical receptor, tumour location	-	-	-	Axillary surgery	-	-
Scheter 2019	Age, smoking status, tumour size, ,	Preoperative bra size, axillary lymph node status	Diabetes, BMI	-	-	Axillary surgery, adjuvant CT, adjuvant ET, adjuvant RT	-	-
Sherwell-Cabello 2006	Tumour size	Age, other comorbidities, axillary node status, tumour location	-	-	Neoadjuvant CT	-	-	-
Srivastava 2018	-	-	Margin of excision	-	-	-	-	-
Tang 2016		Age, BMI, tumour size, stage	-	-	-	Axillary management	-	-
Tenofsky 2014	-	Age, BMI, tumour size	-	-	Adjuvant RT	-	-	-
Tong 2016	Age, diabetes, BMI, other comorbidities, preoperative bra size	Smoking status, tumour size, stage	-	-	Neoadjuvant RT, adjuvant RT	Neoadjuvant CT, adjuvant CT	-	-
Viega 2010	-	Age, BMI, tumour location	-	-	-	Adjuvant RT, adjuvant CT	-	-
Viega 2011	-	Age, BMI, tumour size, tumour location	-	-	-	Adjuvant RT, adjuvant CT, axillary management	-	-
Vieira 2016	-	Age, histological type, stage, immunohistochemical receptor	Tumour size, grade	-	-	Neoadjuvant CT, adjuvant RT	-	-

Table 1. Confounding variables *(Continued)*

Wijgman 2017	Tumour size, tumour location	Age, menopausal status, smoking, diabetes, BMI, other medical comorbidities, histological type, sample volume resected, sample weight resected	-	-	Adjuvant CT, adjuvant ET	Neoadjuvant CT, adjuvant RT, axillary surgery	-	-
Wong 2017	Tumour size	-	-	-	-	-	-	-
Zhou 2019	Tumour size	Age, BMI, preoperative bra size, histological type, tumour location, multifocality, axillary node status	-	-	-	Adjuvant RT, axillary management	-	-

BCS: breast-conserving surgery
BMI: body mass index
CT: chemotherapy
ER: oestrogen receptor
ET: endocrine therapy
HER2: human epidermal growth factor receptor 2
IR: immediate reconstruction
Mx: mastectomy
PR: progesterone receptor
R: reconstruction
RT: radiotherapy
TN: triple negative

Table 2. Risk of bias for local recurrence

Study	Control	Confounding	Selection	Classification of intervention	Deviations from intended intervention	Missing data	Measurement of outcomes	Selection of reported results	Overall
Acea-Nebril 2017	S-BCS	Serious	Low	Low	Moderate	Low	Low	Moderate	Serious
		Some clinicopathological variables significantly different (age, menopausal status, tumour size, tumour stage, axillary lymph node status, location of tumour, multifocality). Some co-interventions balanced (neoadjuvant CT and axillary management), some missing	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Some aspects may be	Deviation from intended co-intervention (adjuvant therapy time)	All patients followed up	Objective outcome measure	No indication of selected reporting	

Table 2. Risk of bias for local recurrence *(Continued)*

				determined retrospectively					
Amitai 2018	S-BCS	Serious	Moderate	Low	Low	Moderate	Low	Moderate	Serious
		Most clinicopathological variables significantly different (age, axillary node status, immunohistochemical receptors). Adjuvant RT demonstrated balanced, most co-interventions missing	Selection may be related to the outcome (those with Mx eventually excluded)	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Analysis unlikely to have removed risk of bias from missing data	Objective outcome measure	No indication of selected reporting	
Borm 2019	S-BCS	Serious	Low	Low	Low	Moderate	Low	Moderate	Serious
		Most clinicopathological variables significantly different: age, tumour size, tumour grade, axillary node status, immunohistochemical receptors (ER status). Important co-interventions (adjuvant CT, adjuvant ET) not balanced across intervention group and may affect the outcome	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Analysis unlikely to have removed risk of bias from missing data	Objective outcome measure	No indication of selected reporting	
Carter 2016	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Most clinicopathological variables significantly different (age, BMI, tumour size, stage, axillary node status, immunohistochemical receptors (ER, PR, multifocality). Adjusted for in LR calculation. Important co-interventions not balanced across intervention group and may affect the outcome (neoadjuvant CT (all), adjuvant RT (Mx/Mx+R), adjuvant CT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Cassi 2016	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some clinicopathological variables demonstrated balance (age, BMI, tumour size), most missing. Important	All participants el-	Classification of interventions clear and de-	All patients received the surgical in-	Most patients followed up	Objective outcome measure	No indication of se-	

Table 2. Risk of bias for local recurrence *(Continued)*

		co-interventions balanced across intervention group (adjuvant RT) some information missing	igible included	termined at the start of intervention. Operative details given clearly	tervention described in the methods			lected reporting	
Chakravorty 2012	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some clinicopathological variables demonstrated balance (age, axillary node status) and some different (histological type, tumour size, grade, sample weight), most missing. Important co-interventions balanced across intervention group (adjuvant RT, adjuvant CT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Chauhan 2016 (1)	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some clinicopathological variables demonstrated balance (histological type, grade, axillary node status, immunohistochemical receptors) and some different (age, tumour size, tumour location), most missing Important co-interventions predefined and uniform across studies	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Chauhan 2016 (2)	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Axillary node status demonstrated balance and some clinicopathological variables different (age, tumour size, tumour location), most missing. Important co-interventions predefined and uniform across studies	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	
DeLorenzi 2016 (1)	S-BCS	Low	Low	Low	Low	Low	Low	Moderate	Moderate

Table 2. Risk of bias for local recurrence *(Continued)*

		Important clinicopathological factors demonstrated balance (menopausal, histological type, grade, axillary node status, immunohistochemical receptors, lymphovascular invasion) or matched (age (within 5 years), year of surgery (within 2 years), tumour size. Important co-interventions balanced across intervention group (adjuvant CT, adjuvant RT, adjuvant ET)	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure - due to margin status	No indication of selected reporting	
DeLorenzi 2018	S-BCS	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (age, BMI, tumour size, immunohistochemical receptors, multifocality), some significantly different (menopausal, grade) Some co-interventions balanced across intervention group (adjuvant RT, any adjuvant therapy)	Selection may be related to the outcome (Mx eventually excluded)	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure - due to margin status	No indication of selected reporting	
Down 2013	S-BCS	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Some clinicopathological variables demonstrated balance (age, histological type, grade), tumour size different, some missing adjuvant RT balanced across intervention group, some co-interventions missing	All patients included. Patients were selected for intervention if cosmetic outcome with control would be bad (selection bias but does not affect this outcome)	Classification of interventions clear and determined at the start of intervention, details of operations described	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	

Table 2. Risk of bias for local recurrence *(Continued)*

Fan 2019	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors matched (age, BMI, stage) or demonstrated balance (histological type), some missing Important co-interventions demonstrated balance (neoadjuvant CT, adjuvant RT, adjuvant CT, adjuvant ET)	All participants eligible included, control selected for	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods	All patients followed up for 30 days and for re-excisions specifically	Objective outcome measure	No indication of selected reporting	
Gulcelik 2013	S-BCS	Moderate	Low	Low	Moderate	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (age, tumour size, immunohistochemical receptor), most missing. Important co-interventions demonstrated balance (adjuvant CT, adjuvant ET, axillary management, adjuvant RT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. Included from the beginning of uptake of intervention	All patients included but some did not have sufficient follow-up so excluded. Details not given	Objective outcome measure	No indication of selected reporting	
Hashimoto 2019*	S-BCS	Serious	Low	Low	No information	No information	Low	Moderate	Serious
		Rate of advanced cases of cancer higher in intervention -	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Some aspects maybe determined retrospectively	-	-	Objective outcome measure	No indication of selected reporting	
Keleman 2019	S-BCS	Moderate	Low	Low	Low	Moderate	Low	Moderate	Serious

Table 2. Risk of bias for local recurrence *(Continued)*

		Some variables demonstrated balance (age, smoking status, diabetes, BMI, type of cancer, tumour size, grade, stage, immunohistochemical receptor) some different (preoperative bra size, axillary node status) but unlikely to affect outcome Important co-intervention of adjuvant RT demonstrated balance, some significantly different (neoadjuvant CT, adjuvant CT, adjuvant ET, axillary management) but less of an impact on outcome	All intervention participants eligible included, random patients selected for control	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. Two experienced breast surgeons	Patients missed due to loss to follow-up and did not respond to outcome, equal numbers in both groups so impact may be similar across groups	Objective outcome measure	No indication of selected reporting	
Lee 2018	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance (age, BMI), some significantly different (tumour size and stage). No breakdown between control and study groups for data on cancer treatment	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. Centre with large numbers	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Losken 2009	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance, some significantly different: age, histological type, stage. Important co-interventions demonstrated balance, some significantly different: adjuvant CT, axillary surgery	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. Experienced surgeon	All patients included followed up	Objective outcome measure	No indication of selected reporting	

Table 2. Risk of bias for local recurrence *(Continued)*

Malhaire 2015	S-BCS	No information	Serious	Low	Low	Low	Low	Moderate	Serious
		-	Selection based on localisation techniques	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. All surgeons had training in O-BCS	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Mansell 2017	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors significantly different: age, histological type, tumour size, grade, axillary node status, immunohistochemical receptor (ER, PR). Important co-interventions balanced, some significantly different: adjuvant CT, adjuvant ET	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up until June 2015	Objective outcome measure	No indication of selected reporting	
Matrai 2014	S-BCS	Serious	Serious	Low	Low	Moderate	Low	Moderate	Serious
		Tumour size significantly different. Some variables demonstrated balance (age, histological type, grade, tumour location, bra size, immunohistochemical receptor, axillary lymph node status). Matching of patients reported but not defined: "the same clinicopathological parameters of 60 traditional breast-conserving surgeries operated by the same breast surgeon were used". Important co-interventions including adjuvant RT demonstrated balance. Adjuvant CT significantly different	Unclear why these 60 patients selected (not consecutive, some retrospective and some prospective), controls matched	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. Experienced surgeon	Groups followed up for different amounts of time: "The mean follow-up time was 32.2 months in the BCS group compared to only 8.7	Objective outcome measure	No indication of selected reporting	

Table 2. Risk of bias for local recurrence *(Continued)*

						months in the OPS group"			
Mazouni 2013	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors balance: histological type, tumour size, grade, axillary node status, immunohistochemical receptor (PR). Important co-interventions predefined and uniform across studies (axillary surgery, neoadjuvant CT, adjuvant RT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Niinikoski 2019 (2)	S-BCS	Serious	Moderate	Low	Low	Moderate	Low	Moderate	Serious
		Important clinicopathological factors significantly different: age, tumour size, grade, axillary node status, immunohistochemical status (ER, TN), multifocality Important co-intervention demonstrated balance (adjuvant RT), some significantly different (adjuvant CT and ET)	All participants eligible included. Excluded on basis on diagnosis by biopsy/incidental. Excluded those without adjuvant therapy nor axillary surgery. Also excluded if follow-up < 3 years	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in methods.	Some loss to follow-up for local recurrence free survival: 140/611 in intervention group, 249/1189 in control group	Objective outcome measure	No indication of selected reporting	
Piper 2016	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious

Table 2. Risk of bias for local recurrence *(Continued)*

		Some variables demonstrated balance (BMI, histological type), age matched for and stage significantly different Important co-interventions missing	Patients without negative margins excluded, minimum 2 years follow-up (O-BCS done more recently)	Classification of interventions clear and determined at the start of intervention: "All reduction mammoplasties were performed either via an inferior or superior-medial pedicle approach, with a Wise pattern or vertical skin pattern incision, based on tumour location"	All patients received the surgical intervention described in methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Vieira 2016	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance. Matched for demographic and oncological aspects Important co-interventions demonstrated balance, missing data on axillary management of cases (97.4% for control group)	All O-BCS participants eligible included, matched standard breast conserving surgery: "cases were matched to decrease a possible bias selection"	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	

Table 2. Risk of bias for local recurrence *(Continued)*

Carter 2016	Mx	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Most clinicopathological variables significantly different (age, BMI, tumour size, stage, axillary node status, immunohistochemical receptors (ER, PR, TN), multifocality). Adjusted for in local recurrence calculation. Important co-interventions not balanced across intervention group and may affect the outcome (neoadjuvant CT (all), adjuvant RT (Mx/MxR), adjuvant CT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Gendy 2003	Mx	Moderate	Moderate	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors balanced (Age, grade, axillary node status), some significantly different (histological type, tumour size), some missing. Important co-interventions different across intervention group, likely to influence outcome. All those that recurred had had RT	All contactable participants	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Lee 2018	Mx	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance (age, BMI), some significantly different (tumour size and stage). No breakdown between control and study groups for data on cancer treatment	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Nakagomi 2019	Mx	Serious	Low	Low	Low	Low	Serious	Moderate	Serious
		Some variables demonstrated balance (histological type, axillary node status, immunohistochemical receptor status), some significantly different (age, tumour size, stage), many missing. Im-	All participants eligible included	Classification of interventions clear and determined at the start of inter-	All patients received the surgical intervention	All patients included followed up	Objective outcome measure but details of fol-	No indication of selected reporting	

Table 2. Risk of bias for local recurrence *(Continued)*

		portant co-interventions missing (RT, axillary management), neoadjuvant CT significantly different		vention: latissimus dorsi mini flap or mastectomy	described in methods.		low-up time not given		
Ren 2014	Mx	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (histological type and location) or matched (age, tumour size, axillary lymph node status, immunohistochemical receptor, (ER, HER2)). Co-intervention information missing for control group	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in methods	Most patients included: "The median follow-up time was 83 months in s-BCS and 81 months in mastectomy"	Objective outcome measure	No indication of selected reporting	
Carter 2016	Mx + R	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Most clinicopathological variables significantly different (age, BMI, tumour size, stage, axillary node status, immunohistochemical receptors (ER, PR, TN), multifocality). Adjusted for in LR calculation. Important co-interventions not balanced across intervention group and may affect the outcome (neoadjuvant CT (all), adjuvant RT (Mx/MxR), adjuvant CT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	
DeLorenzi 2016 (2)	Mx + R	Low	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (grade, immunohistochemical receptors) or matched (age (within 5 years), year of surgery (within 2 years), number of positive axillary lymph nodes, tumour subtype). Important co-interventions	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure - due to margin status	No indication of selected reporting	

Table 2. Risk of bias for local recurrence *(Continued)*

		balanced across intervention group (adjuvant CT, adjuvant ET), adjuvant RT different							
Lee 2018	Mx + R	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance (age, BMI), some significantly different (tumour size and stage). No breakdown between control and study groups for data on cancer treatment	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Mansell 2017	Mx + R	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Some clinicopathological significantly different: age, immunohistochemical receptor (ER, PR). Other important clinicopathological factors balance: histological type, tumour size, grade, axillary node status, immunohistochemical receptor (HER2). Important co-interventions demonstrated balance, adjuvant RT significantly different	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up until June 2018	Objective outcome measure	No indication of selected reporting	
Mustonen 2004	Mx + R	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Age demonstrated balance, tumour size significantly different, most missing. Adjuvant CT balanced, adjuvant radiotherapy significantly different, other co-interventions missing	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in methods.	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Ozmen 2020	Mx + R	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors balance, some different (age, menopausal status, BMI, tumour size, grade, axillary node status, immuno-	Women chose their operation after	Classification of interventions clear and determined at the	All patients received the surgical intervention	Most patients included: "Median	Objective outcome measure	No indication of selected reporting	

Table 2. Risk of bias for local recurrence *(Continued)*

		histochemical receptor status (ER), multifocality), some missing. Important co-interventions significantly different (adjuvant RT and axillary management), some missing (neoadjuvant RT + CT, adjuvant CT + ET)	being told the potential risks and benefits. Bias in assignment: "Both two procedures were explained to patients, and their choices were recorded."	start of intervention	described in methods. All interventions done by a single surgeon with more than 30 years of experience in breast surgery.	follow-up time was 56 (14-116) months."			

BMI: body mass index
CT: chemotherapy
ER: oestrogen receptor
ET: endocrine therapy
HER2: human epidermal growth factor receptor 2
Mx: mastectomy
PR: progesterone receptor
R: reconstruction
RT: radiotherapy
LR: local recurrence

Table 3. Risk of bias for disease-free survival

Study	Control	Confounding	Selection	Classification of intervention	Deviations from intended intervention	Missing data	Measurement of outcomes	Selection of reported results	Overall
Acea-Nebril 2017	S-BCS	Serious	Low	Low	Moderate	Low	Low	Moderate	Serious
		Some clinicopathological variables significantly different (age, menopausal status, tumour size, tumour stage, axillary lymph node status, location of tumour, multifocali-	All participants eligible included	Classification of interventions clear and determined at the start of inter-	Deviation from intended co-intervention (adjuvant therapy time),	All patients followed up	Objective outcome measure	No indication of selected reporting	

Table 3. Risk of bias for disease-free survival *(Continued)*

		ty). Some co-interventions balanced (neoadjuvant CT and axillary management), some missing		vention. Some aspects maybe determined retrospectively	co-interventions significantly different				
Borm 2019	S-BCS	Serious	Low	Low	Low	Moderate	Low	Moderate	Serious
		Most clinicopathological variables significantly different: age, tumour size, tumour grade, axillary node status, immunohistochemical receptors (ER status). Important co-interventions (adjuvant CT, adjuvant ET) not balanced across intervention group and may affect the outcome	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Analysis unlikely to have removed risk of bias from missing data	Objective outcome measure	No indication of selected reporting	
DeLorenzi 2016 (1)	S-BCS	Low	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (menopausal, histological type, grade, axillary node status, immunohistochemical receptors, lymphovascular invasion) or matched (age (within 5 years), year of surgery (within 2 years), tumour size. Important co-interventions balanced across intervention group (adjuvant CT, adjuvant RT, adjuvant ET)	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure - due to margin status	No indication of selected reporting	
DeLorenzi 2018	S-BCS	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (age, BMI, tumour size, immunohistochemical receptors, multifocality), some significantly different (menopausal, grade). Some co-interventions balanced across intervention group (adjuvant RT, any adjuvant therapy)	Selection may be related to the outcome (mastectomy eventually excluded)	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure - due to margin status	No indication of selected reporting	

Table 3. Risk of bias for disease-free survival *(Continued)*

Gulcelik 2013	S-BCS	Moderate	Low	Low	Moderate	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (age, tumour size, immunohistochemical receptor), most missing. Important co-interventions demonstrated balance (adjuvant CT, adjuvant ET, axillary management, adjuvant RT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. Included from the beginning of uptake of intervention	All patients included but some did not have sufficient follow-up so excluded. Details not given	Objective outcome measure	No indication of selected reporting	
Mansell 2017	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors significantly different: age, histological type, tumour size, grade, axillary node status, immunohistochemical receptor (ER, PR). Important co-interventions balanced, some significantly different: adjuvant CT, adjuvant ET	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up until June 2016	Objective outcome measure	No indication of selected reporting	
Mazouni 2013	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors balance: histological type, tumour size, grade, axillary node status, immunohistochemical receptor (PR). Important co-interventions predefined and uniform across studies (axillary surgery, neoadjuvant CT, adjuvant RT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Rose 2019	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors statistically adjusted for. Location of surgeries different in inter-	All participants eligible included	Classification of interventions clear and determined at the	All patients received the surgical intervention	Most patients included	Objective outcome measure	No indication of selected reporting	

Table 3. Risk of bias for disease-free survival *(Continued)*

		vention and control. Some co-interventions balanced, some missing		start of intervention	described in methods				
Vieira 2016	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance. Matched for demographic and oncological aspects. Important co-interventions demonstrated balance, missing data on axillary management of cases (97.4% for control group)	All OPS participants eligible included, matched BCS 'cases were matched to decrease a possible bias selection'	Classification of interventions clear and determined at the start of intervention: standard surgical treatment was quadrantectomy combined with level III axillary node dissection with was performed in 97.4% of patients	All patients received the surgical intervention described in methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Nakagomi 2019	Mx	Serious	Low	Low	Low	Low	Serious	Moderate	Serious
		Some variables demonstrated balance (histological type, axillary node status, immunohistochemical receptor status), some significantly different (age, tumour size, stage), many missing. Important co-interventions missing (RT, axillary management), neoadjuvant CT significantly different	All participants eligible included	Classification of interventions clear and determined at the start of intervention: latisimus dorsi mini flap or mastectomy	All patients received the surgical intervention described in methods	All patients included followed up	Objective outcome measure but details of follow-up time not given	No indication of selected reporting	
DeLorenzi 2016 (2)	Mx + R	Low	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (grade, immunohistochemical receptors) or matched (age (within 5 years), year of surgery (within 2 years), number of positive axillary lymph nodes, tumour subtype). Important co-inter-	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure - due to margin status	No indication of selected reporting	

Table 3. Risk of bias for disease-free survival *(Continued)*

		ventions balanced across intervention group (adjuvant CT, adjuvant ET), adjuvant RT different							
Mansell 2017	Mx + R	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Some clinicopathological significantly different: age, immunohistochemical receptor (ER, PR). Other important clinicopathological factors balance: histological type, tumour size, grade, axillary node status, immunohistochemical receptor (HER2). Important co-interventions demonstrated balance, adjuvant RT significantly different	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up until June 2019	Objective outcome measure	No indication of selected reporting	
Ozmen 2020	Mx + R	Serious	Moderate	Low	Moderate	Low	Low	Moderate	Serious
		Important clinicopathological factors balance, some different (age, menopausal status, BMI, tumour size, grade, axillary node status, immunohistochemical receptor status (ER), multifocality), some missing. Important co-interventions significantly different (adjuvant RT and axillary management), some missing (neoadjuvant RT + CT, adjuvant CT + ET)	Women chose their operation after being told the potential risks and benefits. Bias in assignment: "Both two procedures were explained to patients, and their choices were recorded."	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in methods. All operations done by a single surgeon with more than 30 years of experience in breast surgery.	Most patients included: "Median follow-up time was 56 (14-116) months."	Objective outcome measure	No indication of selected reporting	

BMI: body mass index

CT: chemotherapy
ER: oestrogen receptor
ET: endocrine therapy
HER2: human epidermal growth factor receptor 2
PR: progesterone receptor
R: reconstruction
RT: radiotherapy

Table 4. Risk of bias for overall survival

Study	Control	Confounding	Selection	Classification of intervention	Deviations from intended intervention	Missing data	Measurement of outcomes	Selection of reported results	Overall
Acea-Nebril 2017	S-BCS	Serious	Low	Low	Moderate	Low	Low	Moderate	Serious
		Some clinicopathological variables significantly different (age, menopausal status, tumour size, tumour stage, axillary lymph node status, location of tumour, multifocality). Some co-interventions balanced (neoadjuvant CT and axillary management), some missing	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Some aspects maybe determined retrospectively	Deviation from intended co-intervention (adjuvant therapy time), co-interventions significantly different	All patients followed up	Objective outcome measure	No indication of selected reporting	
Borm 2019	S-BCS	Serious	Low	Low	Low	Moderate	Low	Moderate	Serious
		Most clinicopathological variables significantly different: age, tumour size, tumour grade, axillary node status, immunohistochemical receptors (ER status). Important co-interventions (adjuvant CT, adjuvant ET) not balanced across intervention group and may effect the outcome	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Analysis unlikely to have removed risk of bias from missing data	Objective outcome measure	No indication of selected reporting	
Carter 2016	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious

Table 4. Risk of bias for overall survival *(Continued)*

		Most clinicopathological variables significantly different (age, BMI, tumour size, stage, axillary node status, immunohistochemical receptors (ER, PR, TN), multifocality). Important co-interventions not balanced across intervention group and may affect the outcome (neoadjuvant CT (all), adjuvant RT (Mx/Mx+R), adjuvant CT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	
DeLorenzi 2016 (1)	S-BCS	Low	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (menopausal, histological type, grade, axillary node status, immunohistochemical receptors, lymphovascular invasion) or matched (age (within 5 years), year of surgery (within 2 years), tumour size. Important co-interventions balanced across intervention group (adjuvant CT, adjuvant RT, adjuvant ET)	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure - due to margin status	No indication of selected reporting	
DeLorenzi 2018	S-BCS	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (Age, BMI, tumour size, immunohistochemical receptors, multifocality), some significantly different (menopausal, grade). Some co-interventions balanced across intervention group (adjuvant RT, any adjuvant therapy)	Selection may be related to the outcome (mastectomy eventually excluded)	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure - due to margin status	No indication of selected reporting	
Gulcelik 2013	S-BCS	Moderate	Low	Low	Moderate	Low	Low	Moderate	Moderate

Table 4. Risk of bias for overall survival *(Continued)*

		Important clinicopathological factors demonstrated balance (age, tumour size, immunohistochemical receptor), most missing. Important co-interventions demonstrated balance (adjuvant CT, adjuvant ET, axillary management, adjuvant RT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. Included from the beginning of uptake of intervention	All patients included but some did not have sufficient follow-up so excluded. Details not given	Objective outcome measure	No indication of selected reporting	
Lee 2018	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance (age, BMI), some significantly different (tumour size and stage). No breakdown between control and study groups for data on cancer treatment	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. Centre with large numbers	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Mansell 2017	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors significantly different: age, histological type, tumour size, grade, axillary node status, immunohistochemical receptor (ER, PR). Important co-interventions balanced, some significantly different: adjuvant CT, adjuvant ET	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up until June 2017	Objective outcome measure	No indication of selected reporting	
Mazouni 2013	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors balance: Histological type, tumour size, grade, axillary node status, immunohistochemical receptor (PR). Important co-interventions predefined and uniform	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	

Table 4. Risk of bias for overall survival *(Continued)*

		across studies (axillary surgery, neoadjuvant CT, adjuvant RT)							
Niinikoski 2019 (2)	S-BCS	Serious	Moderate	Low	Low	Moderate	Low	Moderate	Serious
		Important clinicopathological factors significantly different: age, tumour size, grade, axillary node status, immunohistochemical status (ER), multifocality. Important co-intervention demonstrated balance (adjuvant RT), some significantly different (adjuvant CT and ET)	All participants eligible included. Excluded on basis on diagnosis by biopsy/incidental. Excluded those without adjuvant therapy nor axillary surgery. Also excluded if follow-up < 3 years	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods	Some loss to follow-up for local recurrence free survival: 140/611 in intervention group, 249/1189 in control group	Objective outcome measure	No indication of selected reporting	
Piper 2016	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance (BMI, histological type), age matched for and stage significantly different. Important co-interventions missing	Patients without negative margins excluded, minimum 2 years follow-up (O-BCS done more recently)	Classification of interventions clear and determined at the start of intervention: "All reduction mammoplasties were performed either via an inferior or superior-medial pedicle approach, with a Wise pattern or	All patients received the surgical intervention described in methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	

Table 4. Risk of bias for overall survival *(Continued)*

				vertical skin pattern incision, based on tumour location"					
Rose 2019	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors statistically adjusted for. Location of surgeries different in intervention and control. Some co-interventions balanced (adjuvant RT, adjuvant CT, adjuvant ET), axillary surgery different	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods	Most patients included	Objective outcome measure	No indication of selected reporting	
Vieira 2016	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance. Matched for demographic and oncological aspects. Important co-interventions demonstrated balance, missing data on axillary management of cases (97.4% for control group)	All O-BCS participants eligible included, matched s-BCS: "cases were matched to decrease a possible bias selection"	Classification of interventions clear and determined at the start of intervention: "Oncoplastic procedures used encompass Clough level I and II techniques", "The 'standard lumpectomy' performed in this study, consists of removal of the tumour, with or without simple closure of the glandular tissue, without mobilization of surrounding tissue."	All patient received the surgical intervention described in methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Carter 2016	Mx	Serious	Low	Low	Low	Low	Low	Moderate	Serious

Table 4. Risk of bias for overall survival *(Continued)*

		Most clinicopathological variables significantly different (age, BMI, tumour size, stage, axillary node status, immunohistochemical receptors (ER, PR, TN), multifocality). Important co-interventions not balanced across intervention group and may affect the outcome (neoadjuvant CT (all), adjuvant RT (Mx/Mx+R), adjuvant CT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Lee 2018	Mx	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance (age, BMI), some significantly different (tumour size and stage). No breakdown between control and study groups for data on cancer treatment	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. Centre with large numbers	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Ren 2014	Mx	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (histological type and location) or matched (age, tumour size, axillary lymph node status, immunohistochemical receptor, (ER, HER2)). Co-intervention information missing for control group	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods	Most patients included: "The median follow-up time was 83 months in BCT and 81 months in mastectomy."	Objective outcome measure	No indication of selected reporting	
Carter 2016	Mx + R	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Most clinicopathological variables significantly different (age, BMI, tumour size, stage, axillary node	All participants el-	Classification of interventions clear and deter-	All patients received the surgical inter-	Most patients followed up	Objective outcome measure	No indication of se-	

Table 4. Risk of bias for overall survival *(Continued)*

		status, immunohistochemical receptors (ER, PR, TN), multifocality). Important co-interventions not balanced across intervention group and may affect the outcome (neoadjuvant CT (all), adjuvant RT (Mx/MxR), adjuvant CT)	igible included	mined at the start of intervention. Operative details given clearly	vention described in the methods			lected reporting	
DeLorenzi 2016 (2)	Mx + R	Low	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (Grade, immunohistochemical receptors) or matched (age (within 5 years), year of surgery (within 2 years), number of positive axillary lymph nodes, tumour subtype) Important co-interventions balanced across intervention group (adjuvant CT, adjuvant ET), adjuvant RT different	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure - due to margin status	No indication of selected reporting	
Lee 2018	Mx + R	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance (age, BMI), some significantly different (tumour size and stage). No breakdown between control and study groups for data on cancer treatment	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. Centre with large numbers	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Mansell 2017	Mx + R	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Some clinicopathological significantly different: age, immunohistochemical receptor (ER, PR). Other important clinicopathological factors balance: histological type, tumour size, grade, axillary node status, immunohistochemical receptor (HER2). Important co-interven-	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up until June 2020	Objective outcome measure	No indication of selected reporting	

Table 4. Risk of bias for overall survival *(Continued)*

		tions demonstrated balance, adjuvant RT significantly different							
Ozmen 2020	Mx + R	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors balance, some different (age, menopausal status, BMI, tumour size, grade, axillary node status, immunohistochemical receptor status (ER), multifocality), some missing. Important co-interventions significantly different (adjuvant RT and axillary management), some missing (neoadjuvant RT + CT, adjuvant CT + ET)	Women chose their operation after being told the potential risks and benefits. Bias in assignment: "Both two procedures were explained to patients, and their choices were recorded."	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods. All operations done by a single surgeon with more than 30 years of experience in breast surgery.	Most patients included: "Median follow-up time was 56 (14-116) months."	Objective outcome measure	No indication of selected reporting	

BMI: body mass index
CT: chemotherapy
ER: oestrogen receptor
ET: endocrine therapy
HER2: human epidermal growth factor receptor 2
Mx: mastectomy
PR: progesterone receptor
R: reconstruction
RT: radiotherapy

Table 5. Risk of bias for re-excision rates

Study	Control	Confounding	Selection	Classification of intervention	Deviations from intend-	Missing data	Measurement of outcomes	Selection of reported results	Overall

Table 5. Risk of bias for re-excision rates *(Continued)*

					ed intervention				
Acea-Nebril 2005	S-BCS	Serious	Moderate	Low	Moderate	Low	Low	Moderate	Serious
		Size significantly different, most clinicopathological variables missing	Selection into the study may have been related to intervention. Selection to which intervention the women had was based on tumour characteristic. This difference at selection may have an effect on the outcome.	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	Deviation from intended intervention (minor changes in operation technique in some patients) but does not impact this outcome	All patients followed up	Objective outcome measure	No indication of selected reporting	
Acea-Nebril 2017	S-BCS	Serious	Low	Low	Moderate	Low	Low	Moderate	Serious
		Some clinicopathological variables significantly different (age, menopausal status, tumour size, tumour stage, axillary lymph node status, location of tumour, multifocality). Some co-interventions balanced (neoadjuvant CT and axillary management), some missing	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Some aspects maybe determined retrospectively	Deviation from intended co-intervention (adjuvant therapy time) and co-interventions significantly different but minimal impact on this outcome	All patients followed up	Objective outcome measure	No indication of selected reporting	
Amitai 2018	S-BCS	Serious	Serious	Low	Low	Moderate	Low	Moderate	Serious

Table 5. Risk of bias for re-excision rates *(Continued)*

		Most clinicopathological variables significantly different (age, axillary node status, immunohistochemical receptors). Adjuvant RT demonstrated balanced, most co-interventions missing	Selection may be related to the outcome (those with Mx eventually excluded)	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Analysis unlikely to have removed risk of bias from missing data	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Atallah 2015*	S-BCS	Moderate	No information	Low	No information	No information	Low	Moderate	Moderate
		Some clinicopathological variables demonstrated balance (age, BMI, menopausal status, tumour size, location, histological type, immunohistochemical receptors), some missing	-	Classification of interventions clear and determined at the start of intervention. Some aspects maybe determined retrospectively	-	-	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Bali 2018	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some clinicopathological variables demonstrated balance (age, histological type, immunohistochemical receptors, tumour locations). Tumour size significantly different, most missing. Important co-interventions (neoadjuvant and adjuvant CT) not balanced across intervention group but unlikely to effect the outcome	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	All patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention. The margins for determining re-excisions changed overtime	No indication of selected reporting	
Cassi 2016	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious

Table 5. Risk of bias for re-excision rates *(Continued)*

		Some clinicopathological variables demonstrated balance, most missing. Important co-interventions balanced across intervention group (adjuvant RT) some information missing	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Chakravorty 2012	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some clinicopathological variables demonstrated balance (age, axillary node status) and some different (histological type, tumour size, grade, sample weight), most missing. Important co-interventions balanced across intervention group (adjuvant RT, adjuvant CT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Chauhan 2016 (1)	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some clinicopathological variables demonstrated balance (histological type, grade, axillary node status, immunohistochemical receptors) and some different (age, tumour size, tumour location), most missing. Important co-interventions predefined and uniform across studies	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Chauhan 2016 (2)	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Axillary node status demonstrated balance and some clinicopathological variables different (age, tumour size, tumour location), most missing. Important	All participants eligible included	Classification of interventions clear and determined at the start of intervention.	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	

Table 5. Risk of bias for re-excision rates *(Continued)*

		co-interventions predefined and uniform across studies		Operative details given clearly					
Crown 2015	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors demonstrated balance (age, histological type), some significantly different (tumour size, immunohistochemical receptors). Different years of intervention. Adjuvant RT balanced	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given and separated by years	All patients received the surgical intervention described in the methods. Study period chosen to allow for learning period after adoption of O-BCS	Most patients followed up	Objective outcome measure - due to margin status	No indication of selected reporting	
DeLorenzi 2016 (1)	S-BCS	Low	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (menopausal, histological type, grade, axillary node status, immunohistochemical receptors, lymphovascular invasion) or matched (age (within 5 years), year of surgery (within 2 years), tumour size). Important co-interventions balanced across intervention group (adjuvant CT, adjuvant RT, adjuvant ET)	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention. Decided on mastectomy after multi disciplinary team discussion	No indication of selected reporting	
Di Micco 2017	S-BCS	Moderate	Serious	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (Smoking status, BMI, histolog-	Selection may be related to the	Classification of interventions clear and deter-	All patients received the surgical inter-	Most patients followed up	Outcome measure likely only	No indication of se-	

Table 5. Risk of bias for re-excision rates *(Continued)*

		ical type, tumour size, immunohistochemical receptor, tumour location), some significantly different (Age, axillary node status). Some co-interventions balanced across intervention group (neoadjuvant CT, adjuvant ET, axillary management, adjuvant RT), some different (radiation boost, adjuvant CT)	outcome (Mx eventually)	mined at the start of intervention	vention described in the methods		minimally influenced by knowledge of intervention. Decided on re-excision after MDT discussion	lected reporting	
Dolan 2015	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some clinicopathological variables demonstrated balance (histological type, grade, immunohistochemical receptor) and some different (age, tumour size, axillary node status), some missing. Some co-interventions balanced across intervention group (adjuvant RT, adjuvant ET, axillary management), adjuvant CT different	All participants eligible included	Classification of interventions clear and determined at the start of intervention, details of operations described	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Down 2013	S-BCS	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Some clinicopathological variables demonstrated balance (age, histological type, grade), tumour size different, some missing. Adjuvant RT balanced across intervention group, some co-interventions missing	All patients included. Patients were selected for intervention if cosmetic outcome with control would be bad (selection bias but does not affect this outcome)	Classification of interventions clear and determined at the start of intervention, details of operations described	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 5. Risk of bias for re-excision rates *(Continued)*

Fan 2019	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors matched (age, BMI, stage) or demonstrated balance (histological type), some missing. Important co-interventions demonstrated balance (neoadjuvant CT, adjuvant RT, adjuvant CT, adjuvant ET)	All participants eligible included, control selected for	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. Surgeries done by experienced plastic and breast surgeons.	All patients followed up for 30 days and for re-excisions specifically	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Farooqi 2019*	S-BCS	Serious	No information	Low	No information	Low	Low	Moderate	Serious
		Tumour size significantly different. Neoadjuvant CT balanced, most co-interventions missing	-	Classification of interventions clear and determined at the start of intervention. Some aspects maybe determined retrospectively	-	All patients followed up for 30 days and for re-excisions specifically	Objective outcome measure (tumour at ink)	No indication of selected reporting	
Gicalone 2007 (1)	S-BCS	Moderate	Moderate	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors demonstrated balance (BMI, histological type, tumour size, grade, axillary node status, immunohistochemical receptor), some missing	Women chose their operation after being told the potential risks and benefits. Bias in assignment	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. All operations done by 2 experienced surgeons	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Gicalone 2007 (2)	S-BCS	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious

Table 5. Risk of bias for re-excision rates *(Continued)*

		Important clinicopathological factors demonstrated balance (BMI, tumour size, tumour location), some missing	Women chose their operation after being told the potential risks and benefits. Bias in assignment	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. All operations done by 2 experienced surgeons	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Gicalone 2015	S-BCS	Moderate	Moderate	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors demonstrated balance (age, smoking status, diabetes, BMI, other medical comorbidities, histological type, tumour size), some missing	Women chose their operation after being told the potential risks and benefits. Bias in assignment	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. Both intervention and control done by experienced surgeons.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Gulcelik 2013	S-BCS	Moderate	Low	Low	Moderate	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (age, tumour size, immunohistochemical receptor), most missing. Important co-interventions demonstrated balance (adjuvant CT, adjuvant ET, axillary management, adjuvant RT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. Included from the beginning of uptake of intervention	All patients included but some did not have sufficient follow-up so excluded. Details not given	Objective outcome measure	No indication of selected reporting	
Hamdi 2008	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious

Table 5. Risk of bias for re-excision rates *(Continued)*

		Important clinicopathological factors different (age, histological type, tumour size), most missing. Axillary management demonstrated balance	Not clear if/why all patients in the time period not selected	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. All reconstruction done by plastic surgeons whilst tumourectomy by gynaecologist	All patients included followed up	All positive margins (tumour cells at surgical margin) re-excised	No indication of selected reporting	
Jiang 2015	S-BCS	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors balanced (age, weight, histology type,tumour size, grade, stage, tumour location)	60 women were picked, study says randomised but not clear how therefore classified as cohort. Risk of selection	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Keleman 2019	S-BCS	Moderate	Moderate	Low	Low	Serious	Low	Moderate	Serious
		Some variables demonstrated balance (age, smoking status, diabetes, BMI, type of cancer, tumour size, grade, stage, immunohistochemical receptor) some different (preoperative bra size, axillary node status) but unlikely to affect outcome. Important co-intervention of adjuvant RT demonstrated balance, some significantly different (neoadjuvant CT, adjuvant CT, adjuvant ET, axillary management) but less of an impact on outcome	All intervention participants eligible included, random patients selected for control	Classification of interventions clear and determined at the start of intervention. The types of intervention were: therapeutic mammaplasty (superior, central, inferior pedicle Wise-pattern), dermoglandular rotation (medial, lateral mammo-	All patients received the surgical intervention described in the methods. Operations done by experienced breast surgeons.	Patients missed due to loss to follow up and did not respond to outcome, equal numbers in both groups so impact may be similar	Objective outcome measure	No indication of selected reporting	

Table 5. Risk of bias for re-excision rates *(Continued)*

				plasty), periareolar (round block, omega) or standard BCS		across groups			
Lansu 2014	S-BCS	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors balance (age, tumour size, tumour location), some missing. Important co-interventions demonstrated balance (adjuvant CT, adjuvant ET, axillary management, adjuvant RT), some significantly different (neoadjuvant CT)	Patients had to be disease-free and alive at the time of inclusion	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Losken 2014	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors balance. Age and BMI significantly different. Neoadjuvant CT significantly different	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. Operation done by experienced surgeon.	All patients included followed up (requirement for patients to have at least 2 months follow-up data from time of surgery)	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Malhaire 2015	S-BCS	No information	Serious	Low	Low	Low	Low	Moderate	Serious
		-	Selection based on localisation techniques	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. All	All patients included followed up	Outcome measure likely only minimally influenced by knowl-	No indication of selected reporting	

Table 5. Risk of bias for re-excision rates *(Continued)*

					surgeons had training in O-BCS.		edge of intervention		
Mansell 2015	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors significantly different: age, histological type, tumour size, grade, axillary node status, immunohistochemical receptor (ER, PR). Important co-interventions significantly different: adjuvant CT, adjuvant ET	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Matrai 2014	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Tumour size significantly different. Some variables demonstrated balance (age, histological type, grade, tumour location, bra size, immunohistochemical receptor, axillary lymph node status). Matching of patients reported but not defined: "the same clinicopathological parameters of 60 traditional breast-conserving surgeries operated by the same breast surgeon were used." Important co-interventions including adjuvant RT demonstrated balance. Adjuvant CT significantly different	Unclear why these 60 patients selected (not consecutive, some retrospective and some prospective), controls matched	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. Operation done by experienced surgeon.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Mazouni 2013	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors balance: histological type, tumour size, grade, axillary node status, immunohistochemical receptor (PR). Important co-interventions predefined and uniform	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	Outcome measure likely only minimally influenced by knowl-	No indication of selected reporting	

Table 5. Risk of bias for re-excision rates *(Continued)*

		across studies (axillary surgery, neoadjuvant CT, adjuvant RT)					edge of intervention		
Mukhtar 2018	S-BCS	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factor significantly different: shows that when tumour size is matched for then there is no difference in re-excisions due to O-BCS. No information on other clinicopathological factors or co-interventions	All participants eligible included. Possible bias in assignment: "Surgical procedures were performed according to surgeon recommendation and patient choice."	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Niinikoski 2019 (2)	S-BCS	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors significantly different: age, tumour size, grade, axillary node status, immunohistochemical status (ER, TN), multifocality. Important co-intervention demonstrated balance (adjuvant RT), some significantly different (adjuvant CT and ET)	All participants eligible included. Excluded on basis on diagnosis by biopsy/incidental. Excluded those without adjuvant therapy nor axillary surgery. Also excluded if follow-up < 3 years	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 5. Risk of bias for re-excision rates *(Continued)*

Ojala 2017	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors significantly different (tumour size, tumour location, axillary node status, multifocality, histological type). Important co-interventions missing, adjuvant RT demonstrated balance, axillary management significantly different	All participants eligible included: "All patients having breast conserving surgery (BCS) due to primary breast cancer at the Helsinki and Uusimaa Hospital District during 2010 were included in this study"	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Palsoditlir 2018	S-BCS	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance, some significantly different (e.g. tumour size), some missing (grade, stage, location of tumour). Adjuvant ET balanced, some co-interventions missing: radiotherapy, chemotherapy, axillary management	All women included according to selection criteria. Selection criteria excluded level 2 O-BCS procedures assigning these as minimal: "Level 1 and level 2 oncoplastic procedures (minimal gland mo-	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 5. Risk of bias for re-excision rates *(Continued)*

			bilization techniques) were not included in the study group."						
Piper 2016	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance (BMI, histological type), age matched for and stage significantly different. Important co-interventions missing	Patients without negative margins excluded, minimum 2 years follow-up (OPS done more recently)	Classification of interventions clear and determined at the start of intervention: "All reduction mammoplasties were performed either via an inferior or superior-medial pedicle approach, with a Wise pattern or vertical skin pattern incision, based on tumour location"	All patient received the surgical intervention described in methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Tang 2016	S-BCS	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (tumour size, stage, BMI, age). Some co-interventions balanced (axillary management), some missing (medical cancer treatment)	All participants eligible included	Classification of interventions clear and determined at the start of intervention: "Standard Breast Conservation Surgery (SBCS) group had surgery conducted according to the National Surgical Adjuvant Breast and Bowel Project (NSABP)	All patient received the surgical intervention described in methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 5. Risk of bias for re-excision rates *(Continued)*

				standard guidelines."					
Tenofsky 2014	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance, some significantly different, some missing (histological type, grade, stage, axillary node status). Important co-interventions significantly different (adjuvant RT), some missing (neoadjuvant RT + CT, adjuvant CT + ET, axillary management)	Quote: "Patients were excluded if they received a mastectomy within 6 months of the lumpectomy, and/or if they received 6 months of follow-up after their procedure."	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods. Operation done by experienced surgeon.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Vieira 2016	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance. Matched for demographic and oncological aspects. Important co-interventions demonstrated balance, missing data on axillary management of cases (97.4% for control group)	All OPS participants eligible included, matched s-BCS: "cases were matched to decrease a possible bias selection"	Classification of interventions clear and determined at the start of intervention: "Oncoplastic procedures used encompass Clough level I and II techniques", "The 'standard lumpectomy' performed in this study, consists of removal of the tumour, with or without simple closure of the glandular tissue, without mobiliza-	All patients received the surgical intervention described in methods.	All patients included followed up	Objective outcome measure	No indication of selected reporting	

Table 5. Risk of bias for re-excision rates *(Continued)*

				tion of surrounding tissue."					
Wijgman 2017	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance, some significantly different (tumour size), some missing. Important co-interventions demonstrated balance, some different	All participants eligible included	Classification of interventions clear and determined at the start of intervention: "Oncoplastic procedures used encompass Clough level I and II techniques", "The 'standard lumpectomy' performed in this study, consists of removal of the tumour, with or without simple closure of the glandular tissue, without mobilization of surrounding tissue."	All patients received the surgical intervention described in the methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Wong 2017*	S-BCS	Serious	Low	Low	No information	Low	Low	Moderate	Serious
		Tumour size significantly different, most clinicopathological variables missing	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Some aspects maybe determined retrospectively	-	All patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

BMI: body mass index
CT: chemotherapy

ER: oestrogen receptor
ET: endocrine therapy
Mx: mastectomy
PR: progesterone receptor
R: reconstruction
RT: radiotherapy

Table 6. Risk of bias for complications

Study	Control	Confounding	Selection	Classification of intervention	Deviations from intended intervention	Missing data	Measurement of outcomes	Selection of reported results	Overall
Acea-Nebril 2005	S-BCS	Serious	Moderate	Low	Moderate	Low	Low	Moderate	Serious
		Size significantly different, most clinicopathological variables missing	Selection into the study may have been related to intervention. Selection to which intervention the women had was based on tumour characteristic. This difference at selection may have an effect on the outcome.	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	Deviation from intended intervention (minor changes in operation technique in some patients) but does not impact this outcome	All patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Acea-Nebril 2017	S-BCS	Serious	Low	Low	Moderate	Low	Low	Moderate	Serious
		Some clinicopathological variables significantly different (age, menopausal status, tumour size, tumour stage, axillary lymph node status, location of tumour, multifocality), Some co-interventions balanced (neoadjuvant CT	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Some aspects maybe	Deviation from intended co-intervention (adjuvant therapy time) and co-interventions	All patients followed up	Objective outcome measure	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

		and axillary management), some missing		determined retrospectively	significantly different				
Acosta-Marin 2014	S-BCS	Serious	Serious	Low	low	Serious	Low	Moderate	Serious
		Some clinicopathological variables demonstrated balance (age, BMI) and some significantly different (preoperative bra size, tumour size), most missing	Selection may be related to the outcome (mastectomy eventually)	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Analysis unlikely to have removed risk of bias from missing data - missed women with complications in short term. If major may have had to have mastectomy and therefore excluded	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Amitai 2018	S-BCS	Serious	Serious	Low	Low	Serious	Low	Moderate	Serious
		Most clinicopathological variables significantly different (age, axillary node status,immunohistochemical receptors), adjuvant RT demonstrated balanced, most co-interventions missing	Selection may be related to the outcome (those with mastectomy eventually excluded)	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Analysis unlikely to have removed risk of bias from missing data - missed women with complications in short term. If major may	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

						have had to have mastectomy and therefore excluded			
Angarita 2020	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Most clinicopathological variables significantly different (age, BMI, race, smoking status, alcohol consumption, COPD, PCI, HTN, bleeding disorder, steroid use, previous vascular disease, previous cardiac surgery, dialysis, hemiplegia, TIA, CVA, ASA status, histological type). Adjusted risk analysis for some comorbidities not extractable for our study, Important co-interventions (axillary management, neoadjuvant chemotherapy, anaesthetic technique) not balanced across intervention group but unlikely to effect the outcome	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	All patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention. Difficulties with how complications recorded in the database. If axillary surgery undergone affects the study and this was not balanced across the two. Authors accounted for difficulties/differences in the database	No indication of selected reporting	
Carter 2016	S-BCS	Serious	Low	Low	low	Low	Low	Moderate	Serious

Table 6. Risk of bias for complications *(Continued)*

		Most clinicopathological variables significantly different (age, BMI, tumour size, stage, axillary node status, immunohistochemical receptors (ER, PR, TN), multifocality), Important co-interventions not balanced across intervention group and may affect the outcome (neoadjuvant CT (all), adjuvant RT (Mx/Mx+R), adjuvant CT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Cassi 2016	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some clinicopathological variables demonstrated balance, most missing, Important co-interventions balanced across intervention group (adjuvant RT), some information missing	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Chauhan 2016 (1)	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some clinicopathological variables demonstrated balance (histological type, grade, axillary node status, immunohistochemical receptors) and some different (age, tumour size, tumour location), most missing, Important co-interventions predefined and uniform across studies	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Chauhan 2016 (2)	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Axillary node status demonstrated balance and some clinicopathological variables different (age, tumour size, tumour location), most missing, Important	All participants eligible included	Classification of interventions clear and determined at the start of inter-	All patients received the surgical intervention described	Most patients followed up	Outcome measure likely only minimally influenced	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

		co-interventions predefined and uniform across studies		vention. Operative details given clearly	in the methods		by knowledge of intervention		
Crown 2019	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors demonstrated balance (age, smoking, BMI, histological type), some significantly different (tumour size, immunohistochemical receptors). Different years of intervention, adjuvant CT balanced across intervention group, neoadjuvant CT significantly different, some co-interventions missing	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given and separated by years	All patients received the surgical intervention described in the methods. Study period chosen to allow for learning period after adoption of O-BCS	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
DeLorenzi 2016 (1)	S-BCS	Low	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (menopausal, histological type, grade, axillary node status, immunohistochemical receptors, lymphovascular invasion) or matched (age (within 5 years), year of surgery (within 2 years), tumour size). Important co-interventions balanced across intervention group (adjuvant CT, adjuvant RT, adjuvant ET)	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention. Decided on mastectomy after multi-disciplinary discussion	No indication of selected reporting	
Di Micco 2017	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors demonstrated balance (smoking status, BMI, histological	Selection may be related to the outcome	Classification of interventions clear and de-	All patients received the surgical in-	Most patients followed up	Outcome measure likely only	No indication of se-	

Table 6. Risk of bias for complications *(Continued)*

		type, tumour size, immunohistochemical receptor, tumour location), some significantly different (age, axillary node status). Some co-interventions balanced across intervention group (neoadjuvant CT, adjuvant ET, axillary management, adjuvant RT), some different (radiation boost, adjuvant CT)	(mastectomy eventually)	termined at the start of intervention	tervention described in the methods		minimally influenced by knowledge of intervention	lected reporting	
Dolan 2015	S-BCS	Serious	Low	Low	Low	Low	Low	Serious	Serious
		Some clinicopathological variables demonstrated balance (histological type, grade, immunohistochemical receptor) and some different (age, tumour size, axillary node status), some missing, Some co-interventions balanced across intervention group (adjuvant RT, adjuvant ET, axillary management), adjuvant CT different	All participants eligible included	Classification of interventions clear and determined at the start of intervention, details of operations described	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	Only reports complications requiring re-excisions	
Down 2013	S-BCS	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Some clinicopathological variables demonstrated balance (age, histological type, grade), tumour size different, some missing. Adjuvant RT balanced across intervention group, some co-interventions missing	All patients included. Patients were selected for intervention if cosmetic outcome with control would be bad (selection bias but does not affect this outcome)	Classification of interventions clear and determined at the start of intervention, details of operations described	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

Gicalone 2007 (1)	S-BCS	Moderate	Serious	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors demonstrated balance (BMI, histological type, tumour size, grade, axillary node status, immunohistochemical receptor), some missing	Women chose their operation after being told the potential risks and benefits. Bias in assignment	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. All operations done by 2 experienced surgeons.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Gicalone 2007 (2)	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors demonstrated balance (BMI, tumour size, tumour location), some missing	Women chose their operation after being told the potential risks and benefits. Bias in assignment	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. All operations done by 2 experienced surgeons.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Gicalone 2015	S-BCS	Moderate	Serious	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors demonstrated balance (age, smoking status, diabetes, BMI, other medical comorbidities, histological type, tumour size), some missing	Women chose their operation after being told the potential risks and benefits. Bias in assignment	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. Both intervention and control done by ex-	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

					perienced surgeons.				
Jiang 2015	S-BCS	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors balanced (age, weight, histology type, tumour size, grade, stage, tumour location)	60 women were picked, study says randomised but not clear how; therefore classified as cohort. Risk of selection	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Keleman 2019	S-BCS	Moderate	Moderate	Low	Low	Serious	Low	Moderate	Serious
		Some variables demonstrated balance (age, smoking status, diabetes, BMI, type of cancer, tumour size, grade, stage, immunohistochemical receptor), some different (preoperative bra size, axillary node status) but unlikely to affect outcome. Important co-intervention of adjuvant RT demonstrated balance, some significantly different (neoadjuvant CT, adjuvant CT, adjuvant ET, axillary management) but less of an impact on outcome	All intervention participants eligible included, random patients selected for control	Classification of interventions clear and determined at the start of intervention. The types of intervention were: Therapeutic mammaplasty (superior, central, inferior pedicle Wise-pattern), Dermoglandular rotation (medial, lateral mammoplasty), Periareolar (round block, omega) or standard BSC	All patients received the surgical intervention described in the methods. Operations done by experienced breast surgeons.	Patients missed due to loss to follow-up and did not respond to outcome, equal numbers in both groups so impact may be similar across groups	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Kimball 2018	S-BCS	Serious	Moderate	Low	Moderate	Low	Moderate	Moderate	Serious

Table 6. Risk of bias for complications *(Continued)*

		Some clinicopathological variables demonstrated balance (BMI) and some different (age, medical comorbidities, histological type), some missing - issue with the database, Important co-interventions significantly different (adjuvant RT, adjuvant CT, axillary management)	Selection based on coding - not standardised for O-BCS yet	Classification of intervention based on codes - not uniform across sites. Types of intervention: partial mastectomy ('lumpectomy') and three breast reconstructive/repair procedures	All patient received the surgical intervention described in methods. All operations done by a single surgeon with more than 30 years of experience in breast surgery. Notes that uptake of novel techniques not uniform across centres	All patients included followed up	Coding not uniform for complications	No indication of selected reporting	
Lansu 2014	S-BCS	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors balance (age, tumour size, tumour location), some missing. Important co-interventions demonstrated balance, some significantly different	Patients had to be disease-free and alive at the time of inclusion	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Matrai 2014	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Tumour size significantly different. Some variables demonstrated balance (age, histological type, grade, tumour location, bra size, immunohistochemical receptor, axillary lymph node status). Matching of patients report-	Unclear why these 60 patients selected (not consecutive, some retrospective	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. Opera-	All patients included followed up	Outcome measure likely only minimally influenced by knowl-	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

		ed but not defined: "the same clinicopathological parameters of 60 traditional breast-conserving surgeries operated by the same breast surgeon were used". Important co-interventions including adjuvant RT demonstrated balance. Adjuvant CT significantly different	and some prospective), controls matched		tion done by experienced surgeon.		edge of intervention		
Nakada 2019	S-BCS	No information	Moderate	Low	Low	Low	Moderate	Moderate	Serious
		-	Participants were excluded if they were lost to follow-up before 5 years	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention. Lovy grading criteria	No indication of selected reporting	
Ojala 2017	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors significantly different (tumour size, tumour location, axillary node status, multifocality, histological type). Important co-interventions missing, adjuvant RT demonstrated balance, axillary management significantly different	All participants eligible included: "All patients having breast conserving surgery (BCS) due to primary breast cancer at the Helsinki and Uusimaa Hospital District during 2010 were included in this study"	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

Ozmen 2016*	S-BCS	Serious	Moderate	Low	No information	Low	Low	Moderate	Serious
		Some clinicopathological variables significantly different (age, BMI, multifocality), adjuvant RT balanced, most co-interventions missing	Selection into the study may have been related to intervention as BCS data were collected before introduction of O-BCS technique before 2010. O-BCS patients after 2010 only	Classification of interventions clear and determined at the start of intervention. Some aspects maybe determined retrospectively	-	All patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Palsoditlir 2018	S-BCS	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance, some significantly different (e.g. tumour size), some missing (grade, stage, location of tumour), adjuvant ET balanced, some co-interventions missing: radiotherapy, chemotherapy, axillary management	All women included according to selection criteria. Selection criteria excluded level 2 O-BCS procedures assigning these as minimal: "Level 1 and level 2 oncoplastic procedures (minimal gland mobilisation techniques) were not included in the study group."	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

PlaFarnos 2018*	S-BCS	Serious	Moderate	Low	No information	No information	Low	Moderate	Serious
		Multifocality significantly different, most clinicopathological variables missing	Selection into the study may have been related to intervention - it is not clear how the 60 patients in the O-BCS group and 120 in the control were selected for in that time period	Classification of interventions clear and determined at the start of intervention. Some aspects maybe determined retrospectively	-	-	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Scheter 2019	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors statistically adjusted for or demonstrated balance. Some significantly different: age, smoking status, tumour size. Some missing: axillary node status, grade, stage. Important co-interventions demonstrated balance (medical cancer treatment and axillary management)	Patients were excluded if they proceeded to have a mastectomy after the intervention: "Patients who had subsequently proceeded to total mastectomy were excluded from the study."	Classification of interventions clear and determined at the start of intervention. Technique clearly described in methods: 'Patients with centrally located tumours who required NAC re- section and had medium- or large-sized ptotic breasts were offered immediate OBR using a breast reduction pattern technique. Patients in the control group	All patient received the surgical intervention described in methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

				underwent primary closure of the NAC area in a horizontal or oblique scar and no oncoplastic reconstruction.'					
Sherwell-Cabello 2006	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance (age, medical comorbidities), some significantly different (tumour size, stage, axillary node status), some missing. Neoadjuvant chemotherapy is significantly different between groups. No information on other important co-interventions (radiotherapy, adjuvant treatment, axillary management)	Patients selected based on those that responded to questionnaire, not clear if/why all patients in the time period not selected: "All patients diagnosed with breast cancer treated under conventional conservative surgery or oncoplastic patterns at the Institute of Breast Diseases, FUCAM AC, with a complete clinical history and had answered a questionnaire of aesthetic satisfactory in person	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

			or by phone were included. Those who did not continue their follow-up at the institution were eliminated from the study."						
Tang 2016	S-BCS	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors demonstrated balance (tumour size, stage, BMI, age). Some co-interventions balanced (axillary management), some missing (medical cancer treatment)	All participants eligible included	Classification of interventions clear and determined at the start of intervention: 'Standard Breast Conservation Surgery(SBCS) group had surgery conducted according to the National Surgical Adjuvant Breast and Bowel Project(NSABP) standard guidelines. '	All patient received the surgical intervention described in methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Tenofsky 2014	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance, some significantly different, some missing (histological type, grade, stage, axillary node status). Important co-interventions significantly different (adjuvant RT), some missing (neoadjuvant RT + CT, adjuvant CT + ET, axillary management)	Participants were excluded if they went on to require mastectomy 6 months after procedure, or if lost to fol-	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods. Operation done by ex-	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

			low-up within 6 months: "Patients were excluded if they received a mastectomy within 6 months of the lumpectomy, and/or if they received 6 months of follow-up after their procedure."		perienced surgeon.				
Wijgman 2017	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance, some significantly different (tumour size), some missing. Important co-interventions demonstrated balance, some different	All participants eligible included	Classification of interventions clear and determined at the start of intervention: 'Oncoplastic procedures used encompass Clough level I and II techniques', 'The 'standard lumpectomy' performed in this study, consists of removal of the tumour, with or without simple closure of the glandular tissue, without mobilization of surrounding tissue. '	All patients received the surgical intervention described in the methods	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

Zhou 2019	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance, some significantly different (tumour size), some missing. Some co-interventions balanced (adjuvant RT, axillary management), some missing (all other cancer treatment)	Patients selected based on those that responded to questionnaire, not clear if/why all patients in the time period not selected. Patients also excluded if failure to complete follow-up	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Acea-Nebril 2005	Mx	Serious	Moderate	Low	Moderate	Low	Low	Moderate	Serious
		Size significantly different, most clinicopathological variables missing	Selection into the study may have been related to intervention. Selection to which intervention the women had was based on tumour characteristic. This difference at selection may have an effect on the outcome.	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	Deviation from intended intervention (minor changes in operation technique in some patients) but does not impact this outcome	All patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Carter 2016	Mx	Serious	Low	Low	low	Low	Low	Moderate	Serious

Table 6. Risk of bias for complications *(Continued)*

		Most clinicopathological variables significantly different (age, BMI, tumour size, stage, axillary node status, immunohistochemical receptors (ER, PR), multifocality). Important co-interventions not balanced across intervention group and may affect the outcome (neoadjuvant CT (all), adjuvant RT (Mx/Mx+R), adjuvant CT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Gendy 2003	Mx	Moderate	Moderate	Low	low	Low	Low	Moderate	Serious
		Important clinicopathological factors balanced (age, grade, axillary node status), some significantly different (histological type, tumour size), some missing. Important co-interventions different across intervention group, unlikely to influence outcome	All contactable participants	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. All surgeries done by an experienced surgeon/under their supervision.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Potter 2020	Mx	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors significantly different (age, diabetes, BMI, other medical comorbidities, histological type,grade, axillary node status, immunohistochemical receptors, multifocality). Tumour size missing. Clinicopathological factors e.g. size shown to effect the aesthetic outcome. Important co-interventions significantly different	Selection from participants in other studies (iBRA-2 and TeaM studies)	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods. As per protocols for other studies.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention. BIRADs tool used to limit bias	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

		(neoadjuvant CT, adjuvant RT, adjuvant CT, axillary surgery)							
Carter 2016	Mx + R	Serious	Low	Low	low	Low	Low	Moderate	Serious
		Most clinicopathological variables significantly different (age, BMI, tumour size, stage, axillary node status, immunohistochemical receptors (ER, PR, TN), multifocality). Important co-interventions not balanced across intervention group and may affect the outcome (neoadjuvant CT (all), adjuvant RT (Mx/MxR), adjuvant CT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Mustonen 2004	Mx + R	Serious	Low	Low	Low	Low	Moderate	Moderate	Serious
		Age demonstrated balance, tumour size significantly different, most missing. Adjuvant CT balanced, adjuvant radiotherapy significantly different, other co-interventions missing	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods.	All patients included followed up	Reperfusion measured different with transverse rectus abdominus muscle and latissimus dorsi flaps	No indication of selected reporting	
Ozmen 2020	Mx + R	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors balance, some different (age, menopausal status, BMI, tumour size, grade, axillary node status, immunohistochemical receptor status (ER), multifocality), some missing. Important co-interventions significantly different (adjuvant RT and axillary management), some missing (neoadjuvant RT + CT, adjuvant CT + ET)	Women chose their operation after being told the potential risks and benefits. Bias in assignment: "Both two procedures were ex-	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods.	Most patients included: "Median follow-up time was 56 (14-116) months."	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

Table 6. Risk of bias for complications *(Continued)*

			plained to patients, and their choices were recorded."						
Peled 2014	Mx + R	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance (diabetes, smoking status), some significantly different (e.g. age, BMI), some important clinicopathological variables missing (tumour size, grade, stage, location of tumour). Neoadjuvant chemotherapy and adjuvant radiotherapy balanced, other important co-interventions missing, including axillary management	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Potter 2020	Mx + R	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors significantly different (age, diabetes, BMI, other medical comorbidities, histological type,grade, axillary node status, immunohistochemical receptors, multifocality). Tumour size missing. Clinicopathological factors e.g. size shown to effect the aesthetic outcome. Important co-interventions significantly different (neoadjuvant CT, adjuvant RT, adjuvant CT, axillary surgery)	Selection from participants in other studies (iBRA-2 and TeaM studies)	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods. All operations done by a single surgeon with more than 30 years of experience in breast surgery	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention. BIRADs tool used to limit bias	No indication of selected reporting	
Tong 2016	Mx + R	Serious	Low	Low	Low	Moderate	Low	Moderate	Serious
		Some variables demonstrated balance, some significantly different (age, diabetes, BMI, other	All participants eligible included	Classification of interventions clear and de-	All patient received the surgical in-	All patients included fol-	Outcome measure likely only	No indication of se-	

Table 6. Risk of bias for complications *(Continued)*

	comorbidities, preoperative bra size), some missing. Important co-interventions significantly different (neoadjuvant RT, adjuvant RT), some missing	termined at the start of intervention	tervention described in methods.	lowed up, but median follow-up was significantly different between groups. "Median follow-up was 4 months longer for the oncoplastic breast reconstruction group than for the immediate breast reconstruction group (18.7 months versus. 14.0 months, respectively; P < 0.001)"	minimally influenced by knowledge of intervention	lected reporting	

BMI: body mass index
CT: chemotherapy
ER: oestrogen receptor
ET: endocrine therapy
Mx: mastectomy
PR: progesterone receptor
R: reconstruction
RT: radiotherapy
S-BCS: standard breast-conserving surgery
COPD: chronic obstructive pulmonary disease
PCI: primary coronary intervention

HTN: hypertension
TIA: transient ischaemic attack
CVA: cerebral vascular accident
ASA: American Society of anesthesiology
BIRADS: Breast Imaging-Reporting and Data System

Table 7. Risk of bias for recall rates

Study	Control	Confounding	Selection	Classification of intervention	Deviations from intended intervention	Missing data	Measurement of outcomes	Selection of reported results	Overall
Amitai 2018	S-BCS	Serious	Moderate	Low	Low	Moderate	Moderate	Moderate	Serious
		Most clinicopathological variables significantly different (age, axillary node status, immunohistochemical receptors), adjuvant RT demonstrated balanced, most co-interventions missing	Selection may be related to the outcome (those with mastectomy eventually excluded)	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Analysis unlikely to have removed risk of bias from missing data	Outcome measure likely only minimally influenced by knowledge of intervention. BIRADs tool used to limit bias	No indication of selected reporting	
Dolan 2015	S-BCS	Serious	Low	Low	Low	Low	Moderate	Moderate	Serious
		Some clinicopathological variables demonstrated balance (histological type, grade, immunohistochemical receptor) and some different (age, tumour size, axillary node status), some missing. Some co-interventions balanced across intervention group (adjuvant RT, adjuvant ET, axillary management), adjuvant CT different	All participants eligible included	Classification of interventions clear and determined at the start of intervention, details of operations described	All patients received the surgical intervention described in the methods	Most patients followed up	Outcome measure likely only minimally influenced by knowledge of intervention. BIRADs tool used to limit bias	No indication of selected reporting	
Fan 2019	S-BCS	Moderate	Low	Low	Low	Low	Moderate	Moderate	Moderate

Table 7. Risk of bias for recall rates *(Continued)*

		Important clinicopathological factors matched (age, BMI, stage) or demonstrated balance (histological type), some missing. Important co-interventions demonstrated balance (neoadjuvant CT, adjuvant RT, adjuvant CT, adjuvant ET)	All participants eligible included, control selected for	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. Surgeries done by experienced plastic and breast surgeons.	All patients followed up for 30 days and for re-excisions specifically	Outcome measure likely only minimally influenced by knowledge of intervention. BIRADs tool used to limit bias	No indication of selected reporting	
Hu 2019	S-BCS	Moderate	Low	Low	Low	Low	Moderate	Moderate	Moderate
		Important clinicopathological factors balanced (age, tumour size, immunohistochemical receptor). Important co-interventions demonstrated balance (neoadjuvant CT, axillary management), most missing	All intervention included, control matched for on certain domains	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. All operations done by an experienced surgeon	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention. BIRADs tool used to limit bias	No indication of selected reporting	
Losken 2009	S-BCS	Serious	Low	Low	Low	Low	Moderate	Moderate	Serious
		Some variables demonstrated balance, some significantly different: age, histological type, stage. Important co-interventions demonstrated balance, some significantly different: adjuvant CT, axillary surgery	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. All operations done by an experienced surgeon	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	
Piper 2016	S-BCS	Serious	Serious	Low	Low	Low	Moderate	Moderate	Serious
		Some variables demonstrated balance (BMI, histological type), age matched for and	Patients without negative margins ex-	Classification of interventions clear and de-	All patients received the surgical in-	All patients in-	Outcome measure likely only min-	No indication of se-	

Table 7. Risk of bias for recall rates *(Continued)*

		stage significantly different. Important co-interventions missing	cluded, minimum 2 years follow-up (O-BCS done more recently)	termined at the start of intervention: "All reduction mammoplasties were performed either via an inferior or superior-medial pedicle approach, with a Wise pattern or vertical skin pattern incision, based on tumour location"	tervention described in methods	cluded followed up	imally influenced by knowledge of intervention	lected reporting	
Tenofsky 2014	S-BCS	Serious	Serious	Low	Low	Low	Moderate	Moderate	Serious
		Some variables demonstrated balance, some significantly different, some missing (histological type, grade, stage, axillary node status). Important co-interventions significantly different (adjuvant RT), some missing (neoadjuvant RT + CT, adjuvant CT + ET, axillary management)	Participants were excluded if they went on to require mastectomy 6 months after procedure, or if lost to follow-up within 6 months: "Patients were excluded if they received a mastectomy within 6 months of the lumpectomy, and/or if they received, 6 months of follow-up after their procedure."	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in methods. Operation done by experienced surgeon.	All patients included followed up	Outcome measure likely only minimally influenced by knowledge of intervention	No indication of selected reporting	

RT: radiotherapy
ET: endocrine therapy
CT: chemotherapy
BMI: body mass index
BIRADs: Breast Imaging-Reporting and Data System

Table 8. Risk of bias for time to adjuvant therapy

Study	Control	Confouding	Selection	Classification of intervention	Deviations from intended intervention	Missing data	Measurement of outcomes	Selection of reported results	Overall
Acea-Nebril 2017	S-BCS	Serious	Low	Low	Moderate	Low	Low	Moderate	Serious
		Some clinicopathological variables significantly different (age, menopausal status, tumour size, tumour stage, axillary lymph node status, location of tumour, multifocality). Some co-interventions balanced (neoadjuvant CT and axillary management), some missing	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Some aspects maybe determined retrospectively	Deviation from intended co-intervention (adjuvant therapy time) but does not impact this outcome	All patients followed up	Objective outcome measure (from date of surgery to date of treatment)	No indication of selected reporting	
Borm 2019	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Most clinicopathological variables significantly different: age, tumour size, tumour grade, axillary node status, immunohistochemical receptors (ER status). Important co-interventions (adjuvant CT, adjuvant ET) not balanced across intervention group and may effect the outcome	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	All patients followed up	Objective outcome measure	No indication of selected reporting	
Cassi 2016	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious

Table 8. Risk of bias for time to adjuvant therapy *(Continued)*

		Some clinicopathological variables demonstrated balance, most missing. Important co-interventions balanced across intervention group (adjuvant RT,) some information missing	All participants eligible included	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Di Micco 2017	S-BCS	Moderate	Serious	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors demonstrated balance (smoking status, BMI, histological type, tumour size, immunohistochemical receptor, tumour location), some significantly different (age, axillary node status). Some co-interventions balanced across intervention group (neoadjuvant CT, adjuvant ET, axillary management, adjuvant RT), some different (radiation boost, adjuvant CT)	Selection may be related to the outcome (mastectomy eventually)	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Objective outcome measure	No indication of selected reporting	
Kahn 2013	S-BCS	Serious	Low	Moderate	No information	Low	Serious	Moderate	Serious
		Clinicopathological factors missing. Adjuvant CT balanced	All participants eligible included, consecutive patients to reduce selective bias	Some plane mobilisation without skin reduction counted as WLE. This is standard practice so minor risk of bias due to this	-	All patients included followed up	Date calculated from when MDT decided to give CT, this is not an objective date and could be different across the two groups	No indication of selected reporting	

Table 8. Risk of bias for time to adjuvant therapy *(Continued)*

Keleman 2019	S-BCS	Moderate	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
		Some variables demonstrated balance (age, smoking status, diabetes, BMI, type of cancer, tumour size, grade, stage, immunohistochemical receptor) some different (preoperative bra size, axillary node status) but unlikely to affect outcome. Important co-intervention of adjuvant RT demonstrated balance, some significantly different (neoadjuvant CT, adjuvant CT, adjuvant ET, axillary management) but less of an impact on outcome	All intervention participants eligible included, random patients selected for control	Classification of interventions clear and determined at the start of intervention. The types of intervention were: therapeutic mammaplasty (superior, central, inferior pedicle Wise-pattern), Dermoglandular rotation (medial, lateral mammoplasty), Periareolar (round block, omega) or standard BSC	All patients received the surgical intervention described in the methods	Patients missed due to loss to follow-up and did not respond to outcome, equal numbers in both groups so impact may be similar across groups	Objective outcome measure	No indication of selected reporting	
Kimball 2018	S-BCS	Serious	Moderate	Moderate	Low	Low	Moderate	Moderate	Serious
		Some clinicopathological variables demonstrated balance (BMI) and some different (age, medical comorbidities, histological type), some missing - issue with the database. Important co-interventions significantly different (adjuvant RT, adjuvant CT, axillary management)	Selection based on coding - not standardised for OPS yet	Classification of intervention based on codes - not uniform across sites. Types of intervention: partial mastectomy ('lumpectomy') and three breast reconstructive/repair procedures	All patient received the surgical intervention described in methods	All patients included followed up	From coding in insurance companies	No indication of selected reporting	
Klit 2017	S-BCS	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious

Table 8. Risk of bias for time to adjuvant therapy *(Continued)*

		Some differences in clinicopathological characteristics (age, BMI, tumour size, axillary node status), unlikely to have major impact on outcome. Important co-interventions significantly different (axillary management), some balanced (adjuvant CT)	Excluded patients with unclear resection margins, needs for further surgery (could influence outcome)	Classification of interventions clear and determined at the start of intervention. Surgical treatment consisted of mastectomy, lumpectomy or O-BCS in combination with either sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND)	All patients received the surgical intervention described. The surgical and adjuvant treatments were standardized according to DBCG guidelines	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Matrai 2014	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Tumour size significantly different. Some variables demonstrated balance (age, histological type, grade, tumour location, bra size, immunohistochemical receptor, axillary lymph node status). Matching of patients reported but not defined: "the same clinicopathological parameters of 60 traditional breast-conserving surgeries operated by the same breast surgeon were used". Important co-interventions including adjuvant RT demonstrated balance. Adjuvant CT significantly different	Unclear why these 60 patients selected (not consecutive, some retrospective and some prospective), controls matched	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Mazouni 2013	S-BCS	Moderate	Low	Low	Low	Low	Serious	Moderate	Serious
		Important clinicopathological factors balance: histological type, tumour size, grade, axillary node status, immunohistochemical receptor (PR). Important co-interventions predefined and uniform across studies	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention de-	All patients included followed up	Unclear date from which time until adjuvant	No indication of selected reporting	

Table 8. Risk of bias for time to adjuvant therapy *(Continued)*

		(axillary surgery, neoadjuvant CT, adjuvant RT)			scribed in the methods		therapy calculated		
Morrow 2019	S-BCS	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance (histological type (MxIR), tumour size (MxIR), grade (MxIR), axillary node status, immunohistochemical receptors), some significantly different (age (all), histological type (BCS, Mx), tumour size (BCS, Mx), grade (BCS, Mx), axillary node status (Mx, MxIR)). Important co-interventions significantly different (adjuvant RT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Palsoditlir 2018	S-BCS	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance, some significantly different (e.g. tumour size), some missing (grade, stage, location of tumour). Adjuvant ET balanced, some co-interventions missing: radiotherapy, chemotherapy, axillary management	All women included according to selection criteria. Selection criteria excluded level 2 O-BCS procedures assigning these as minimal: "Level 1 and level 2 oncoplastic procedures (minimal gland mobilization techniques) were not included in	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	

Table 8. Risk of bias for time to adjuvant therapy *(Continued)*

			the study group."						
Rose 2019	S-BCS	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
		Important clinicopathological factors statistically adjusted for. Location of surgeries different in intervention and control. Accounted for by measuring time to adjuvant therapy in all locations. Some co-interventions balanced (adjuvant RT, adjuvant CT, adjuvant ET), axillary surgery different	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods	Most patients included	Objective outcome measure: time from day of surgery to first day of therapy	No indication of selected reporting	
Tenofsky 2014	S-BCS	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance, some significantly different, some missing (histological type, grade, stage, axillary node status). Important co-interventions significantly different (adjuvant RT), some missing (neoadjuvant RT + CT, adjuvant CT + ET, axillary management)	Participants were excluded if they went on to require mastectomy 6 months after procedure, or if lost to follow-up within 6 months: "Patients were excluded if they received a mastectomy within 6 months of the lumpectomy, and/or if they received 6 months of follow-up	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	

Table 8. Risk of bias for time to adjuvant therapy *(Continued)*

			after their procedure."						
Kahn 2013	Mx	Serious	Low	Moderate	No information	Low	Serious	Moderate	Serious
		Clinicopathological factors missing. Adjuvant CT balanced	All participants eligible included, consecutive patients to reduce selective bias	Some plane mobilisation without skin reduction counted as WLE. This is standard practice so minor risk of bias due to this	-	All patients included followed up	Date calculated from when the multi-disciplinary team decided to give CT, this is not an objective date and could be different across the two groups	No indication of selected reporting	
Klit 2017	Mx	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
		Some differences in clinicopathological characteristics (age, BMI, tumour size, axillary node status), unlikely to have major impact on outcome. Important co-interventions significantly different (axillary management), some balanced (adjuvant CT)	Excluded patients with unclear resection margins, needs for further surgery (could influence outcome)	Classification of interventions clear and determined at the start of intervention. Surgical treatment consisted of mastectomy, lumpectomy or OBS in combination with either SLNB or ALND	All patients received the surgical intervention described. The surgical and adjuvant treatments were standardised according to DBCG guidelines	All patients included followed up	Objective outcome measure	No indication of selected reporting	

Table 8. Risk of bias for time to adjuvant therapy *(Continued)*

Morrow 2019	Mx	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance (histological type (MxIR), tumour size (MxIR), grade (MxIR), axillary node status (BCS), immunohistochemical receptors), some significantly different (age (all), histological type (BCS, Mx), tumour size (BCS, Mx), grade (BCS, Mx), axillary node status (Mx, MxIR)). Important co-interventions significantly different (adjuvant RT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Potter 2020	Mx	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors significantly different (age, diabetes, BMI, other medical co-morbidities, histological type,grade, axillary node status, immunohistochemical receptors, multifocality). Tumour size missing. Important co-interventions significantly different (neoadjuvant CT, adjuvant RT, adjuvant CT, axillary surgery)	Selection from participants in other studies (iBRA-2 and TeaM studies)	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Kahn 2013	Mx + R	Serious	Low	Moderate	No information	Low	Serious	Moderate	Serious
		Clinicopathological factors missing. Adjuvant CT balanced	All participants eligible included, consecutive patients to reduce selective bias	Some plane mobilisation without skin reduction counted as WLE. This is standard practice so minor risk of bias due to this	-	All patients included followed up	Date calculated from when MDT decided to give CT, this is not an objective date and could be different across	No indication of selected reporting	

Table 8. Risk of bias for time to adjuvant therapy *(Continued)*

							the two groups		
Morrow 2019	Mx + R	Serious	Low	Low	Low	Low	Low	Moderate	Serious
		Some variables demonstrated balance (histological type (MxIR), tumour size (MxIR), grade (MxIR), axillary node status (BCS), immunohistochemical receptors), some significantly different (Age (all), histological type (BCS, Mx), tumour size (BCS, Mx), grade (BCS, Mx), axillary node status (Mx, MxIR)). Important co-interventions significantly different (adjuvant RT)	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Potter 2020	Mx + R	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious
		Important clinicopathological factors significantly different (age, diabetes, BMI, other medical co-morbidities, histological type,grade, axillary node status, immunohistochemical receptors, multifocality). Tumour size missing. Important co-interventions significantly different (neoadjuvant CT, adjuvant RT, adjuvant CT, axillary surgery)	Selection from participants in other studies (iBRA-2 and TeaM studies)	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods	All patients included followed up	Objective outcome measure	No indication of selected reporting	
Tong 2016	Mx + R	Serious	Low	Low	Low	Moderate	Moderate	Moderate	Serious
		Some variables demonstrated balance, some significantly different (age, Diabetes, BMI, other comorbidities, preoperative bra size), some missing. Important co-interventions significantly different (neoadjuvant RT, adjuvant RT), some missing	All participants eligible included	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods	All patients included followed up, but median follow-up was significantly different between	Objective outcome measure. Unclear why delay is defined as over 6 weeks "Complications that de-	No indication of selected reporting	

Table 8. Risk of bias for time to adjuvant therapy *(Continued)*

			groups. "Median follow-up was 4 months longer for the oncoplastic breast reconstruction group than for the immediate breast reconstruction group (18.7 months versus 14.0 months, respectively; P < 0.001)"			layed the initiation of adjuvant chemotherapy or radiation therapy for greater than 6 weeks postoperatively were recorded." Outcome measure likely only minimally influenced by knowledge of intervention

BMI: body mass index
CT: chemotherapy
ER: oestrogen receptor
ET: endocrine therapy
Mx: mastectomy
MxIR: mastectomy and immediate reconstruction
PR: progesterone receptor
R: reconstruction
RT: radiotherapy
DBCG: Danish Breast Cancer Co-operative Group
SLNB - Sentinel lymph node biopy
ALND - Axillary lymph node dissection
iBRA-2: Immediate breast reconstruction and therapy audit
TeaM: Tamoxifen Exemestane Adjuvant Multinational Study

Table 9. Risk of bias for cosmetic evaluation

Study	Control	Confounding	Selection	Classification of intervention	Deviations from intended intervention	Missing data	Measurement of outcomes	Selection of reported results	Overall
Acosta-Marin 2014	S-BCS	Serious	Serious	Low	Low	Serious	Serious	Moderate	Serious
		Some clinicopathological variables demonstrated balance (age, BMI) and some significantly different (preoperative bra size, tumour size), most missing	Selection may be related to the outcome (mastectomy eventually)	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Analysis unlikely to have removed risk of bias from missing data - missed women with complications in short term. If major may have had to have mastectomy and therefore excluded	Validated reporting tool but vulnerable bias from subjective knowledge of intervention	No indication of selected reporting	
Gicalone 2007 (2)	S-BCS	Serious	Serious	Low	Low	Low	Critical	Moderate	Critical
		Important clinicopathological factors demonstrated balance (BMI, tumour size, tumour location), some missing	Women chose their operation after being told the potential risks and benefits. Bias in assignment	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. All operations done by 2 experienced surgeons.	All patients included followed up	2 person panel of experts, bias likely to influence outcome	No indication of selected reporting	

Table 9. Risk of bias for cosmetic evaluation *(Continued)*

Hilli-Betz 2014	S-BCS	Serious	Serious	Low	Low	Low	Moderate	Moderate	Serious
		Some clinicopathological variables demonstrated balance (axillary node status) and some different (tumour size, pre-operative bra size), some missing. Axillary management demonstrated balance, most co-interventions missing	Women were invited to return, not all of them did	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	Objective software/panel assessment	No indication of selected reporting	
Jiang 2015	S-BCS	Moderate	Serious	Low	Low	Low	Critical	Moderate	Critical
		Important clinicopathological factors balanced (age, weight, histology type,tumour size, grade, stage, tumour location)	60 women were picked, study says randomised but not clear how therefore classified as cohort. Risk of selection	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	3 person panel of experts, bias likely to influence outcome	No indication of selected reporting	
Keleman 2019	S-BCS	Moderate	Serious	Low	Low	Low	Critical	Serious	Critical
		Some variables demonstrated balance (age, smoking status, diabetes, BMI, type of cancer, tumour size, grade, stage, immunohistochemical receptor) some different (preoperative bra size, axillary node status) but unlikely to affect outcome. Important co-intervention of adjuvant RT demonstrated balance, some significantly different (neoadjuvant CT, adjuvant CT, adjuvant ET, axillary	Not all patients responded	Classification of interventions clear and determined at the start of intervention. The types of intervention were: Therapeutic mammaplasty (superior, central, inferior pedicle Wise-pattern), Dermoglandular rotation (medial, lateral mammoplasty), Periareolar (round block,	All patients received the surgical intervention described in the methods. Operations done by experienced breast surgeons.	Patients missed due to loss to follow up and did not respond to outcome, equal numbers in both groups so impact may be similar	3 person panel of experts, bias likely to influence outcome	Details not given	

Table 9. Risk of bias for cosmetic evaluation *(Continued)*

		management) but less of an impact on outcome		omega) or standard BSC		across groups			
Lansu 2014	S-BCS	Moderate	Moderate	Low	Low	Low	Moderate	Moderate	Moderate
		Important clinicopathological factors balance (age, tumour size, tumour location), some missing. Important co-interventions demonstrated balance, some significantly different	Patients had to be disease free and alive at the time of inclusion	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described	Most patients responded and followed up	Objective BCCT.core score	No indication of selected reporting	
Santos 2015	S-BCS	Serious	Serious	Low	Low	Low	Moderate	Moderate	Serious
		Some variables matched and demonstrated balance, stage significantly different: BMI, histological type, axillary node status. Intervention and control from different locations. Axillary management balanced, important co-interventions missing: medical cancer treatment	Patients selected based on those that responded to questionnaire, not clear if/why all patients in the time period not selected	Classification of interventions clear and determined at the start of intervention: 'first group underwent level 2 O-BCS techniques (bilateral surgeries with mammaplasty techniques', 'second group underwent lumpectomy with incisions over the tumour, without removing skin (except in cases where the tumours where close to skin)'	All patients received the surgical intervention described in methods	All patients included followed up	Objective BCCT.core score. Cosmesis also evaluated by two independent plastic surgeons and two breast surgeons using Garbay's criteria	No indication of selected reporting	
Scheter 2019	S-BCS	Serious	Serious	Low	Low	Low	Serious	Serious	Serious
		Important clinicopathological factors statistically adjusted for or demonstrated balance. Some significantly different: age, smoking status, tumour size. Some	Patients were excluded if they proceeded to have a mas-	Classification of interventions clear and determined at the start of intervention. Technique clearly described in	All patients received the surgical intervention described in methods	All patients included followed up	13 person panel of experts, bias likely to influence outcome	Selective reporting of certain domains	

Table 9. Risk of bias for cosmetic evaluation *(Continued)*

		missing: axillary node status, grade, stage. Important co-interventions demonstrated balance (medical cancer treatment and axillary management)	tectomy after the intervention: "Patients who had subsequently proceeded to total mastectomy were excluded from the study."	methods: 'Patients with centrally located tumours who required NAC re- section and had medium- or large-sized ptotic breasts were offered immediate OBR using a breast reduction pattern technique. Patients in the control group underwent primary closure of the NAC area in a horizontal or oblique scar and no oncoplastic reconstruction.'					
Viega 2011	S-BCS	Moderate	Serious	Low	Low	Moderate	Serious	Moderate	Serious
		Important clinicopathological factors demonstrated balance (age, BMI, tumour size, tumour location) and "matched for demographic and oncologic aspects". Important co-interventions demonstrated balance (adjuvant RT, adjuvant CT, axillary management), says some demographic and oncological aspects matched for	Unclear why these 45 patients were selected	Classification of interventions clear and determined at the start of intervention: "All patients underwent quadrantectomy and in most of them sentinel lymph node biopsy was performed. Breast reconstruction procedures included local flaps or breast reduction techniques. Neither distant flaps nor prosthesis were used."	All patients received the surgical intervention described in methods	Some patients were lost to follow-up at 12 months: PParticipation rates at the follow-up assessments of oncoplastic group were 100% at the 6th month and 88.9% at the 12th month follow-up."	4 person panel of experts, bias likely to influence outcome but tried to limit by standardisation and blinding of methods: "The aesthetic results of control group and oncoplastic group at 6 and 12 months postoperatively were evaluated through photographs of pre and postoperative, by a pan-	No indication of selected reporting	

Table 9. Risk of bias for cosmetic evaluation *(Continued)*

							el of four independent raters, according to the criteria shown on Table 1, modified from Garbay et al"		
Gendy 2003	Mx	Moderate	Serious	Low	Low	Low	Serious	Moderate	Serious
		Important clinicopathological factors balanced (age, grade, axillary node status), some significantly different (histological type, tumour size), some missing. Important co-interventions different across intervention group	All contactable participants	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. All surgeries done by an experienced surgeon/under their supervision	All patients included followed up	5 person panel of experts, bias likely to influence outcome	No indication of selected reporting	
Ozmen 2020	Mx +R	Serious	Serious	Low	Low	Low	Serious	Moderate	Serious
		Important clinicopathological factors balance, some different (age, menopausal status, BMI, tumour size, grade, axillary node status, immunohistochemical receptor status (ER), multifocality), some missing. Important co-interventions significantly different (adjuvant RT and axillary management), some missing (neoadjuvant RT + CT, adjuvant CT + ET)	Women chose their operation after being told the potential risks and benefits. Bias in assignment: "Both two procedures were explained to patients, and their	Classification of interventions clear and determined at the start of intervention	All patient received the surgical intervention described in methods. All operations done by a single surgeon with more than 30 years of experience in breast surgery.	Most patients included: "Median follow-up time was 56 (14-116) months."	Cosmetic evaluation reporting tool validated but vulnerable to bias from subjective knowledge of intervention. Carried out by a single surgeon: "The cosmetic evaluation was conducted by a plastic	No indication of selected reporting	

Table 9. Risk of bias for cosmetic evaluation *(Continued)*

			choic-es were recorded."				surgeon who was not part of the surgical team."		

BMI: body mass index
CT: chemotherapy
ER: oestrogen receptor
ET: endocrine therapy
Mx: mastectomy
PR: progesterone receptor
R: reconstruction
RT: radiotherapy
NAC: neoadjuvant chemotherapy

Table 10. Risk of bias for patient-reported outcome measures

Study	Control	Confounding	Selection	Classification of intervention	Deviations from intended intervention	Missing data	Measurement of outcomes	Selection of reported results	Overall
Acea-Nebril 2017	S-BCS	Serious	Serious	Low	Moderate	Moderate	Serious	Critical	Critical
		Some clinicopathological variables significantly different (age, menopausal status, tumour size, tumour stage, axillary lymph node status, location of tumour, multifocality). Some co-interventions balanced (neoadjuvant CT and axillary management), some missing	Selection into the study may have been related to intervention and follow-up time may miss initial time as questionnaire at 12 and 24 months. Only reported intervention results	Classification of interventions clear and determined at the start of intervention. Some aspects maybe determined retrospectively	Deviation from intended co-intervention (adjuvant therapy time)	Analysis unlikely to have removed risk of bias from missing data - not all women returned the form. Reasons due to recurrence, death, completion mas-	Validated reporting tool but vulnerable bias from subjective knowledge of intervention	Selective questionnaire results reported only of intervention	

Table 10. Risk of bias for patient-reported outcome measures *(Continued)*

						tectomy (all things that would have likely affected PROMs)			
Acosta-Marin 2014	S-BCS	Serious	Serious	Low	Low	Moderate	Serious	Moderate	Serious
		Some clinicopathological variables demonstrated balance (age, BMI) and some significantly different (preoperative bra size, tumour size), most missing	Selection may be related to the outcome (mastectomy eventually)	Classification of interventions clear and determined at the start of intervention. Operative details given clearly	All patients received the surgical intervention described in the methods	Analysis unlikely to have removed risk of bias from missing data - missed women with complications in short term. If major may have had to have mastectomy and therefore excluded	Validated reporting tool but vulnerable bias from subjective knowledge of intervention	No indication of selected reporting	
Di Micco 2017	S-BCS	Serious	Serious	Low	Low	Low	Serious	Moderate	Serious
		Important clinicopathological factors demonstrated balance (smoking status, BMI, histological type, tumour size, immunohistochemical receptor, tumour location), some significantly different (age, axillary node status). Some co-interventions balanced across intervention group (neoadjuvant CT, adju-	Selection may be related to the outcome (mastectomy eventually)	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients followed up	Validated reporting tool but vulnerable bias from subjective knowledge of intervention	No indication of selected reporting	

Table 10. Risk of bias for patient-reported outcome measures *(Continued)*

		vant ET, axillary management, adjuvant RT), some different (radiation boost, adjuvant CT)							
Eichler 2013	S-BCS	Moderate	Serious	Low	Low	Moderate	Critical	Moderate	Critical
		Some clinicopathological variables demonstrated balance (age, histological type, grade), tumour size different, some missing. Adjuvant CT balanced across intervention group, neoadjuvant CT significantly different	Patients selected based on those that responded to questionnaire, not clear if/why all patients in the time period not selected	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Not all patients responded to questionnaire	PROMs reporting tool not validated and vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	
Gicalone 2007 (2)	S-BCS	Serious	Serious	Low	Low	Low	Critical	Moderate	Critical
		Important clinicopathological factors demonstrated balance (BMI, tumour size, tumour location), some missing	Women chose their operation after being told the potential risks and benefits. Bias in assignment	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods	All patients included followed up. All surgeries done by an experienced surgeon/under their supervision	PROMs reporting tool not validated and vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	
Hilli-Betz 2014	S-BCS	Serious	Serious	Low	Low	Low	Critical	Moderate	Critical
		Some clinicopathological variables demonstrated balance (axillary node status) and some different (tumour size, preoperative bra size), some missing. Axillary management demon-	Women were invited to return, not all of them did	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in	All patients included followed up	PROMs reporting tool not validated and vulnerable to bias from subjective	No indication of selected reporting	

Table 10. Risk of bias for patient-reported outcome measures *(Continued)*

		strated balance, most co-interventions missing			the methods		knowledge of intervention		
Jiang 2015	S-BCS	Moderate	Moderate	Low	Low	Low	Critical	Moderate	Critical
		Important clinicopathological factors balanced (age, weight, histology type,tumour size, grade, stage, tumour location)	60 women were picked, study says randomised but not clear how therefore classified as cohort. Risk of selection	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	PROMs reporting tool not validated and vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	
Keleman 2019	S-BCS	Moderate	Serious	Low	Low	Moderate	Serious	Serious	Serious
		Some variables demonstrated balance (age, smoking status, diabetes, BMI, type of cancer, tumour size, grade, stage, immunohistochemical receptor) some different (preoperative bra size, axillary node status) but unlikely to affect outcome. Important co-intervention of adjuvant RT demonstrated balance, some significantly different (neoadjuvant CT, adjuvant CT, adjuvant ET, axillary management) but less of an impact on outcome	Not all patients responded	Classification of interventions clear and determined at the start of intervention. The types of intervention were: therapeutic mammaplasty (superior, central, inferior pedicle Wise-pattern), Dermoglandular rotation (medial, lateral mammoplasty), Periareolar (round block, omega) or standard BCS	All patients received the surgical intervention described in the methods. Operations done by experienced breast surgeons	Patients missed due to loss to follow-up and did not respond to outcome, equal numbers in both groups so impact may be similar across groups	PROMs reporting tool validated but vulnerable to bias from subjective knowledge of intervention	Selective details not given	
Lansu 2014	S-BCS	Moderate	Moderate	Low	Low	Low	Serious	Moderate	Serious
		Important clinicopathological factors balance (age, tumour	Patients had to be disease-free	Classification of interventions	All patients re-	All patients in-	PROMs reporting tool	No indication of se-	

Table 10. Risk of bias for patient-reported outcome measures *(Continued)*

		size, tumour location), some missing. Important co-interventions demonstrated balance, some significantly different	and alive at the time of inclusion	clear and determined at the start of intervention	ceived the surgical intervention described	cluded followed up	validated but vulnerable to bias from subjective knowledge of intervention	lected reporting	
Matrai 2014	S-BCS	Serious	Serious	Low	Low	Low	Serious	Moderate	Serious
		Tumour size significantly different. Some variables demonstrated balance (age, histological type, grade, tumour location, bra size, immunohistochemical receptor, axillary lymph node status). Matching of patients reported but not defined: "the same clinicopathological parameters of 60 traditional breast-conserving surgeries operated by the same breast surgeon were used". Important co-interventions including adjuvant RT demonstrated balance. Adjuvant CT significantly different	Unclear why these 60 patients selected (not consecutive, some retrospective and some prospective), controls matched	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods. Operation done by experienced surgeon	All patients included followed up	PROMs reporting tool validated but vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	
Mazouni 2013	S-BCS	Moderate	Serious	Low	Low	Moderate	Critical	Moderate	Critical
		Important clinicopathological factors balance: histological type, tumour size, grade, axillary node status, immunohistochemical receptor (PR). Some clinicopathological factors statistically different: tumour location. Some factors missing: age, BMI, preoperative bra size. Important co-interventions predefined and uniform across studies (axillary surgery, neoadjuvant CT, adjuvant RT)	Most participants eligible included, Patients who subsequently underwent mastectomy excluded from survey	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	Most patients responded	PROMs reporting tool not validated and vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	

Table 10. Risk of bias for patient-reported outcome measures *(Continued)*

Ojala 2017	S-BCS	Serious	Moderate	Low	Low	Low	Serious	Moderate	Serious
		Important clinicopathological factors significantly different (tumour size, tumour location, axillary node status, multifocality, histological type). Important co-interventions missing, adjuvant RT demonstrated balance, axillary management significantly different	All participants eligible included: "All patients having breast conserving surgery (BCS) due to primary breast cancer at the Helsinki and Uusimaa Hospital District during 2010 were included in this study, most had PROMs"	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in methods	Most patients responded (279/293 conventional, 86/86 O-BCS)	PROMs reporting tool validated but vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	
Palsoditlir 2018	S-BCS	Serious	Moderate	Low	Low	Moderate	Critical	Serious	Critical
		Some variables demonstrated balance, some significantly different (e.g. tumour size), some missing (grade, stage, location of tumour). Adjuvant ET balanced, some co-interventions missing: radiotherapy, chemotherapy, axillary management	All women included according to selection criteria. Selection criteria excluded level 2 O-BCS procedures assigning these as minimal: "Level 1 and level 2 oncoplastic procedures (minimal gland mobilisation techniques) were not included in the study group."	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in methods	Some patients did not respond to questionnaire, and so were not included: "Question lists were sent to 448 women in total. Of those, 75 were in the O-BCS group and 373 in the S-BCS group. Response rate was 68% in	PROMs reporting tool not validated and vulnerable to bias from subjective knowledge of intervention	Selective reporting of detailed questionnaire	

Table 10. Risk of bias for patient-reported outcome measures *(Continued)*

						the OBCS group but 43% in the SBCS group."			
PlaFarnos 2018*	S-BCS	Serious	Moderate	Low	No information	No information	Serious	Serious	Serious
		Multifocality significantly different, most clinicopathological variables missing	Selection into the study may have been related to intervention and may miss initial follow-up period Selection into the study may have been related to intervention - it is not clear how the 60 patients in the O-BCS group and 120 in the control were selected for in that time period	Classification of interventions clear and determined at the start of intervention. Some aspects maybe determined retrospectively	-	-	Validated reporting tool but vulnerable bias from subjective knowledge of intervention	Details of Breast-Q domains not reported	
Rose 2020	S-BCS	Moderate	Serious	Low	Low	Low	Serious	Moderate	Serious
		Important clinicopathological factors statistically adjusted for: age, tumour size, tumour location, bra size, BMI. Location of surgeries different in intervention and control. Co-intervention statistically adjusted for: axillary management, some medical cancer treatment	Patients selected based on those that responded to questionnaire sent out via post or email: "the response rates for the BCS and OBS cohorts	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in methods	All patients included	PROMs reporting tool validated but vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	

Table 10. Risk of bias for patient-reported outcome measures *(Continued)*

			were 48.4% (631/1304) and 48.0% (96/200), respectively"						
Santos 2015	S-BCS	Serious	Serious	Low	Low	Low	Critical	Moderate	Critical
		Some variables matched and demonstrated balance, stage significantly different: BMI, histological type, axillary node status. Intervention and control from different locations. Axillary management balanced, important co-interventions missing: medical cancer treatment	Patients selected based on those that responded to questionnaire, not clear if/why all patients in the time period not selected	Classification of interventions clear and determined at the start of intervention: "first group underwent level 2 OP techniques (bilateral surgeries with mammaplasty techniques', 'second group underwent lumpectomy with incisions over the tumour, without removing skin (except in cases where the tumours where close to skin)"	All patients received the surgical intervention described in methods	All patients included followed up	PROMs reporting tool not validated and vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	
Scheter 2019	S-BCS	Serious	Serious	Low	Low	Low	Critical	Moderate	Critical
		Important clinicopathological factors statistically adjusted for or demonstrated balance. Some significantly different: age, smoking status, tumour size. Some missing: axillary node status, grade, stage. Important co-interventions demonstrated balance (medical cancer treatment and axillary management)	Patients were excluded if they proceeded to have a mastectomy after the intervention: "Patients who had subsequently proceeded to total mastectomy	Classification of interventions clear and determined at the start of intervention. Technique clearly described in methods: "Patients with centrally located tumours who required NAC	All patients received the surgical intervention described in methods	Almost all patients included in follow-up: The questionnaire response rate was high: 11 of the 12 patients	PROMs reporting tool not validated and vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	

Table 10. Risk of bias for patient-reported outcome measures *(Continued)*

			were excluded from the study."	re- section and had medium- or large-sized ptotic breasts were offered immediate OBR using a breast reduction pattern technique. Patients in the control group underwent primary closure of the NAC area in a horizontal or oblique scar and no oncoplastic reconstruction."		in each group (92%)			
Sherwell-Cabello 2006	S-BCS	Serious	Serious	Low	Low	Low	Critical	Moderate	Critical
		Some variables demonstrated balance (age, medical comorbidities), some significantly different (tumour size, stage, axillary node status), some missing. Neoadjuvant chemotherapy is significantly different between groups. No information on other important co-interventions (radiotherapy, adjuvant treatment, axillary management)	Patients selected based on those that responded to questionnaire, not clear if/why all patients in the time period not selected: "All patients diagnosed with breast cancer treated under conventional conservative surgery or oncoplastic patterns at the Institute of Breast Diseases, FUCAM AC, with a complete clinical history and	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in methods	All patients included followed up	PROMs reporting tool not validated and vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	

Table 10. Risk of bias for patient-reported outcome measures *(Continued)*

			had answered a questionnaire of aesthetic satisfactory in person or by phone were included. Those who did not continue their follow-up at the institution were eliminated from the study."						
Srivastava 2018*	S-BCS	No information	No information	Low	No information	No information	Serious	Serious	Serious
		-	-	Classification of interventions clear and determined at the start of intervention. Some aspects maybe determined retrospectively	-	-	Validated reporting tool but vulnerable bias from subjective knowledge of intervention	Selective questionnaire results reported	
Tang 2016	S-BCS	Moderate	Moderate	Low	Low	Low	Critical	Moderate	Critical
		Important clinicopathological factors demonstrated balance (tumour size, stage, BMI, age). Some co-interventions balanced (axillary management), some missing (medical cancer treatment)	All participants eligible included	Classification of interventions clear and determined at the start of intervention: "Standard Breast Conservation Surgery (SBCS) group had surgery conducted according to the National Surgical Adjuvant Breast and Bowel Project (NSABP)	All patients received the surgical intervention described in methods	All patients included followed up	PROMs reporting tool not validated and vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	

Table 10. Risk of bias for patient-reported outcome measures *(Continued)*

				standard guidelines."					
Tenofsky 2014	S-BCS	Serious	Serious	Low	Low	Low	Critical	Moderate	Critical
		Some variables demonstrated balance, some significantly different, some missing (histological type, grade, stage, axillary node status). Important co-interventions significantly different (adjuvant RT), some missing (neoadjuvant RT + CT, adjuvant CT + ET, axillary management)	Participants were excluded if they went on to require mastectomy 6 months after procedure, or if lost to follow-up within 6 months: "Patients were excluded if they received a mastectomy within 6 months of the lumpectomy, and/or if they received 6 months of follow-up after their procedure."	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in methods. Operations done by experienced surgeon.	All patients included followed up	PROMs reporting tool not validated and vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	
Viega 2011	S-BCS	Moderate	Serious	Low	Low	Moderate	Critical	Moderate	Critical
		Important clinicopathological factors demonstrated balance (age, BMI, tumour location) and "matched for demographic and oncologic aspects." Important co-interventions demonstrated balance (adjuvant RT, adjuvant CT), "some demographic and oncological aspects matched for"	Not clear how patients were enrolled. For case group, allocation to type of procedure was based on patient choice	Classification of interventions clear and determined at the start of intervention: "All patients underwent quadrantectomy, and in most of them, sentinel lymph node biopsy was performed. Breast reconstruction	All patient received the surgical intervention described in methods	Some patients were lost in follow-up: 5 in case group. "Participation rates at the follow-up assessments were 95.5 per cent	PROMs reporting tool validated but not for breast cancer and vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	

Table 10. Risk of bias for patient-reported outcome measures *(Continued)*

				procedures were performed by the same plastic surgery team with the use of adjacent tissues, local flaps, or breast reduction techniques. Neither distant flaps nor prostheses were used."		at the 6-month follow-up and 88.9 per cent at the 12-month follow-up."			
Viega 2010	S-BCS	Moderate	Serious	Low	Low	Moderate	Critical	Moderate	Critical
		Important clinicopathological factors demonstrated balance (age, BMI, tumour location) and 'matched for demographic and oncologic aspects '. Important co-interventions demonstrated balance (adjuvant RT, adjuvant CT), 'some demographic and oncological aspects matched for	Not clear how patients were enrolled. For case group, allocation to type of procedure was based on patient choice	Classification of interventions clear and determined at the start of intervention: "All patients underwent quadrantectomy, and in most of them, sentinel lymph node biopsy was performed. Breast reconstruction procedures were performed by the same plastic surgery team with the use of adjacent tissues, local flaps, or breast reduction techniques. Neither distant flaps nor prostheses were used."	All patients received the surgical intervention described in methods. All surgeries by same team of surgeons	Some patients were lost in follow-up: 5 in case group. "Participation rates at the follow-up assessments were 95.5 per cent at the 6-month follow-up and 88.9 per cent at the 12-month follow-up."	PROMs reporting tool not validated and vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	
Zhou 2019	S-BCS	Serious	Serious	Low	Low	Low	Critical	Moderate	Critical

Table 10. Risk of bias for patient-reported outcome measures *(Continued)*

		Some variables demonstrated balance, some significantly different (tumour size), some missing. Some co-interventions balanced (adjuvant RT, axillary management), some missing (all other cancer treatment)	Patients selected based on those that responded to questionnaire, not clear if/why all patients in the time period not selected. Patients also excluded if failure to complete follow-up	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in the methods	All patients included followed up	PROMs reporting tool not validated and vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	
Gendy 2003	Mx	Moderate	Serious	Low	Low	Moderate	Serious	Serious	Serious
		Important clinicopathological factors balanced (age, grade, axillary node status), some significantly different (histological type, tumour size), some missing. Important co-interventions different across intervention group	All contactable participants	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in the methods. All surgeries done by an experienced surgeon/under their supervision.	Not all patients responded to questionnaire	Various validated scales but subject to bias	All PROMs not mentioned for all patients	
Hart 2015	Mx + R	Serious	Serious	Low	Low	Moderate	Critical	Moderate	Critical
		Some clinicopathological variables significantly different (age, BMI), stage balanced, some missing. Adjuvant RT significantly different, most co-interventions missing	Only some patients responded	Classification of interventions clear and determined at the start of intervention, operative details given clearly	All patients received the surgical intervention described in	Not all patients responded to questionnaire	PROMs reporting tool not validated and vulnerable to bias from subjective knowledge	No indication of selected reporting	

Table 10. Risk of bias for patient-reported outcome measures *(Continued)*

					the methods		of intervention		
Kelsall 2017	Mx + R	Serious	Moderate	Low	Low	Low	Serious	Moderate	Serious
		Important variables matched (age, tumour size, date of surgery, breast size) or demonstrated balance (axillary node status). Important co-interventions demonstrated balance (adjuvant CT, adjuvant ET and neoadjuvant CT) and some significantly different (adjuvant RT)	Selection based on patient reported outcome measures data	Classification of interventions clear and determined at the start of intervention. Surgery was either O-BCS (requiring therapeutic mammaplasty or volume replacement with a local chest wall perforator flap); or mastectomy with immediate reconstruction	All patient received the surgical intervention described in methods	All patients included followed up	PROMs reporting tool validated but vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	
Ozmen 2020	Mx + R	Serious	Serious	Low	Low	Low	Serious	Moderate	Serious
		Important clinicopathological factors balance, some different (age, menopausal status, BMI, tumour size, grade, axillary node status, immunohistochemical receptor status (ER), multifocality), some missing. Important co-interventions significantly different (adjuvant RT and axillary management), some missing (neoadjuvant RT + CT, adjuvant CT + ET)	Women chose their operation after being told the potential risks and benefits. Bias in assignment: "Both two procedures were explained to patients, and their choices were recorded."	Classification of interventions clear and determined at the start of intervention	All patients received the surgical intervention described in methods. All operations done by a single surgeon with more than 30 years of experience in breast surgery.	Most patients responded	PROMs reporting tool validated but vulnerable to bias from subjective knowledge of intervention	No indication of selected reporting	

BMI: body mass index
CT: chemotherapy
ET: endocrine therapy
Mx: mastectomy
PR: progesterone receptor
R: reconstruction
RT: radiotherapy
PROM: Patient-reported outcome measure

Table 11. Countries of studies

Countries	Number
Belgium	1
Brazil	4
China	4
Denmark	3
Europe	2
Finland	3
France	6
Germany	3
Hungary	2
Iceland	1
India	2
Israel	2
Italy	2
Japan	3
Korea	2
Mexico	1
Netherlands	2
Pakistan	1
Spain	3
Turkey	3
UK	13
USA	14
Venezuela	1

Table 12. Matrix of interventions and controls

	Intervention		
Control	**Volume displacement**	**Volume replacement**	**Both**

Table 12. Matrix of interventions and controls *(Continued)*

BCS	39	6	13
Mx	0	3	0
Mx+R	3	2	1
Mx+-R	0	0	1
BCS/Mx	2	0	0
BCS/Mx+-R	0	0	2
BCS/Mx/Mx+R	2	0	2
Mx/Mx+R	1	0	0

BCS: breast-conserving surgery
Mx: mastectomy
R: reconstruction

Table 13. Complications: O-BCS of those compared to S-BCS

Study	Wound infection	Flap necrosis	Dehisence	Fat necrosis	Seroma	Skin	Haematoma	Bleeding	Needed surgery
Acea-Nebril 2017-VD	1 (0.5%)	4 (2.3%)	-	-	3 (1.7%)	-	4 (2.3%)	3 (1.7%)	(1.7%) - bleeding only
Acea-Nebril 2005-VD	2 (4%)	3 (6%)	-	-	3 (6%)	-	4 (8%)	-	-
Acosta-Marin 2014-VD	1 (1.9%)	-	-	1 (1.9%)	-	1 (1.9%)	-	-	-
Amitai 2018-VD	-	-	-	15 (22%)	-	-	-	-	-
Angarita 2020-VD	209 (2.3%)	-	67 (0.7%)	-	-	-	-	22 (0.3%)	-
Carter 2016-VD	45 (4.8%)	-	-	-	126 (13.4%)	-	18 (1.9%)	-	-
Chauhan 2016 (1)-VD and VR	4 (7%)	2 (3.5%)	-	-	1 (1.8%)	-	1 (1.8%)	-	-
Chauhan 2016 (2)-VD and VR	1 (3.67%)	1 (3.7%)	-	-	0 (0%)	-	1 (3.7%)	-	-
Jiang 2015-VD	-	-	1 (3.3%)	-	3 (10%)	-	-	-	-
Tang 2016-VD and VR	0 (0%)	0 (0%)	2 (3%)	0 (0%)	10 (15%)	10 (15%)	3 (4.48%)	0 (0%)	-
Crown 2019-VD	15 (3.3%)	-	14 (3.1%)	-	8 (1.8%)	2 (0.4%)	-	-	-
DeLorenzi 2016 (1)-Both	13 (2.8%)	6 (1.3%)	16 (3.5%)	12 (2.6%)	-	-	11 (2.4%)	-	-
Dolan 2015-VD and VR	-	-	-	-	-	-	-	-	5 (7%)
Down 2013-VD and VR	2 (5.4%)	-	-	-	-	-	-	-	breakdown only
Gicalone 2007 (1)-VD	-	21 (67%)	5 (16%)	-	-	-	2 (6.45%)	-	-
Gicalone 2007 (2)-VD	-	-	2 (5.13%)	-	-	1 (2.6%)	1 (2.6%)	-	-
Gicalone 2015-VD	4 (9.52%)	-	-	-	-	2 (4.8%)	1 (2.4%)	-	-
Keleman 2019-VD	8 (2.3%)	3 (0.9%)	-	2 (0.57%)	5 (1.4%)	-	2 (0.6%)	-	-

Table 13. Complications: O-BCS of those compared to S-BCS *(Continued)*

Kimball 2018-VD	17.7 (2.5%)	33.3 (4.7%)	-	-	-	-	6.4% (includes seroma)	-	< 1%
Mazouni 2013 - VD	-	-	-	-	-	-	-	-	4 (2%)
Nakada 2019-VR	-	68 (16%)	-	-	-	-	-	-	-
Palsodittlir 2018-VD and VR	-	0 (0%)	-	-	-	-	0 (0%)	-	-
Scheter 2019-VD	-	-	2 (16.7%)	1 (8.3%)	-	-	-	-	0
Tenofsky 2014-VD	5 (8.6%)	-	4 (6.9%)	15 (25.9%)	10 (17.2%)	21 (36.2%)	10 (17.2%)	-	-
Wijgman 2017-VD	11 (4%)	-	-	-	17 (6.2%)	-	31 (11.4%)	-	6 (1.9%)
Zhou 2019-VR	-	-	-	-	3 (9.3%)	-	0 (0%)	-	3 (9.3%)

O-BCS: oncoplastic breast-conserving surgery
S-BCS: standard breast-conserving surgery
VD: volume displacement
VR: volume replacement

Table 14. Complications: S-BCS

Study	Wound infection	Flap/skin necrosis	Dehisence	Fat necrosis	Seroma	Skin	Haematoma	Bleeding	Needed surgery
Acea-Nebril 2017- BCS	13 (2%)	1 (0.1%)	-	-	21 (3.3%)	-	22 (3.3%)	-	
Acea-Nebril 2005- BCS	2 (3.5%)	0	-	-	8 (13.9%)	-	5 (8.7%)	-	-
Acosta-Marin 2014- BCS	0	-	-	0	-	0	-	-	-
Amitai 2018- BCS	-	-	-	3 (1%)	-	-	-	22	-
Angarita 2020- BCS	1842 (1.8%)	-	126 (0.1%)	-	-	-	-	-	-
Carter 2016- BCS	32 (1.4%)	-	-	-	406 (18%)	-	57 (2.5%)	-	-
Chauhan 2016 (1)- BCS	2 (3.5%)	-	-	-	1 (1.8%)	-	1 (1.75%)	-	-

Table 14. Complications: S-BCS *(Continued)*

Chauhan 2016 (2) - BCS	2 (4.3%)	1 (2.2%)	-	-	2 (4.3%)	-	-	-	-
Jiang 2015- BCS	-	-	4 (13.3%)	-	2 (6.7%)	-	-	0 (0%)	-
Tang 2016- BCS	3 (2.6%)	0 (0%)	16 (13.7%)	2 (1.71%)	57 (48.7%)	21 (17.9%)	17 (14.5%)	0 (0%)	-
Crown 2019- BCS	21 (8.4%) P = 0.01	-	13 (4.7%)	-	12 (4.4%)	2 (0.7%)	-	-	-
DeLorenzi 2016 (1)- BCS	-	-	-	-	-	-	-	-	3 (2.6%)
Dolan 2015- BCS	-	-	-	-	-	-	-	-	
Down 2013- BCS	3 (2.5%)	-	-	1 (0.8%)	-	-	-	-	-
Gicalone 2007 (1)- BCS	-	-	1 (2.3%)	-	-	-	3 (6.7%)	-	-
Gicalone 2007 (2)- BCS	-	-	3 (3.4%)	-	-	0 (0%)	1 (1.14%)	-	-
Gicalone 2015- BCS	5 (8.8%)	-	-	-	-	0 (0%)	2 (3.5%)	-	-
Keleman 2019- BCS	7 (2%)	2 (0.6%)	-	1 (0.3%)	9 (2.6%)	-	4 (1.1%)	-	<1%
Kimball 2018- BCS	298 (1.7%)	702 (4%)	-	-	-	-	1000 (5.7%)	-	-
Nakada 2019- BCS	-	-	-	-	-	-	-	-	2 (1%)
Palsodittlir 2018- BCS	-	26 (4.6%)	-	-	-	-	-	-	1 (0.2%)
Scheter 2019- BCS	-	5 (0.8%)	-	-	-	-	11 (1.67%)	-	16 (2.4$%)
Tenofsky 2014- BCS	-	-	1 (8.3%)	0 (0%)	-	-	-	-	0 (0%)
Wijgman 2017- BCS	8 (9.5%)	0	4 (4.8%)	8 (9.5)%)	15 (17.2%)	21 (25%)	8 (9.5%)	-	-
Zhou 2019- BCS	12 (2.6%)	-	-	-	23 (5%)	-	59 (12.8%)	-	1 (0.2%)

BCS: breast-conserving surgery

Table 15. Recall rates: O-BCS versus S-BCS

	Intervention details	Intervention results	S-BCS results
Amitai 2018	VD	7/12 due to lump needed more imaging	7/14 due to a lump needed more imaging
Dolan 2015	Both VD and VR	Imaging per patient: 2.19 ultrasound: 20/71 VD: 16/61 VR: 4/10	Imaging per patient: 2.146, ultrasound 17/119
Fan 2019	VR	3.2%	1%
Hu 2019	VR	1/18 1.4%	0
Losken 2009	VD	Further US, MRI imaging: 41.0%	Further US, MRI imaging: 47.0%, 6.0%

MRI: magnestic resonance imaging
O-BCS: oncoplastic breast-conserving surgery
S-BCS: standard breast-conserving surgery
US: ultrasound
VD: volume displacement
VR: volume replacement

Table 16. Time to adjuvant therapy: O-BCS versus S-BCS unextractable values

Intervention details	Time to any adjuvant therapy: intervention	Time to any adjuvant therapy: control	P value	Time to adjuvant chemotherapy: intervention	Time to adjuvant chemotherapy: control	P value	Time to adjuvant radiotherapy: intervention	Time to adjuvant radiotherapy: control	P value
Di Micco 2017- VD	-	-	-	Median (range) 39 (21 to 78)	40 (11 to 81)	0.551	Median (range) 57 (36 to 153)	53 (25 to 126)	0.025
Keleman 2019- VD	Median (range) 29.4 (28 to 84)	28.7 (28 to 84)	0.31	-	-	-	-	-	-
Kimball 2018- VD	-	-	-	Median (IQR) 37 (23.5 to 51.5)	36 (26 to 49)	0.0004	Median (IQR) 41 (28 to 56)	34 (22 to 48)	0.0002
Morrow 2019- VD	-	-	-	Less than 31 days: 14.9%	Less than 31 days: 22.1%	0.171	Median (range) 51 (35 to 125)	50 (10 to 447)	0.088
Palsodittlir 2018- VD and VR	Median (range) 47.5 (22 to 111)	50 (15 to 202)	0.05	-	-	-	-	-	-

IQR: interquartile range
O-BCS: oncoplastic breast-conserving surgery
S-BCS: standard breast-conserving surgery
VD: volume displacement
VR: volume replacement

Table 17. Patient-reported outcome measures: O-BCS versus S-BCS

Study: intervention details	Outcome measure	Intervention: quality of life	Intervention: cosmetic	Intervention: other	Control: quality of life	Control: cosmetic	Control: other	P value	Conclusion
Keleman 2019 - VD	EORTC	Median (range) emotional functioning score: 91.6 (50-100), social functioning score: 83.4 (33-100)	Median (range): body image score: 91.6 (50-100)	-	Emotional functioning score: 83.4 (50-100), Social functioning	Body image score was 75.0 (33-100)	-	< 0.01/< 0.01/< 0.01	OPS significantly better in emotional/social/body image

Table 17. Patient-reported outcome measures: O-BCS versus S-BCS *(Continued)*

					score: 75.0 (50-100)				
Lansu 2014 - VD	EORTC QLQ C30 and BR23 and Young Boost Trial	C30 function scale: 75.9 (22.57) C30 symptom scale: 17.31 (10.2) C30 QOL: 63.45(35.77) BR23 fuction scale: 70.19(16.30) BR23 symptom scale: 20.51 (12.35)	YBT 26.94 (15.03)	-	C30 function scale: 92.34 (5.89) C30 symptom scale: 14.51 (11.18) C30 QOL: 87.96(7.30) BR23 function scale: 84.17(7.3) BR23 symptom scale: 11.9 (8.32)	YBT 31.35 (23.79)	-	0.28/0.57/0.05/0.06/0.07/0.08	PC is significantly better in C30 QOL but otherwise no SD
Matrai 2014 - VD	Q 47-53 of Hungarian EORTC and self-designed cosmetic	The quality of life questions, "Did you feel any arm or shoulder pain?" (P = 0.0399), "Did you have difficulty raising or moving your arm to the side?" (P = 0.0060) and “Did you feel any pain in the affected chest area?” (P = 0.0304) showed a significant advantage in the OPS group.	8.73 (1.023) 61.7% had 9/10 or 10/10	-	-	7.35 (1.5) - 23.3% had 9/10 or 10/10	-	< 0.001	Significantly better PR cosmetic score in OPS than control. Significantly less shoulder disability and chest pain in OPS group.
Acosta-Marin 2014 - VD	Self-designed	-	Mean: 4.4 - 88.4% (4/5 (good) or 5/5 (excellent))	-	-	Mean: 4.2 83.4% (4/5 (good) or 5/5 (excellent))	-	0.644	No SD

Table 17. Patient-reported outcome measures: O-BCS versus S-BCS *(Continued)*

Jiang 2015 - VD	Self-designed	-	28 (93.3%) satisfied	-	-	25 (83.3%) satisfied	-	-	More satisfied in OPS
Tang 2016 - VD and VR	Self-designed	-	62/67 satisfied	-	-	92/117 satisfied	-	0.025	Significantly more satisfied in OPS
Eichler 2013 - VD	Self-designed	Overall satisfaction (4-5/5): 86%	Satisfied with overall appearance: 83%	-	Overall satisfaction (4-5/1-5): 87%	Satisfied with overall appearance: 87%	No significant difference in overall, shape, appearance, size, quality of life, sensitivity in nipple, swelling, self-confidence. Significant better satisfaction with appearance/amount of scar tissue in BCS compared to OPS	Overall satisfaction: 0.48 Cosmetic evaluation: 0.91 Scar satisfaction: 0.013	No SD in most domains. Scar satisfaction better in BCS
Gicalone 2007 (2) - VD	Self-designed	-	32/39 (4-5/5)		-	63/88 (4-5/5)	-	0.23	No SD of cosmetic satisfaction between patient groups
Hilli-Betz 2014 - VD	Self-designed	-	92.8% - very satisfied with the cosmetic appearance of their breasts. No difference in physical attractiveness	More PROMS in paper	-	83.5% - very satisfied with the cosmetic. No difference in physical attractiveness	More PROMS in paper	0.189/0.435	No SD in PROMs in paper

Table 17. Patient-reported outcome measures: O-BCS versus S-BCS *(Continued)*

Mazouni 2013 - VD	Self-designed	-	Moderately satisfied: 12.5%; satisfied: 37.5%; very satisfied: 50%	-	-	Moderately satisfied: 14.5%, satisfied: 47.9%, very satisfied: 37.6%	-	0.52	No SD in cosmetic difference
Palsodittlir 2018 - VD and VR	Self-designed	-	97% happy with aesthetic outcome of surgery	-	-	89% happy	-	-	Greater proportion of patients in OPS happy with the aesthetic outcome
Santos 2015 - VD	Self-designed	-	35 excellent (61.4%)	-	-	45 excellent (69.2%)	-	0.242	No SD in patient-reported cosmetic score
Sherwell-Cabello 2006 - VD	Self-designed	Overall QOL 4.77	4.81	-	4.81	4.72	-	0.256	No SD in any parameters. High levels of aesthetic acceptance and mild psychological and social impact on patients.
Tenofsky 2014 - VD	Self-designed	-	8 complained of unfavourable cosmetic outcomes (13.8%)	-	-	6 (7.1%) complained of unfavourable cosmetic outcome	-	0.191	No SD in patient-reported complaints of cosmetic outcome
Viega 2011 - VD	Self-designed	-	10 (9-10)/10	-	-	10 (5-10)/10	-	< 0.001	OPS is better than standard BCS
Zhou 2019 - VR	Self-designed and DASH	-	28 (87.5) extremely satisfied	DASH 10.57	-	22 (78.6) extremely satisfied	DASH 7.86	NS/0.06	No SD in overall outcome or DASH questionnaires scores

O-BCS: oncoplastic breast-conserving surgery
S-BCS: standard breast-conserving surgery
VD: volume displacement
VR: volume replacement
PROM: Patient-reported outcome measures
DASH: The Disabilities of the Arm, Shoulder and Hand Questionnaire
EORTC: The European Organisation for Research and Treatment of Cancer
YBT: Young Boost Trial

Table 18. Cosmetic-reported outcomes: O-BCS versus S-BCS - subjective panel assesment

Study	Intervention details	Assesment details	Intervention results	Control results	P-value	Conclusion
Acosta-Marin 2014	VD	Self-designed, 4 person panel (1 plastic surgeon, 1 breast surgeon, 2 surgical oncologists)	Mean 4.5/5	4.1/5	< 0.005	O-BCS better than control (S-BCS)
Jiang 2015	VD	Self-designed - grade 1-3 (1 best, 1 and 2 satisfactory) by 1 doctor, 1 nurse, 1 non-professional	93.3% satisfactory	83.3% satisfactory	-	O-BCS better than control (S-BCS)
Gicalone 2007 (2)	VD	Self-designed, panel (1 surgeon, 1 oncologist)	33; 4-5/5	11; 4-5/5	0.006	O-BCS (Donught mastopexy) significantly better cosmetic results than standard lumpectomy (S-BCS)
Hilli-Betz 2014	VD	Self-designed, 1 surgeon evaluation	Excellent in 8.7%, good in 63.8%, moderate in 24.6%, and poor in 0.0%	Excellent in 32.2%, good in 60.9%, moderate in 5.6%, and poor in 0.6%	0.191	O-BCS (Dermoglandular rotation) significantly worse than standard segmentectomy
Keleman 2019	VD	Self-designed - 3 surgeons panel	Median (range) 4.4 (3-5)/5	Median (range) 3.2 (1-5)/5	0.001	O-BCS significantly better than control
Santos 2015	VD	2 plastic surgeon panel	Excellent in 50.9%, good in 40.4%, moderate in 7%, and poor in 1.8%	Excellent in 18.5%, good in 61.5%, moderate in 18.5%, and poor in 1.5%	< 0.001	O-BCS significantly better than control
Scheter 2019	VD	Self-designed, 13 plastic surgeon panel (1-10) 10 excellent	Shape: 7.9; Symmetry: 7.9 Volume: 8.1	Shape: 5.5 Symmetry: 5.4 Volume: 6.2	0.002/0.016/0.012	O-BCS significantly better than control
Viega 2011	VD and VR	Self-designed - 2 breast surgeons, 2 plastic surgeons (male and female of each): FBS/MBS/FPS/MPS	10/9/9/9	9/8/6/6	< 0.001/0.005/ < 0.001/< 0.001	O-BCS significantly better than control

O-BCS: oncoplastic breast-conserving surgery
S-BCS: standard breast-conserving surgery
VD: volume displacement
VR: volume replacement
FBS: female breast surgeon
MBS: male breast surgeon
FPS: female plastic surgeon
MPS: male plastic surgeon

Table 19. Complications: O-BCS of those compared to mastectomies

Study	Intervention type	Wound infection	Flap/skin necrosis	Dehisence	Fat necrosis	Seroma	Skin	Haematoma	Needed surgery
Acea-Nebril 2005	VD	2 (4%)	3 (6%)	-	-	3 (6%)	-	4 (8%)	-
Carter 2016	VD and VR	45 (4.8%)	-	-	-	126 (13.4%)	-	18 (1.9%)	-
Mustonen 2004	VR	1 (8.3%)	1 (8.3%)	-	-	3 (25%)	-	-	-
Ozmen 2020	VR	-	-	-	-	-	3 (5.6%)	-	5 (2%)
Peled 2014	VD	6 (16.2%)	-	4 (10.8%)	-	-	-	-	1 (2.7%)
Potter 2020	VD	-	-	-	-	-	-	-	8 (2.13%)
Tong 2016	VD	11 (8.4%)	0 (0%)	8 (6.1%)	5 (3.8%)	-	18 (13.7%)	4 (3.1%)	3 (2.3%)

O-BCS: oncoplastic breast-conserving surgery
VD: volume displacement
VR: volume replacement

Table 20. Complications: mastectomies

Study	Control Details	Wound infection	Flap/skin necrosis	Dehiscence	Fat necrosis	Seroma	Skin	Haematoma	Needed surgery
Acea-Nebril 2005	Mx	3 (5.6%)	0 (0%)	-	-	14 (26.4%)	-	2 (3.6%)	-
Carter 2016	Mx	133 (5.8%)	-	-	-	305 (13.2%)	-	66 (2.9%)	-
Carter 2016	Mx+R	212 (11.6%)	-	-	-	228 (12.5%)	-	87 (4.8%)	-
Mustonen 2004	Mx+R	1 (8.3%)	1 (8.3%)	-	-	3 (5.6%)	-	-	1 (8.3%)
Ozmen 2020	Mx+R	-	-	-	-	-	-	-	5 (6.7%)
Peled 2014	Mx+R	23 (35.9%)	-	19 (29.7%)	-	-	-	-	24 (37.5%)
Potter 2020	Mx+R	-	-	-	-	-	-	-	96 (9.5%)

Table 20. Complications: mastectomies *(Continued)*

Tong 2016	Mx+R	31 (11.2%)	41 (14.8%)	14 (5.1%)	11 (4%)	32 (11.6%) includes haematoma	14 (5.1%)	-	27.1%

Mx: mastectomy
R: reconstruction

Table 21. Time to adjuvant therapy: O-BCS versus mastectomy alone

Study	Intervention details	Time to adjuvant chemotherapy - intervention	Time to adjuvant chemotherapy - control	P value	Time to adjuvant radiotherapy - intervention	Time to adjuvant radiotherapy - control	P value
Morrow 2019	VD	Less than 31 days: 14.9%	Mx: 16.2% MX+R: 10.8%	0.787/0.386	Median (range) 51 (35-125)	Mx alone: 55 (26-428) Mx+R: 56 (33-122)	0.626/0.747

Mx: mastectomy
R: reconstruction
VD: volume displacement

Table 22. Patient-reported outcome measures: O-BCS versus Mx+R

Study	Intervention details	Assesment details	Intervention results	Control results	P value	Conclusion
Hart 2015	VD	Self-designed	-	-	0.03/0.02/0.09/0.03	Greater gains in satisfaction with body image, more often attributed to their reconstruction than control. Increased ability to wear revealing clothing. More often thought they were perceived as womanly by partner
Kelsall 2017	VD and VR	Hopwood Body Image score/return to activities	Case-matched: large/small breasts mean body image score: 3.3/5.69	Body image score: 5.37/5.34	0.011/0.715	OPS better body image score in large breasts
Ozmen 2020	VR	EORTC	Physical function: 88.6 (26.6-100) emotional function: 83.3 (0-100) body image: 75 (0-100)	Physical function: 93.3 (33.3-100) emotional function: 83.3 (33-100) body image: 58.3 (0-100)	< 0.001, 0.71, 0.012, 0.298	Significantly better physical function, less nausea and vomiting, less sleep disturbance, fewer breast symptoms in M + I. Better body image in MLDF. No SD in emotional or physical function

Mx: mastectomy
O-BCS: oncoplastic breast-conserving surgery
R: reconstruction
VD: volume displacement
VR: volume replacement
EORTC: The European Organisation for Research and Treatment of Cancer Questionnaire

APPENDICES

Appendix 1. CENTRAL

#1 MeSH descriptor: [Breast Neoplasms] explode all trees
#2 breast near cancer*
#3 breast near neoplasm*
#4 breast near carcinoma*
#5 breast near tumour*
#6 breast near tumour*
#7 #1 or #2 or #3 or #4 or #5 or #6
#8 MeSH descriptor: [Mastectomy, Segmental] explode all trees
#9 (Oncoplastic breast-conserving surgery):ti,ab,kw
#10 (Oncoplastic breast conserving surgery):ti,ab,kw
#11 (Oncoplastic breast conservation):ti,ab,kw
#12 Oncoplastic near (breast conserving or breast conservation):ti,ab,kw
#13 oncoplastic surger*:ti,ab,kw
#14 volume displacement near procedur*:ti,ab,kw
#15 volume displacement near tech*:ti,ab,kw
#16 MeSH descriptor: [Mammaplasty] explode all trees
#17 mammaplast* or mammoplast*:ti,ab,kw

#18 therapeutic near (mammaplast* or mammoplast*):ti,ab,kw
#19 Wise pattern near (mammaplast* or mammoplast*):ti,ab,kw
#20 Vertical scar near (mammaplast* or mammoplast*):ti,ab,kw
#21 Circumareolar near (mammaplast* or mammoplast*):ti,ab,kw
#22 Benelli near (mammaplast* or mammoplast*):ti,ab,kw
#23 Round block near (mammaplast* or mammoplast*):ti,ab,kw
#24 Raquet handle near (mammaplast* or mammoplast*):ti,ab,kw
#25 lateral near (mammaplast* or mammoplast*):ti,ab,kw
#26 volume replacement near procedur*:ti,ab,kw
#27 volume replacement near tech*:ti,ab,kw
#28 (Abdominal Adipo-fascial Flap):ti,ab,kw
#29 (Abdominal Adipofascial Flap):ti,ab,kw
#30 abdominal flap*:ti,ab,kw
#31 Adipo-fascial Flap*:ti,ab,kw
#32 Adipofascial Flap*:ti,ab,kw
#33 Thoraco-epigastric Flap*:ti,ab,kw
#34 Thoracoepigastric Flap*:ti,ab,kw
#35 Superior epigastric artery perforator flap*:ti,ab,kw
#36 Medial Intercostal Artery Perforator flap*:ti,ab,kw
#37 Internal Mammary Artery Perforator flap*:ti,ab,kw
#38 Anterior Intercostal Artery Perforator flap*:ti,ab,kw
#39 MeSH descriptor: [Perforator Flap] explode all trees
#40 Lateral Intercostal Artery Perforator flap*:ti,ab,kw
#41 Lateral Thoracic Artery Perforator flap*:ti,ab,kw
#42 Thoracodorsal Artery Perforator Flap*:ti,ab,kw
#43 Mini Latissimus Dorsi:ti,ab,kw
#44 Omental flap*:ti,ab,kw
#45 transverse upper gracilis flap*:ti,ab,kw
#46 MeSH descriptor: [Free Tissue Flaps] explode all trees
#47 "Advancement Flap*":ti,ab,kw
#48 #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47
#49 #7 AND #48 in Trials

Appendix 2. MEDLINE

#	Searches
1	exp Breast Neoplasms/
2	(breast adj6 cancer$).tw.
3	(breast adj6 neoplasm$).tw.
4	(breast adj6 carcinoma$).tw.
5	(breast adj6 tumo?r$).tw.
6	or/1-5
7	exp Surgical Oncology/
8	exp Breast Neoplasms/su [Surgery]
9	or/7-8
10	6 and 9

(Continued)

11	exp Mastectomy, Segmental/mt [Methods]
12	Oncoplastic breast-conserving surgery.tw.
13	Oncoplastic breast conserving surgery.tw.
14	(oncoplastic adj5 breast-conserving adj5 surgery).tw.
15	Oncoplastic breast conservation surgery.tw.
16	(oncoplastic adj5 breast adj5 (conserving or conservation*) adj5 surgery).tw.
17	Oncoplastic breast conservation.mp.
18	(oncoplastic adj5 breast adj5 (conserving or conservation*)).tw.
19	oncoplastic surger*.tw.
20	(volume displacement and (procedur* or tech*)).tw.
21	exp Mammaplasty/
22	therapeutic mamm#plast*.mp.
23	Wise pattern therapeutic mamm#plast*.tw.
24	Vertical scar mamm#plast*.tw.
25	Circumareolar mamm#plast*.tw.
26	Benelli* mamm#plast*.tw.
27	Round block mamm#plast*.tw.
28	Raquet handle mamm#plast*.tw.
29	lateral mamm#plast*.tw.
30	(volume replacement and (procedur* or tech*)).tw.
31	Abdominal Adipo-fascial Flap*.tw.
32	Abdominal Flap*.tw.
33	Adipo-fascial Flap*.tw.
34	Thoraco-epigastric Flap*.tw.
35	Superior epigastric artery perforator flap*.tw.
36	Medial Intercostal Artery Perforator flap*.tw.
37	Internal Mammary Artery Perforator flap*.tw.
38	Anterior Intercostal Artery Perforator flap*.tw.

(Continued)

39	exp Perforator Flap/
40	Lateral Intercostal Artery Perforator flap*.tw.
41	Lateral Thoracic Artery Perforator flap*.tw.
42	Thoracodorsal Artery Perforator Flap*.tw.
43	(mini adj5 Latissimus Dorsi).tw.
44	Omental flap*.tw.
45	transverse upper gracilis flap*.tw.
46	exp Free Tissue Flaps/
47	Advancement Flap*.tw.
48	or/11-46
49	10 and 48
50	randomized controlled trial.pt.
51	controlled clinical trial.pt.
52	randomized.ab.
53	placebo.ab.
54	Clinical Trials as Topic/
55	randomly.ab.
56	trial.ti.
57	(crossover or cross-over).tw.
58	Pragmatic Clinical Trials as Topic/
59	pragmatic clinical trial.pt.
60	or/50-59
61	Case-Control Studies/
62	Control Groups/
63	Matched-Pair Analysis/
64	Retrospective Studies/
65	((case* adj5 control*) or (case adj3 comparison*) or control group*).ti,ab.
66	or/61-65

(Continued)

67	Cohort Studies/
68	Longitudinal Studies/
69	Follow-Up Studies/
70	Prospective Studies/
71	Retrospective Studies/
72	cohort.ti,ab.
73	longitudinal.ti,ab.
74	prospective.ti,ab.
75	retrospective.ti,ab.
76	or/67-75
77	49 and 60
78	49 and 66
79	49 and 76
80	77 or 78 or 79
81	animals/ not humans/
82	80 not 81
83	remove duplicates from 82

Appendix 3. Embase

#	Searches
1	exp breast/
2	exp breast disease/
3	(1 or 2) and exp neoplasm/
4	exp breast tumor/
5	exp breast cancer/
6	exp breast carcinoma/
7	(breast$ adj5 (neoplas$ or cancer$ or carcin$ or tumo$ or metasta$ or malig$)).ti,ab.

(Continued)

8	or/3-7
9	exp breast cancer/su [Surgery]
10	exp cancer surgery/
11	9 or 10
12	8 and 11
13	exp partial mastectomy/
14	oncoplastic breast surgery/
15	Oncoplastic breast-conserving surgery.tw.
16	Oncoplastic breast conserving surgery.tw.
17	(oncoplastic adj5 breast-conserving adj5 surgery).tw.
18	oncoplastic breast conservation surgery/
19	Oncoplastic breast conservation surgery.tw.
20	(oncoplastic adj5 breast adj5 (conserving or conservation*) adj5 surgery).tw.
21	Oncoplastic breast conservation.tw.
22	(oncoplastic adj5 breast adj5 (conserving or conservation*)).tw.
23	(oncoplastic adj5 (procudur* or tech* or surger*)).tw.
24	(volume displacement and (procedur* or tech*)).tw.
25	exp breast reconstruction/ and partial.tw.
26	therapeutic mamm#plast*.tw.
27	Wise pattern therapeutic mamm#plast*.tw.
28	Vertical scar mamm#plast*.tw.
29	Circumareolar mamm#plast*.tw.
30	Benelli* mamm#plast*.tw.
31	Round block mamm#plast*.tw.
32	Raquet handle mamm#plast*.tw.
33	lateral mamm#plast*.tw.
34	(volume replacement and (procedur* or tech*)).tw.
35	Abdominal Adipo-fascial Flap*.tw.

(Continued)

36	Abdominal Flap*.tw.
37	exp adipofascial flap/
38	((Adipo-fascial or adipofascial) and Flap*).tw.
39	((Thoraco-epigastric or Thoracoepigastric) and Flap*).tw.
40	Superior epigastric artery perforator flap*.tw.
41	Medial Intercostal Artery Perforator flap*.tw.
42	Internal Mammary Artery Perforator flap*.tw.
43	Anterior Intercostal Artery Perforator flap*.tw.
44	exp perforator flap/
45	Lateral Intercostal Artery Perforator flap*.tw.
46	Lateral Thoracic Artery Perforator flap*.tw.
47	exp thoracodorsal artery perforator flap/
48	Thoracodorsal Artery Perforator Flap*.tw.
49	Mini Latissimus Dorsi.tw.
50	Omental flap*.tw.
51	transverse upper gracilis flap*.tw.
52	exp free tissue graft/
53	Advancement Flap*.tw.
54	or/13-53
55	12 and 54
56	Randomized controlled trial/
57	Controlled clinical study/
58	Random$.ti,ab.
59	randomization/
60	intermethod comparison/
61	placebo.ti,ab.
62	(compare or compared or comparison).ti.
63	(open adj label).ti,ab.

(Continued)

64	((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab.
65	double blind procedure/
66	parallel group$1.ti,ab.
67	(crossover or cross over).ti,ab.
68	((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab.
69	(assigned or allocated).ti,ab.
70	(controlled adj7 (study or design or trial)).ti,ab.
71	(volunteer or volunteers).ti,ab.
72	trial.ti.
73	or/56-72
74	exp case control study/
75	case control study.ti,ab.
76	((case control or case base or case matched or retrospective) adj1 (analys* or design* or evaulation* or research or stud* or survey* or trial*)).ti,ab.
77	or/74-76
78	exp retrospective study/
79	exp prospective study/
80	((cohort or concurrent or incidence or longitudinal or followup or 'follow up' or prospective or retrospective) adj1 (analys* or design* or evaluation* or research or stud* or survey* or trial*)).ti,ab.
81	or/78-80
82	55 and 73
83	55 and 77
84	55 and 81
85	82 or 83 or 84
86	limit 85 to (human and (conference abstracts or embase))
87	remove duplicates from 86

Appendix 4. WHO ICTRP

Basic search:

1. Oncoplastic breast-conserving surger*

2. Breast cancer AND volume displacement

3. Breast cancer AND volume replacement

4. Breast cancer AND flap

Advanced search:

1. Condition: breast cancer
Intervention: oncoplastic breast surgery OR oncoplastic technique OR oncoplastic procedure
Recruitment Status: ALL

2. Condition: breast cancer
Intervention: volume displacement OR wise pattern mammaplasty OR therapeutic mammaplasty OR vertical scar mammaplasty OR Circumareolar mammoplasty OR benelli mammoplasty OR round block mammoplasty OR raquet handle mammoplasty OR lateral mammoplasty
Recruitment Status: ALL

3. Condition: breast cancer
Intervention: volume replacement OR Abdominal adipo-fascial flap OR advancement flap OR Lateral intercostal artery perforator flap OR Lateral thoracic artery perforator OR Thoracodorsal artery perforator flap
Recruitment Status: ALL

4. Condition: breast cancer
Intervention: Latissimus dorsi mini flap OR Thoraco-epigastric Flap OR Superior epigastric artery perforator flap OR Medial intercostal artery perforator OR Internal mammary artery perforator OR Anterior inter-costal artery perforator OR omental flap OR transverse upper gracilis flap
Recruitment Status: ALL

Appendix 5. ClinicalTrials.gov

Basic search:

1. Condition or disease: Breast cancer
Other terms: Oncoplastic breast-conserving surgery

2. Condition or disease: Breast cancer
Other terms: volume displacement technique

3. Condition or disease: Breast cancer
Other terms: volume replacement technique

4. Condition or disease: Breast cancer
Other terms: flap (consider adding ‘reconstruction’)

Advanced search:

1. Condition or disease: Breast cancer
Intervention: Oncoplastic breast-conserving surgery
Study type: all studies

2. Condition or disease: Breast cancer
Intervention: volume displacement technique
Study type: all studies

3. Condition or disease: Breast cancer
Intervention: therapeutic mammoplasty OR wise pattern mammoplasty OR vertical scar mammoplasty OR Circumareolar mammoplasty OR benelli mammoplasty OR round block mammoplasty OR raquet handle mammoplasty OR lateral mammoplasty
Study type: all studies

4. Condition or disease: Breast cancer
Intervention: volume replacement technique
Study type: all studies

5. Condition or disease: Breast cancer

Intervention: Abdominal Adipo-fascial Flap OR advancement flap OR Lateral intercostal artery perforator flap OR Lateral thoracic artery perforator OR Thoracodorsal artery perforator flap
Study type: all studies

6. Condition or disease: Breast cancer
Intervention: Latissimus dorsi mini flap OR Thoraco-epigastric Flap OR Superior epigastric artery perforator flap OR Medial intercostal artery perforator OR Internal mammary artery perforator OR Anterior inter-costal artery perforator OR omental flap OR transverse upper gracilis flap
Study type: all studies

HISTORY

Protocol first published: Issue 7, 2020

CONTRIBUTIONS OF AUTHORS

- Draft the protocol: AN, JH, SH, PGR, RR
- Study selection: AN, JH
- Extract data from studies: AN, JH, SA
- Enter data into RevMan: AN, SA
- Carry out the analysis: AN, SH
- Interpret the analysis: AN, JH, SH, PGR, RR
- Draft the final review: AN, JH, PGR, SA, SH, RR
- Disagreement resolution: PGR, RR
- Update the review: AN, PGR

DECLARATIONS OF INTEREST

Akriti Nanda: none known.
Jesse Hu: none known.
Sarah Hodgkinson: none known.
Sanah Ali: none known
Richard Rainsbury: none known.
Pankaj Roy: none known.

SOURCES OF SUPPORT

Internal sources

- No sources of support provided

External sources

- No sources of support provided

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Criteria for considering studies for this review

Authors planned to exclude studies with fewer than 20 women with O-BCS. The original reasoning had been to eliminate bias created by learning curves of the surgeons performing the procedure. It was then agreed, prior to full-text review, that to avoid creating study selection bias by this restrictive criterion we agreed to remove this restriction.

Authors included studies in all languages and did not limit to English only.

In the control, authors expanded the wide local excision (WLE) group to include any breast conservation surgery. Some studies used terminology such as "lumpectomy", "quadrantectomy", "segmentectomy" or "partial mastectomy" that in practice are almost identical operations to a WLE, but the term "breast-conserving surgery" better encompasses all of these operations.

Outcomes

Local recurrence was reported as 'local recurrence rate' or 'local recurrence-free survival' so both were extracted but not pooled as authors felt they were two different outcomes.

For primary outcomes follow-up, we included the addition of '1 to 5 years' and '10 years' to display all studies and be clear on follow-up periods.

We replaced the secondary outcome 'need for further surgery to address aesthetics or symmetry (for example, symmetrisation or fat transfer)' with 'time to adjuvant therapy; time in days from surgery to initiation of adjuvant chemotherapy and/or radiotherapy.' This was done prior to data extraction as it was felt this outcome was more important to assess whether oncoplastic surgery results in a hastening or delay of treatment compared to other surgeries. The need for further aesthetic surgeries or symmetrisation was deemed a less important outcome and repetition of information captured by the patient-reported cosmetic evaluation and independent cosmetic evaluation. This change in protocol was approved by the editorial group.

Shortened titles of outcomes added for ease of writing in the review. Definitions have not been altered in any way between protocol and review.

Selection of studies

Studies with multiple publications of duplicate data sets: we excluded the study with the shorter follow-up time or fewer participant numbers for outcomes of interest so as not to duplicate data in the analysis.

Dealing with missing data

We had previously not specified what data sets we would seek from authors and deemed it sensible that, given we included 78 studies with varying outcomes we would take a selective approach. When studies reported one primary outcome but other primary outcome data were missing, we contacted the authors to request further information.

Risk of bias

In our protocol, we planned to use the ROBINS-I tool. We planned to included bias 'due to centre-specific experience and post-operative follow-up' in the analysis. Risk of bias due to the follow-up period is covered in the 'selection of participants domain'. Centre experience would have been appropriate to analyse in the subgroup analysis, but not enough studies reported information on this for it to be conducted.

Author contributions

Another author (SA) was added to the review to help with data extraction, risk of bias and uploading of data and references to RevMan.

Author JH (not SH) analysed the risk of bias with AN. Author SH (not JH) constructed the summary of findings tables with AN.

Sensitivity analysis

We did not do any sensitivity analysis with "missing data that require assumptions and/or imputations (removing studies where assumptions have been made)" as we had no studies with missing data or assumptions.

INDEX TERMS

Medical Subject Headings (MeSH)

*Breast Neoplasms [surgery]; Cohort Studies; Disease-Free Survival; Mastectomy; *Mastectomy, Segmental

MeSH check words

Female; Humans