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Different types of implants for reconstructive breast surgery (Review)

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[Intervention Review]

Different types of implants for reconstructive breast surgery

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ABSTRACT

Background

Breast cancer is the most common cancer in women worldwide, and is a leading cause of cancer death among women. Prophylactic or curative mastectomy is often followed by breast reconstruction for which there are several surgical approaches that use breast implants with which surgeons can restore the natural feel, size and shape of the breast.

Objectives

To assess the effects of different types of breast implants on capsular contracture, surgical short- and long-term complications, postoperative satisfaction level and quality of life in women who have undergone reconstructive breast surgery after mastectomy.

Search methods

We searched the Cochrane Breast Cancer Group's Specialised Register on 20 July 2015, MEDLINE (1985 to 20 July 2015), EMBASE (1985 to 20 July 2015) and the Cochrane Central Register of Controlled Trials (CENTRAL; Issue 8, 2015). We also searched the World Health Organization's International Clinical Trials Registry Platform (WHO ICTRP) and ClinicalTrials.gov on 16 July 2015.

Selection criteria

We included randomised controlled trials (RCTs) and quasi-RCTs that compared different types of breast implants for reconstructive surgery. We considered the following types of intervention: implant envelope surfaces - texturised versus smooth; implant filler material - silicone versus saline, PVP-Hydrogel versus saline; implant shape - anatomical versus round; implant volume - variable versus fixed; brands - different implant manufacturing companies and implant generation (fifth versus previous generations).

Data collection and analysis

Two review authors independently assessed methodological quality and extracted data. We used standard Cochrane methodological procedures. The quality of the evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.

Main results

Five RCTs with 202 participants met the inclusion criteria. The women participants were typically in their 50s, and the majority of them (about 82%) received reconstructive surgery following breast cancer, while the others had reconstructive surgery after prophylactic mastectomy. The studies were heterogenous in terms of implant comparisons, which prevented us from pooling the data.

The studies were judged as being at an unclear risk of bias for most risk of bias items owing to poor quality of reporting in the trial publications. Three of the five RCTs were judged to be at high risk of attrition bias, and one at high risk of detection bias.

Textured silicone versus smooth silicone implants: textured implants were associated with worse outcomes when compared to smooth implants (capsular contracture: risk ratio (RR) 0.82, 95% CI 0.14 to 4.71; 1 study, 20 participants; *very low quality evidence;* reintervention: RR 0.82, 95% CI 0.14 to 4.71; 1 study, 20 participants; *very low quality evidence*). No results in this comparison were statistically significant.

Silicone versus saline implants: saline-filled implants performed better than silicone-filled implants for some outcomes; specifically, they produced less severe capsular contracture (RR 3.25, 95% CI 1.24 to 8.51; 1 study, 60 participants; *very low quality evidence*) and increased patient satisfaction (RR 0.60, 95% CI 0.41 to 0.88; 1 study, 58 participants; *very low quality evidence*). However reintervention was significantly more frequent in the saline-filled implant group than in the silicone-filled group (OR 0.08, 95% CI 0.01 to 0.43; 1 study, 60 participants; *very low quality evidence*).

Poly(N-vinyl-2-pyrrolidone) hydrogel-filled (PVP-hydrogel) versus saline-filled implants: PVP-hydrogel-filled implants were associated with worse outcomes when compared to saline-filled implants (capsular contracture: RR 3.50, 95% CI 0.83 to 14.83; 1 study, 40 participants; *very low quality evidence*; short-term complications: RR 2.10, 95% CI 0.21 to 21.39; 1 study, 41 participants; *very low quality evidence*).

Anatomical versus round implants: anatomical implants were associated with worse outcomes than round implants (capsular contracture: RR 2.00, 95% CI 0.20 to 20.15; 1 study, 36 participants; *very low quality evidence*; short-term complications: RR 2.00, 95% CI 0.42 to 9.58; 1 study, 36 participants; *very low quality evidence;* reintervention: RR 1.50, 95% CI 0.51 to 4.43; 1 study, 36 participants; *very low quality evidence*). No results in this comparison were statistically significant.

Variable-volume versus fixed-volume implants: data about one-stage reconstruction using variable-volume implants were compared with data about fixed-volume implants positioned during the second surgical procedure of two-stage reconstructions. Fixed-volume implant reconstructions were possibly associated with a greater number of women reporting that their reconstruction corresponded with expected results (RR 0.25, 95% CI 0.10 to 0.62; 1 study, 40 participants; *very low quality evidence*) and fewer reinterventions (RR 7.00, 95% CI 1.82 to 26.89; 1 study, 40 participants; *very low quality evidence*) when compared to variable-volume implants. A higher patient satisfaction level (rated from 1 to 6, with 1 being very bad and 6 being very good) was found with the fixed-volume implants for overall aesthetic result (mean difference (MD) -1.10, 95% CI -1.59 to -0.61; 1 study, 40 participants; *very low quality evidence*).

There were no studies that examined the effects of recent (fifth) generation silicone implants versus previous generations or different implant manufacturing companies.

Authors' conclusions

Despite the central role of breast reconstruction in women with breast cancer, the best implants to use in reconstructive surgery have been studied rarely in the context of RCTs. Furthermore the quality of these studies and the overall evidence they provide is largely unsatisfactory. Some of our results can be interpreted as early evidence of potentially large differences between different surgical approaches, which should be confirmed in new high-quality RCTs that include a larger number of women. These days - even after a few million women have had breasts reconstructed - surgeons cannot inform women about the risks and complications of different implant-based breast reconstructive options on the basis of results derived from RCTs.

PLAIN LANGUAGE SUMMARY

Different types of implants for reconstructive breast surgery after mastectomy

Review question

We assessed the effects of different types of breast implants on short-term and long-term surgical complications, cosmetic outcomes, satisfaction with the surgical procedure and the quality of life in women undergoing breast reconstruction following a mastectomy (breast removal).

Background

An estimated 28% to 60% of women affected by breast cancer will undergo a mastectomy (i.e. surgical removal of the breast). Following a mastectomy, women can choose from many breast reconstruction options and achieve a natural feel with appropriate size and shape of the breast, according to individual needs. These reconstruction options are also available for the increasing number of women at high risk of developing hereditary breast cancer who undergo risk-reducing mastectomy. Options include implants that are silicone-filled (filled with an inert, man-made polymer in gel form), saline-filled (a silicone shell, filled with sterile salt water), anatomically shaped or round, textured or smooth, and of fixed-volume or variable-volume. We wanted to examine if different types of breast implants are associated with better or worse surgical outcomes and patient satisfaction.

Study characteristics

The evidence is current to July 2015. We conducted a review to compare short- and long-term surgical complications (such as scar tissue forming around the implant and squeezing it - referred to as 'capsular contracture', and 'implant rupture'), cosmetic outcomes, women's postoperative quality of life and satisfaction with different types of breast implants used in breast reconstruction. We found five randomised studies involving 202 women that provided data for five different comparisons: rough versus smooth surface, implant filler materials compared to each other (silicone versus saline, and hydrogel versus saline), anatomical versus round shape, and variable- versus fixed-volume. Four studies included women who received a mastectomy for breast cancer and one study included women who had bilateral mastectomies for preventive purposes.

The authors of two studies reported that they did not have competing interests; the authors of three studies did not report this information. Three studies reported that their studies received financial support from research foundations; the other studies did not report any information regarding the source of their funding.

Key results

Only two studies reported differences between types of implants for some of the outcomes we considered.

One study on 65 women compared silicone-filled implants with saline-filled implants and showed that saline implants resulted in fewer cases of capsular contracture and a higher number of women who were satisfied with the reconstructed breast. However more women in the saline-filled implant group required further operations on the reconstructed breast than in the silicone-filled implant group.

Another study on 40 women compared variable-volume implants (inserted in a single surgical procedure) with fixed-volume implants (inserted in the second of two separate surgical procedures) and showed that there were significantly higher satisfaction levels and significantly lower reoperation rates with the fixed-volume implants.

The remaining three studies reported on the following comparisons: rough versus smooth silicone-filled implants (20 women), PVP-hydrogel versus saline-filled implants (41 women) and anatomically shaped versus round implants (36 women). These studies reported no differences between implant types for outcomes such as capsular contracture, other short-term complications or reoperation rates.

There were no studies that compared recent generation silicone implants with earlier versions or implants from different manufacturing companies.

Quality of the evidence

The evidence we found was limited: only a negligible, tiny fraction of women who undergo breast reconstruction have been studied in randomised controlled trials. The quality of evidence is very low, as the studies we identified suffered from major methodological limitations.

Despite the fact that several million women have had their breasts reconstructed over the last 20 years, the small number of studies and the low numbers of women included in these studies does not allow us to draw any definitive conclusions about the which is the best type of breast implant. This lack of evidence should be discussed when informing women about the risks and complications of

different implant-based breast reconstruction options. There is a need for further studies, which include a larger number of women and compare different types of implants, to free women from decisions made on the basis of surgical opinion alone.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Textured versus smooth implants for reconstructive breast surgery

Patient or population: women having reconstructive breast surgery
Settings: cancer centres
Intervention: textured implants
Comparison: smooth implants

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Smooth implants	Textured implants				
Capsular contracture Number of women with capsular contracture Follow-up: mean 3 years	**Study population**		**RR 0.82** (0.14 to 4.71)	20 (1 study)	⊕◯◯◯ **very low**[1,2]	
	222 per 1000	**182 per 1000** (31 to 1000)				
	Moderate					
	222 per 1000	**182 per 1000** (31 to 1000)				
Reintervention Number of women with reinterventions Follow-up: mean 3 years	**Study population**		**RR 0.82** (0.14 to 4.71)	20 (1 study)	⊕◯◯◯ **very low**[1,2]	
	222 per 1000	**182 per 1000** (31 to 1000)				
	Moderate					
	222 per 1000	**182 per 1000** (31 to 1000)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (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; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]We downgraded twice based on unclear risk of selection, performance and detection bias.
[2]We downgraded once because the result was based on only one study with 20 participants.

BACKGROUND

Description of the condition

Breast cancer is the most common cancer in women worldwide (excluding cancers of the skin), and represents the second leading cause of cancer death among women (after lung cancer) in high-income countries (American Cancer Society 2014; Siegel 2015). Since the 1940s, the incidence of breast cancer has gradually increased in Western countries at a rate of approximately 1% per year (Boyle 2005). Despite this increase, mortality from breast cancer has declined in countries with organised, population-based mammography screening (Jonsson 2007), even if trials with optimal randomisation do not show a significant reduction in breast cancer mortality and although substantial over-diagnosis and over-treatment cannot be ruled out (Gøtzsche 2013). New and efficient therapeutic regimens have led to the prolonged survival of women and an improved quality of life (Hortobagyi 2005). These interventions have increased the number of breast cancer survivors considerably; a further increase of 31% is expected in the 10-year period between 2005 and 2015 (De Angelis 2009).

Novel approaches in oncological breast surgery and new technologies in the global management of women diagnosed with breast cancer will allow patients to access the best, individually tailored treatment (Cordeiro 2008). Nevertheless, an estimated 28% to 60% of women affected by breast cancer will undergo a mastectomy (McGuire 2009). Breasts represent a strong symbol of femininity, the loss of which can lead to important psychological consequences that potentially damage a woman's self-image and leading her to question her desirability as a sexual partner (Marin-Gutzke 2010). Following a surgical procedure to remove breast cancer, women face the challenge of deciding what to do about breast reconstruction.

After oncological surgery for breast cancer, women can choose from many options for breast reconstruction in order to achieve a reconstructed breast that has a natural feel combined with a size and shape that meets their individual needs (Djohan 2008; Thiruchelvam 2013). Women also have the option of deciding which type of breast reconstruction they prefer, and can select alternative measures, such as external prostheses.

The same reconstructive options are available for the increasing number of women who undergo risk-reducing mastectomy because they are at high risk of developing breast cancer (i.e. hereditary breast cancer) (Nelson 2012).

Women who undergo a mastectomy should be aware of all available reconstructive options and should discuss the benefits and limitations of each technique with their physician and plastic surgeon before making decisions about the best course of action.

Description of the intervention

The demand for reconstructive breast surgery is increasing among women: The number of procedures performed in the USA presented a 30% increase over the last decade, from 78,800 in 2000 to nearly 102,200 procedures in 2014, according to the American Society of Plastic Surgeons (ASPS 2014).

Breast reconstruction can be performed at the same time that the oncological procedure is carried out to remove the breast cancer (immediate reconstruction), or it can be delayed until all adjuvant treatments have been completed (postoperative chemotherapy or radiotherapy) (Champaneria 2012; D'Souza 2011).

Both immediate and delayed reconstruction can be performed using autologous tissue (i.e. tissue used for surgical reconstruction that comes from the patient's own body, such as the musculocutaneous pedicle or free flaps) or using implants. Reconstruction with implants can occur in a one-stage (direct-to-implant reconstruction) or two-stage (tissue expander followed by permanent implant) intervention. The one-stage reconstruction option has been improved by the recent introduction of meshes (biological or synthetic) in breast surgery (Ho 2012).

Implant-based breast reconstruction usually involves the placement of breast implants filled with silicone gel or saline. The best results with implant-based reconstruction are achieved in patients with small or moderate breast volume and a low degree of ptosis (i.e. age-related drooping) due to easier achievable symmetry between natural and reconstructed breasts (Spear 2007).

Five generations of silicone breast implants have been developed since silicon implants were introduced in 1961 (Blocksma 1965), each leading to better results in terms of both short- and long-term surgical and aesthetic outcomes (Champaneria 2012).

While silicone implants are now routinely used in breast surgery, they have been the subject of controversy. This was particularly true in the USA, where there was a moratorium on their use from 1992 to 2006 due to safety concerns. Following subsequent scientific validation of their safety, silicone implants have regained widespread acceptance for clinical use (Chao 2016).

How the intervention might work

Implant-based breast reconstruction allows restoration of a woman's lost physical image with excellent cosmetic results (Spear 2007).

Moreover, breast implant positioning after a mastectomy represents a minimally invasive procedure compared with autologous tissue breast reconstruction, and carries no risk of distant donor site-related morbidity (Jewell 2012).

However, the use of breast implants can be associated with some short- and long-term complications, including capsular contracture (i.e. development of problems caused by scar tissue), infection, haematoma (collection of clotted blood), seroma (collection of fluid), rupture of the implant, and migration of the filler material (Accurso 2008; Barnsley 2006; Henriksen 2003). These complications can lead to reinterventions to replace the implant, which

result in additional costs to the patient, potentially suboptimal results, and a higher probability of repeated adverse events (Baker 1978; Nahabedian 2009a).

In particular, capsular contracture can span from simple breast induration (hardening) to the development of a painful breast, with total distortion of its shape and volume. This can severely compromise the aesthetic outcome, and is the most significant reason for patient dissatisfaction following breast implant surgery (Handel 2006; Nahabedian 2009b). Capsular contracture rates after breast reconstruction range from 4% to 17% (Spear 2007). Radiotherapy increases the risk of complications by more than 40% in prosthetic-based reconstructions, increasing the rate of capsular contractures to between 25% and 30% of patients (Kronowitz 2009; Nava 2011).

In addition, different types of implants (e.g. textured, smooth, silicone- or saline-filled) exhibit different rates of complications (Hammond 2012; Maxwell 2012), although no consensus has been reached about the best type of implant-based reconstruction. Women undergoing this type of surgery should be aware of all of the possible complications and pitfalls related to these procedures.

Why it is important to do this review

Breast cancer control represents a major objective in public health, and breast reconstruction following oncological procedures is one of the main health objectives of the European Community for the coming years (EU 2012). The European Society of Breast Cancer Specialists (EUSOMA) has defined the requirement for specialist breast units, and stressed the importance of reconstruction after oncological surgery (EUSOMA 2012).

Since surgical techniques for breast reconstruction are almost standardised worldwide (Nahabedian 2009b; Querci della Rovere 2010), researchers' efforts should be directed at finding evidence of the best implants in terms of patient satisfaction, postoperative quality of life, women's safety, and cosmetic outcomes.

There are currently no systematic reviews in the scientific literature on this topic.

OBJECTIVES

To assess the effects of different types of breast implants on capsular contracture, surgical short- and long-term complications, postoperative satisfaction level and quality of life in women who have undergone reconstructive breast surgery after mastectomy.

METHODS

Criteria for considering studies for this review

Types of studies

We considered any randomised or quasi-randomised controlled trials (RCTs or qRCTs) that compared different types of breast implants. Quasi-randomised trials were defined as those presenting a predictable non-concealed allocation (e.g. simple alternation, date of birth, hospital admission number).

Types of participants

Women undergoing reconstructive breast surgery with implants following mastectomy for treatment of breast cancer or for risk reduction.

Types of interventions

Different types of breast implants and different surgical procedures for reconstructive purposes.

We compared:

- implant envelope surfaces: texturised versus smooth; different types of texturisation;
- implant filler material: silicone versus saline; poly(N-vinyl-2-pyrrolidone) hydrogel-filled (PVP-hydrogel) versus saline;
- implant shape: anatomical versus round;
- implant volume: variable versus fixed;
- brands: different implant manufacturing companies;
- implant generation: fifth versus previous generations of silicone implants.

We excluded the data from trials if flaps or other interventions (except oncological excisions) were performed along with implant positioning.

We planned to perform cross-comparisons if the number of participants in each group allowed it.

Types of outcome measures

Primary outcomes

- Capsular contracture rate and severity.
    - If assessed by a surgeon, we used Baker, Gylbert, and Spear classifications to identify contracture severity at a minimum of one year of follow-up (Baker 1978; Gylbert 1989; Spear 1995).
    - We considered participants' subjective self-assessments, or objective measurements of firmness (applanation tonometry), as other valid methods of identifying contracture severity at a minimum of one year of follow-up.
- Participant-reported outcomes: postoperative quality of life (psychosocial, physical, and sexual well-being) or satisfaction level (satisfaction with breast and reconstructive outcome), as measured by BREAST-Q, EORTC QLQC30 (Br23), and 36-Item Short-Form Health Survey (SF-36).

Secondary outcomes

- Implant rupture and filler material migration rates.
    - We considered migration of filler material as evidence of filler material outside the capsule surrounding the implant that was visible during magnetic resonance imaging (MRI) or surgery.
- Short-term complication rates: implant infection, seroma, haematoma, implant extrusion, and implant malpositioning.
- Reintervention and long-term complication rates: late seroma (i.e. seroma presenting more than one month after surgery), double-capsule formation (i.e. the presence of a double-layered capsule surrounding the implant at reintervention), and chronic pain (i.e. pain that persists for more than three months after surgery).
- Cosmetic outcomes not reported by participants (i.e. evaluation of reconstructive outcomes, e.g. breast shape and symmetry, by the operating surgeon or by other clinicians).

Search methods for identification of studies

Electronic searches

We searched the following databases.

- The Cochrane Breast Cancer Group'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 in the Group's module (http://www.mrw.interscience.wiley.com/cochrane/clabout/articles/BREASTCA/frame.html). Trials with the key words "breast reconstruction," "breast reconstructive surgery," "implant-based breast reconstruction," "mammaplasty," "silicone implant," "saline implant," "silicone breast implant," "saline breast implant," "breast implants," "implants," "silicone," "saline," "texturized implant," "smooth implant," "variable volume implant," and "fixed volume implant" were extracted and considered for inclusion in the review.
- MEDLINE (via Ovid SP; from 1985 until 20 July 2015). See Appendix 1.
- EMBASE (via EMBASE.com; from 1985 until 20 July 2015). See Appendix 2.
- The Cochrane Central Register of Controlled Trials (CENTRAL; Issue 8, 2015). See Appendix 3.
- The World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal (http://apps.who.int/trialsearch/Default.aspx) for all prospectively registered and ongoing trials on 16 July 2015. See Appendix 4.
- Clinicaltrials.gov (http://clinicaltrials.gov/) on 16 July 2015. See Appendix 5.

Searching other resources

We tried to identify further studies by reviewing reference lists of relevant trials or reviews. We obtained a copy of the full article for each reference that reported a potentially eligible trial. When this was not possible, we attempted to contact study authors to request additional information.

Data collection and analysis

Selection of studies

We screened all abstracts identified by the search strategies described above for duplicates. Then two independent review authors (CR and NR) assessed the deduplicated abstracts to exclude studies that did not meet the inclusion criteria. Disagreements were resolved through discussion between the two review authors; in cases of persistent disagreement, they consulted a third review author (ST). The full publications of all potentially relevant abstracts were obtained and formally assessed for inclusion. Trials in languages other than English were included as well. Review authors were not blinded to the names of the study authors, their corresponding institutions, the journal of publication, or the results.

Data extraction and management

We developed a tailored data extraction form to record the following details of the studies.

- Methods: study design, year, country, language, duration, sequence generation, allocation concealment, blinding.
- Participants: source of participants, demographic characteristics, inclusion/exclusion criteria, numbers of participants at baseline and completion, setting.
- Interventions and controls: number of arms, definitions of interventions, materials, surgical techniques, timing of surgery.
- Outcomes: list of assessed outcomes, definition of each outcome, outcome assessor, blinding of the assessor.
- Results: follow-up data, analyses (intention-to-treat or per-protocol), withdrawals, and losses to follow-up.

Data were extracted independently by two review authors (LI and ST); differences of opinion between these review authors were resolved through discussion with a third review author (LM). Missing or updated information was sought through contact with the study authors.
Quantitative data from trials with more than one publication were extracted from all publications; the most recent publication was considered as the primary reference.
All data were managed by using the Review Manager Software version 5.2 (RevMan 2012).

Assessment of risk of bias in included studies

Two review authors independently evaluated each study for risk of bias using the criteria recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* for the domains of sequence generation; allocation concealment; blinding of health professionals, participants, and outcome assessors; incomplete outcome data; selective outcome reporting; and other potential threats to validity (Higgins 2011d). Each domain was judged as having a low, high or unclear risk of bias. We compared the judgements and resolved any inconsistencies in the assessments.

Sequence generation for randomisation

We assessed randomisation as being at low risk of bias if the procedure for sequence generation was explicitly described and was considered likely to produce comparable groups. Examples of suitable methods include computer-generated random numbers, a random numbers table, and coin tossing. If no description was given, we contacted the study authors, and if no response was received, we made a judgment of unclear risk of bias. With regard to our inclusion criteria for this review, if a response suggested that a study was not randomised, we excluded it. If the study used a predictable allocation (e.g. simple alternation, date of birth, hospital admission number) it was rated as being at high risk of bias for this domain.

Allocation concealment

We assessed concealment of treatment allocation as being at low risk of bias if the procedure was explicitly described and was considered likely to ensure that intervention allocations could not have been foreseen in advance of, or during, enrolment. Examples of suitable methods include centralised randomisation, numbered or coded containers, and sealed, opaque envelopes. Procedures with a high risk of bias include alternation and references to case record numbers or dates of birth. If no description was given, we contacted study authors; if no response was received, we made a judgment of unclear risk. If allocation was not concealed, we made a judgment of high risk of bias for this domain.

Blinding of health professionals, participants, and outcome assessors

In this context, surgeons are not usually blinded to the surgical procedure and associated elements (e.g. type of implant). We assessed the risk of bias associated with blinding of health professionals and participants primarily on the basis of the likelihood that such blinding was sufficient to ensure that caregivers and women had no knowledge of which intervention had been received.

Even if the surgeon could not be blinded, it is possible that the healthcare professionals who followed participants after the procedure could have been blinded, and contact between other caregivers and the surgeon could have been avoided. Other blinding techniques that we evaluated were those in which participants were instructed that they should not tell outcome assessors the surgery received.

For each included study we described the methods used, if any, to blind the outcome assessor from knowledge of which intervention a participant received. We judged studies to be at low risk of bias if the outcome assessors were blinded, or if we ascertained that lack of blinding may not have affected the results. If authors stated that blinding was not possible because of the nature of the intervention, we judged the study to be at high risk of bias because it is possible that lack of blinding influenced the results. Blinding of health professionals was signalled if reported.

If no description was given, we contacted study authors, and if no response was received, we made a judgment of unclear risk.

Incomplete outcome data

Incomplete outcome data included attrition, exclusions, and missing data.

We made a judgement of low risk of bias if participants included in the analysis were exactly those who had been randomly assigned into the trial, and if missing outcome data were balanced in numbers across intervention groups, with similar reasons for missing data across groups, or if no outcome data were missing. We made a judgement of low risk of bias if, for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk was not enough to have a clinically relevant impact on the intervention effect estimate; and for continuous outcome data, when plausible effect size (difference in means or standardised difference in means) among missing outcomes was not enough to have a clinically relevant impact on observed effect size; or if missing data had been imputed using appropriate methods.

We made a judgement of high risk of bias for any of the following: when reasons for missing outcome data were likely to be related to the true outcome, with imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, when the proportion of missing outcomes compared with observed event risk was enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, when plausible effect size (difference in means or standardised difference in means) among missing outcomes was enough to induce clinically relevant bias in observed effect size; and when 'as-treated' analysis was done with a substantial departure of the intervention received from that assigned at randomisation, with a potentially inappropriate application of simple imputation.

We made a judgement of unclear (uncertain risk of bias) when reporting of attrition/exclusions was insufficient to permit judgment of low or high risk of bias, or when the study did not address this outcome, and also, when the numbers randomly assigned into intervention and control groups were not clearly reported.

Selective outcome reporting

We assessed reporting of outcomes as being at low risk of bias when all study outcomes declared in the Methods section were reported in the Results. We also evaluated whether different reports of the study were available, including protocols, and examined them to ensure that no suggestion of selective outcome reporting was made. If no description was given, we contacted study authors, and if no response was received, we made a judgment of unclear risk of bias. If evidence suggested selective reporting, we made a judgment of high risk of bias for this domain.

Other potential threats to validity

We assessed other threats to validity as being at low risk of bias if the study appeared to be free of other sources of bias, such as being stopped early because of a data-dependent process or having a baseline imbalance between the groups. Examples that may pose a risk of bias could include sources of sponsorship or funding.
When the risk of bias was unclear from published information, we attempted to contact study authors for clarification. If a response was not forthcoming, we assessed studies as being at unclear risk of bias for this domain.
The review authors were not blinded to the titles of journals or the identities of study authors, as they are familiar with the field. When the two review authors scored items differently, they attempted to establish agreement by discussion. A third review author resolved any persisting disagreement.

Grading the evidence

The overall quality of evidence was assessed using the GRADE approach (Guyatt 2008). The GRADE approach appraises the quality of a body of evidence based on the extent to which one can be confident that an estimate of effect or association reflects the item being assessed. Randomised trials start as high-quality evidence but may be downgraded because of risk of bias (methodological quality), indirectness of evidence, unexplained heterogeneity, imprecision (sparse data), and publication bias. We determined the overall quality of the evidence for each outcome after considering each of these factors and graded our confidence in the results as follows.

- High: further research is very unlikely to change our confidence in the estimate of effect.
- Moderate: further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
- Low: further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
- Very low: any estimate of effect is very uncertain.

Measures of treatment effect

Dichotomous outcomes

We reported dichotomous outcomes (e.g. presence/absence of infection) as risk ratios (RRs) with 95% confidence intervals (CIs). For comparisons with zero events we used odds ratios (OR). For future review updates, using control event risks from the included trials, the number needed to treat for an additional beneficial outcome (NNTB) and the associated 95% confidence interval will be calculated for statistically significant dichotomous outcomes. Also, for unwanted effects (eg, adverse events), the NNTB will become the number needed to treat for an additional harmful outcome (NNTH) and will be calculated in the same way.

Ordinal outcomes

When outcome data were provided on an ordinal scale (e.g. for severity of capsular contracture: minimal, moderate, severe), we selected a threshold based on the definition of clinically significant contracture and converted these data into a dichotomous form. When it was not possible to split ordinal data into dichotomous outcomes to meet our a priori definition, we assigned a numeric score to each category and analysed the results as continuous data.

Continuous outcomes

We calculated mean differences (MDs) of change scores when all studies used the same measurement scale. When studies used different scales, we calculated the standardised mean differences (SMDs), using Hedges' g. When necessary, we calculated effect estimates from P values, t statistics analysis of variance (ANOVA) tables, or other statistics (Higgins 2011b).
For this analysis, we used, according to need, either change scores or final values without combining them.

Unit of analysis issues

We had considered that the unit of analysis needed to be the individual participant instead of number of breasts.
For each included study, we determined whether the unit of analysis was appropriate for the unit of randomisation and the design of each study (i.e. whether the number of observations matched the number of units randomly assigned). In the case of inclusion of cluster randomised trials, we planned to use the intraclass correlation coefficient (ICC) to convert trials to their effective sample size before incorporating them into the meta-analysis, according to the recommendation in the *Cochrane Handbook for Systematic Review of Interventions* (Higgins 2011c). When the ICC was not provided, we planned to use values for ICCs available in the published literature (Campbell 2000). We did not find any cluster randomised trials.

Studies with multiple treatment arms

In the primary analysis, we planned to combine results across all eligible intervention arms and to compare them with combined

results across all eligible control arms (alternative surgical procedure), making single, pair-wise comparisons. When such a strategy would prevent investigation of potential sources of heterogeneity, we planned to analyse each surgical procedure separately (against a common control group) but dividing the sample size for common comparator arms proportionately across each comparison (Higgins 2011c). This simple approach allows the use of standard software (including RevMan 2012) and prevents inappropriate double-counting of individuals. We did not perform meta-analyses because the studies used very different comparison arms.

Dealing with missing data

When data were missing, we contacted the corresponding authors of included studies to request any unreported data. For all outcomes in all studies, we carried out analyses as far as possible on an intention-to-treat basis (i.e. we attempted to include all participants randomly assigned to each group in the analyses), and we analysed all participants in the groups to which they were allocated, regardless of whether they received the allocated intervention. For continuous data that were missing, we estimated standard deviations from other available data such as standard errors, or we imputed them using the methods suggested in Higgins 2011c. We made no assumptions about loss to follow-up for continuous data, and we based analyses on those participants completing the trial. If a discrepancy was noted between the number randomly assigned and the number analysed in each treatment group, we calculated and reported the percentage lost to follow-up in each group. When it was not possible to obtain missing data, we recorded this fact on the data collection form and reported it in the 'Risk of bias' table; we discussed the extent to which the missing data could alter the results/conclusions of the review.

Assessment of heterogeneity

We considered both clinical and statistical heterogeneity. When studies appeared similar in terms of the level of participants, intervention type, and outcome type, we planned to pool the data in a meta-analysis.

We assessed heterogeneity of effect sizes using the I^2 statistic and the Chi^2 statistic (Higgins 2003).

I^2 indicates the percentage of variability due to between-study (or inter-study) variability as opposed to within-study (or intra-study) variability.

We interpreted I^2 as suggested in Higgins 2011a.

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

We also evaluated the confidence interval for I^2.

The significance level of the Chi^2 statistic was set at $P < 0.10$ because of the low statistical power of the test.

Assessment of reporting biases

We planned to use a funnel plot to explore reporting bias if there were at least 10 trials for our primary outcome (Egger 1997; Macaskill 2001). Asymmetry in the funnel plot of trial size against treatment effect would be an indicator of this bias. We planned to undertake a linear regression approach as described by Egger 1997 to determine funnel plot asymmetry in the presence of at least 10 trials for the outcome. In this review, we included only five trials, did not perform meta-analysis, and so a funnel plot was not used.

Data synthesis

We planned to combine results unless diversity (surgical and/or statistical heterogeneity) suggested that combining them was unreasonable. If both a continuous outcome and a dichotomous outcome were available for an outcome, we included only the dichotomous outcome (i.e. risk ratio (RR)) in the primary analysis. We planned to summarise capsular contracture rates using risk differences if these events were found to be rare (i.e. less than 10%). If some studies reported an outcome as a continuous measure and others used a dichotomous measure for the same construct, we planned to convert results for the former from the continuous measure to a dichotomous measure, provided that we could assume a positive/negative threshold based on the definition of clinically significant contracture (otherwise, we planned to carry out two separate analyses). If outcomes were reported at different time points that exceeded one year, we planned to pool data for each point and to combine these with data from other trials at similar time points. This would lead to an estimate of the onset and persistence of treatment effect, at least over the time points available for the combination of data. A decision regarding the time points to be included in the final analysis were made by consensus after the data had been collected.

We planned to use inverse variance methods, with the variance including between-study variation (i.e. DerSimonian 1986 random-effects model) to combine results across the studies because a certain degree of heterogeneity was expected. If high statistically heterogeneity was found we planned: 1) to redo the analysis using the homogenous subgroup (only if a clear and compelling reason to exclude the heterogeneous data could be found); and 2) to abandon statistical combination of the trials in favour of providing a narrative review of the literature.

We planned to carry out statistical analysis using Review Manager software (RevMan 2012) according to the recommendations of the*Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). However, because the included studies were composed of very heterogeneous comparisons, we did not perform meta-analysis and provided a narrative description of the results.

The GRADE approach was used to assess the quality of the evidence for the main outcomes. The main outcomes assessed were capsular contracture, patient satisfaction, reintervention and short-term complications. We created five Summary of Findings

tables (one for each comparison) using GRADEproGDT.

Subgroup analysis and investigation of heterogeneity

We planned to do subgroup analyses to explore effect size differences, as follows.

- Trials at low risk of bias versus trials at high risk of bias (allocation concealment versus lack of allocation concealment, blinding versus lack of blinding).
- One- versus two-stage reconstruction.
- Radiotherapy-treated participants versus non-radiotherapy-treated participants.
- Reconstruction after breast cancer treatment versus reconstruction after risk-reducing procedures.
- Early breast cancer versus locally advanced breast cancer.

We planned to use the 'test for interaction' to identify differences between subgroups. We planned to use meta-regression (in the presence of adequate numbers of trials) to determine the influence of different factors on the effect estimate.
Subgroup analysis was not performed because only five studies were included and meta-analysis was not performed.

Sensitivity analysis

We planned to conduct sensitivity analyses to determine whether our findings were sensitive to restricting the analyses to studies judged to be at low risk of bias for generation of allocation sequence and for allocation concealment. We planned to explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analyses. In addition, we planned to assess the sensitivity of findings to any imputed data by calculating the treatment effect while including and excluding imputed data to see whether this altered the outcome of the analysis. We planned to investigate the effects of dropouts and exclusions by conducting worst-case versus best-case scenario analyses.
Sensitivity analysis was not performed because we described the results narratively only.

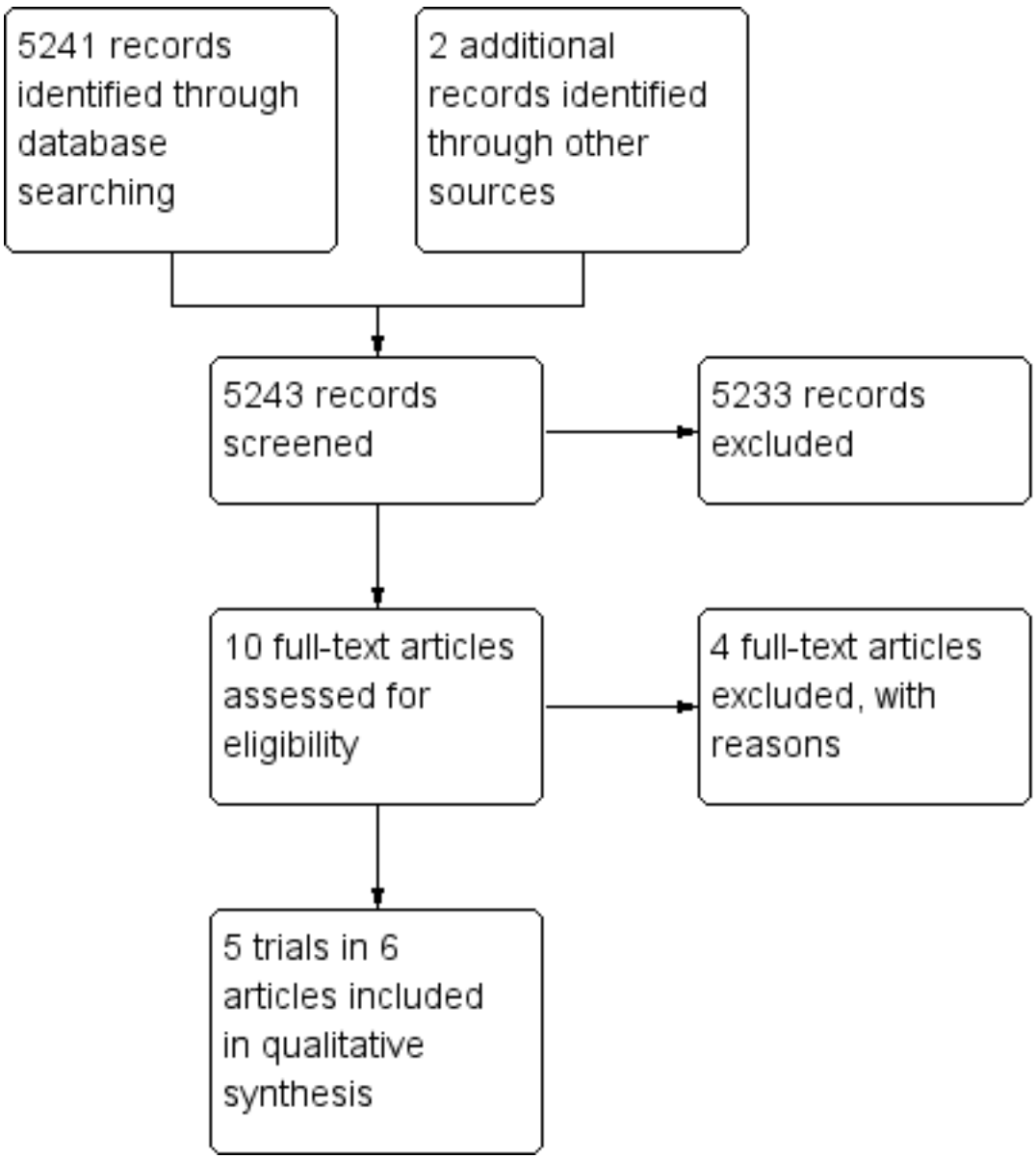
RESULTS

Description of studies

Results of the search

The search was conducted in July 2015. After removal of duplicates, we found 5241 records from the following databases: EMBASE (2725), MEDLINE (2082), Cochrane Central Register of Controlled Trials (CENTRAL) (140), Cochrane Breast Cancer Group Specialised Register (110), the World Health Organisation's International Clinical Trials Registry Platform (WHO ICTRP) (75) and ClinicalTrials.gov (109).
We also performed a search across references of published studies, and found two other reports.
After screening the titles and abstracts, we identified 10 potentially eligible articles. We sought the full texts for the 10 articles. We excluded four studies because they did not meet the inclusion criteria (Benediktsson 2006; Hammerstad 1996; Macadam 2010; Macadam 2013) (see 'Characteristics of excluded studies' table).
Five trials with six reports contributed to this review (Benediktsson 2000; Eriksen 2012; Gahm 2010; Gylbert 1990; Thuesen 1995).
A flow diagram summarising the study selection process is shown in Figure 1.

Figure 1. Study flow diagram.



Included studies

We included four trials that compared different types of implants for breast reconstruction after surgery for breast cancer (Benediktsson 2000; Eriksen 2012; Gylbert 1990; Thuesen 1995), and one trial that followed risk-reduction procedures (Gahm 2010).

The five trials included a total of 202 female participants, with a mean of 40 women in each trial.

All trials were conducted in Northern Europe (Sweden and Denmark).

Summaries of the five trials are given below. All the studies reported submuscular placement of the implant following the mastectomy except for Benediktsson 2000 which used subcutaneous implant positioning. For further details, see the Characteristics of included studies tables.

Benediktsson 2000 included 41 women (mean age 55 years) having modified radical mastectomies (MRM) with immediate reconstruction (IR) and compared subcutaneous positioning of textured PVP-hydrogel-filled implants versus subcutaneous positioning of textured saline-filled implants. Follow-up assessment for the primary outcome (capsular contracture) was at 12 months.

Eriksen 2012 randomised 70 women, 40 of whom were included in this analysis (mean age 50 years). This trial compared MRM with IR using submuscular positioning of textured round variable volume Becker implants versus MRM and two-stage reconstruction with submuscular positioning of textured crescent-shaped expanders, later replaced by textured silicone-filled fixed volume implants. Mean follow-up assessment for the primary outcome (quality of life) was three and a half years.

Gylbert 1990 included 65 women (mean age 49 years) and compared MRM with IR using submuscular positioning of smooth silicone-filled implants versus MRM with IR using submuscular positioning of smooth saline-filled implants. Mean follow-up assessment for the primary outcome (capsular contracture) was six years.

Thuesen 1995 included 20 women (mean age 50 years) and compared MRM with IR using submuscular positioning of textured silicone-filled implants versus MRM with IR using submuscular positioning of smooth silicone-filled implants. Mean follow-up assessment for the primary outcome (capsular contracture) was three years.

Gahm 2010 included 36 women (mean age 38 years) and compared bilateral prophylactic mastectomies with IR using sub-muscular positioning of textured anatomically-shaped permanent expander implants (saline-filled) versus bilateral prophylactic mastectomies with IR using sub-muscular positioning of textured round permanent expander implants (saline-filled). Mean follow-up assessment for the primary outcome was 30 months.

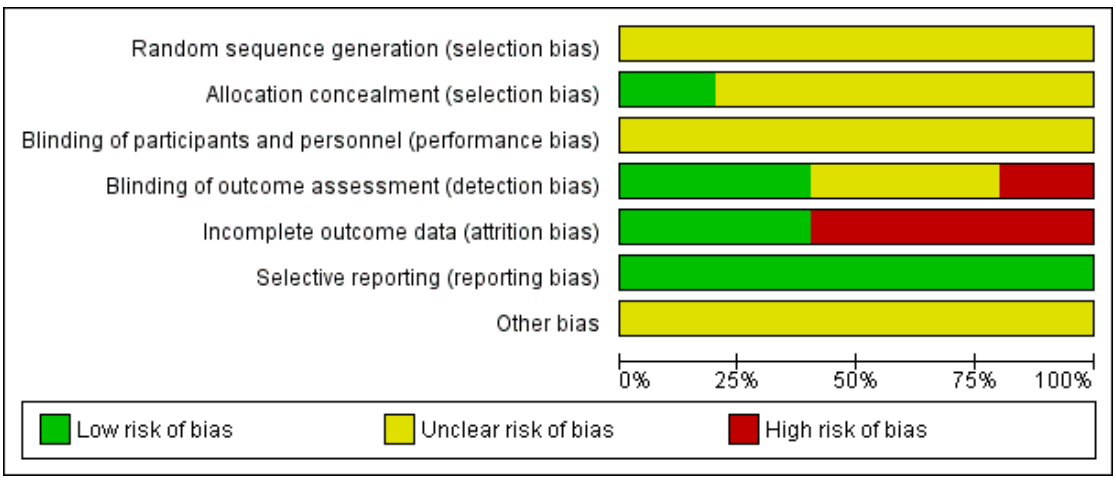
Excluded studies

We excluded four studies because they were not RCTs (Benediktsson 2006; Hammerstad 1996; Macadam 2010; Macadam 2013). See Characteristics of excluded studies.

Risk of bias in included studies

Summaries of our risk of bias assessment of the included studies are presented in Figure 2.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

None of the trials gave details about their method of random sequence generation and allocation concealment; so we considered them to be at unclear risk of bias. Only Eriksen 2012 reported a valid allocation concealment strategy.

Blinding

Due to the surgical nature of the intervention, the operators could not be blinded to the type of implant used.

None of the studies reported information about blinding of the participants.

Two studies did not report any information about the blinding of outcome assessors and were judged to be at unclear risk of bias (Benediktsson 2000; Thuesen 1995). One study reported that there was an independent outcome assessor who was unaware of the implant used (Gylbert 1990), but the investigation could not be labelled as strictly blinded, as experienced surgeons could easily detect the difference between a saline- and a silicone-filled implant, so we rated it as being at high risk of bias. Gahm 2010 and Eriksen 2012 used a blinded expert panel of assessors to evaluate standardised photographs of each breast and we rated them as being at low risk of bias for this domain.

Incomplete outcome data

None of the trials reported their method of analysis (intention-to-treat or by protocol). Considering the significant percentage of losses to follow-up and women excluded from the analysis for various reasons, we judged that three studies were at high risk of bias (Eriksen 2012; Gahm 2010; Gylbert 1990). We judged two studies to be at low risk of bias: Benediktsson 2000 because women excluded from the analysis were few, the reasons were reported and were balanced between groups; and Thuesen 1995 because women were all included in the follow-up.

Selective reporting

Published trial registration information or protocols were not available for any of the five trials. However, all the outcomes that were listed in the Methods sections were reported in the Results sections, so we judged all the trials to be at low risk of bias for this domain.

Other potential sources of bias

Two studies reported that they had no competing interests (Eriksen 2012; Gahm 2010); the other studies did not report information of this kind. The source of financial support was reported in three studies (Benediktsson 2000; Eriksen 2012; Gahm 2010), and was provided by research foundations with no involvement in the study. The other studies did not report any information. Baseline characteristics considered in the included trials were mostly balanced between treatment groups but the number of covariates explored was limited. We judged all the studies to be at unclear risk of bias for this domain.

Effects of interventions

See: **Summary of findings for the main comparison** Textured versus smooth implants for reconstructive breast surgery; **Summary of findings 2** Silicone-filled versus saline-filled implants for reconstructive breast surgery; **Summary of findings 3** PVP-hydrogel-filled versus saline-filled implants for reconstructive breast surgery; **Summary of findings 4** Anatomical versus round implants for reconstructive breast surgery; **Summary of findings 5** Variable- versus fixed-volume implants for reconstructive breast surgery

Capsular contracture*rate and severity*

Four studies considered capsular contracture (Benediktsson 2000; Gahm 2010; Gylbert 1990; Thuesen 1995). When the Baker grade classes were reported, we dichotomised the outcome and considered Baker classes 3 and 4 as indicating severe contracture, and Baker classes 1 and 2 as acceptable.

Implant envelope surfaces: textured versus smooth implants

In Thuesen 1995 no significant difference in capsular contracture was found between textured versus smooth implants groups (RR 0.82, 95% CI 0.14 to 4.71; 20 participants; Analysis 1.1). Baker class 3 or 4 was found in two out of 11 women in the textured implants group versus two out of nine women in the smooth implants group.

Implant filler material: silicone-filled versus saline-filled implants

Gylbert 1990 reported significantly more severe capsular contracture with a RR of 3.25 (95% CI 1.24 to 8.51; 60 participants; Analysis 1.2), in women with silicone-filled compared to saline-filled implants. Severe capsular contracture (class 3 or 4) was found in 17/34 (50%) of women who had silicone-filled breast implants, compared with 4/26 (16%) of women who had saline-filled implants.

Implant filler material: PVP-hydrogel-filled implants versus saline-filled implants

In Benediktsson 2000 no significant difference in severe capsular contracture rate was found between women with PVP-hydrogel-filled implants and women with saline-filled implants (RR 3.50, 95% CI 0.83 to 14.83; 40 participants; Analysis 1.3). Seven out of 20 women who had PVP-hydrogel-filled implants reported a Baker class 3 or 4 compared with two out of 20 women who had saline-filled implants. No significant difference in applanation tonometry was observed between groups.

Implant shape: anatomical versus round implants

Gahm 2010 reported a non significant difference in severe capsular contracture (Baker class not specified) for women with anatomical versus round implants (RR 2.0, 95% CI 0.20 to 20.15; 36 participants; Analysis 1.4). Two out of 18 women developed severe capsular contracture in the anatomical implants group compared to one out of 18 women in the round implants group.

Implant volume: variable- versus fixed-volume implants

No study examined this outcome for this comparison.

Brands: different implant manufacturing companies

No study made this comparison.

Implant generation: fifth versus previous generations of silicone implants

No study made this comparison.

Participant-reported outcomes: postoperative quality of life or satisfaction level

Three studies considered participant-reported outcomes (Eriksen 2012; Gahm 2010; Gylbert 1990).

Implant envelope surfaces: textured versus smooth implants

No study examined this outcome for this comparison.

Implant filler material: silicone-filled versus saline-filled implants

Gylbert 1990 reported no significant differences concerning tenderness of the reconstruction area, palpable wrinkling and sound emanating from the implants in 58 women. Women with silicone-filled implants were significantly less satisfied with the consistency of the reconstructed breast when compared to women with saline-filled implants (RR 0.60, 95% CI 0.41 to 0.88; 58 participants; Analysis 2.1). A slightly higher number of women in the saline group reported a decrease in size during the five years of follow-up compared to women in the silicone-filled implant group (RR 0.55, 95% CI 0.24 to 1.27; 58 participants; Analysis 2.2).

Implant filler material: PVP-hydrogel-filled versus saline-filled implants

No study examined this outcome for this comparison.

Implant shape: anatomical versus round implants

Gahm 2010 reported patients' satisfaction level data in 26 out of 36 women (12 in the anatomical implant group and 14 in the round implant group). Six women from the anatomical group and four women from the round group had their implant exchanged and these women were excluded from the aesthetic evaluation. Satisfaction was expressed using a scale ranging from 1 ("not at all [satisfied]") to 7 ("absolutely [satisfied]"), with a score of 4 considered "acceptable". The median overall aesthetic result score was 6 for both the anatomical and round implant group.

Implant volume: variable- versus fixed-volume implants

Eriksen 2012 reported a higher level of patient satisfaction (rated from 1 to 6, with 1 being very bad and 6 being very good) in the two-stage fixed-volume implants group compared with the one-stage variable-volume implants group; overall aesthetic result (MD -1.10, 95% CI -1.59 to -0.61; 40 participants; Analysis 2.3). Eighty per cent of the women in the two-stage fixed-volume implants group said that the results corresponded "very much" to their expectations versus 20% in the one-stage variable-volume implants group (RR 0.25, 95% CI 0.10 to 0.62; 40 participants; Analysis 2.4). All women would definitely recommend their operation to another woman in the two-stage fixed-volume implants group, compared to 75% in the one-stage variable-volume implants group (RR 0.76, 95% CI 0.58 to 0.98, 40 participants; Analysis 2.5). No significant differences in quality of life were found between the two groups (raw data were not reported).

Brands: different implant manufacturing companies

No study dealt with this comparison.

Implant generation: fifth versus previous generations

No study dealt with this comparison.

Implant rupture and filler material migration rates

No studies reported data on this outcome.

Short-term complication rates (implant infection, seroma, haematoma, implant extrusion, and implant malpositioning)

Two studies reported data on this outcome (Benediktsson 2000; Gahm 2010).

Implant envelope surfaces: textured versus smooth implants

No study examined this outcome for this comparison.

Implant filler material: silicone-filled versus saline-filled implants

No study examined this outcome for this comparison.

Implant filler material: PVP-hydrogel-filled implants versus saline-filled implants

Benediktsson 2000 reported no significant difference in implant infection rates when comparing PVP-hydrogel-filled implants to saline-filled implants (RR 2.10, 95% CI 0.21 to 21.39; 41 participants; Analysis 3.1).

Implant shape: anatomical versus round implants

Gahm 2010 reported no significant difference in short-term complications when comparing anatomical versus round implants (RR 2.00, 95% CI 0.42 to 9.58; 36 participants; Analysis 3.2).

Implant volume: variable- versus fixed-volume implants

No study examined this outcome for this comparison.

Brands: different implant manufacturing companies

No study dealt with this comparison.

Implant generation: fifth versus previous generations

No study dealt with this comparison.

Reintervention and long-term complication rates: late seroma double-capsule formation and chronic pain

Four studies reported data about reinterventions required because of various complications or insufficiently aesthetic results (Eriksen 2012; Gahm 2010; Gylbert 1990; Thuesen 1995).

Implant envelope surfaces: textured versus smooth implants

Thuesen 1995 reported that two women in each group had to be reoperated on because of Baker 3 capsular contracture (RR 0.82, 95% CI 0.14 to 4.71; 20 participants; Analysis 4.1).

Implant filler material: silicone-filled versus saline-filled implants

Gylbert 1990 reported that no silicone-filled implants were removed for any reason while six women had their saline-filled implants removed because of deflation (OR 0.08, 95% CI 0.01 to 0.43; 60 participants; Analysis 4.2).

Implant filler material: PVP-hydrogel-filled implants versus saline-filled implants

No study examined these outcomes for this comparison.

Implant shape: anatomical versus round implants

Gahm 2010 reported no significant difference in reintervention rates when comparing anatomically-shaped versus round implants (RR 1.50, 95% CI 0.51 to 4.43; 36 participants; Analysis 4.3).

Implant volume: variable- versus fixed-volume implants

Eriksen 2012 reported significantly fewer reinterventions in women undergoing two-stage reconstructions with fixed-volume implants compared to one-stage variable-volume reconstructions (RR 7.00, 95% CI 1.82 to 26.89; 40 participants; Analysis 4.4).

Brands: different implant manufacturing companies

No study dealt with this comparison.

Implant generation: fifth versus previous generations

No study dealt with this comparison.

Cosmetic outcomes not reported by participants

Two studies reported data about cosmetic outcomes evaluated by an independent panel through digital standardised photographs (Eriksen 2012; Gahm 2010).

Implant envelope surfaces: textured versus smooth implants

No study examined this outcome for this comparison.

Implant filler material: silicone-filled versus saline-filled implants

TNo study examined this outcome for this comparison.

Implant filler material: PVP-hydrogel-filled implants versus saline-filled implants

No study examined this outcome for this comparison.

Implant shape: anatomical versus round implants

In Gahm 2010, the median outcome scores for each category did not show any significant difference between the two implant groups: the median overall aesthetic result was 4.88 and 4.50 for anatomically-shaped and round implants, respectively (analysis not performed). Agreement between the outcome assessors was moderate (mean kappa values between 0.36 and 0.57).

Implant volume: variable- versus fixed-volume implants

In Eriksen 2012, expert panels awarded the highest scores for overall aesthetic result to the two-stage fixed-volume implants group compared to the one-stage variable-volume implants group (expert panel: MD -0.70, 95% CI -1.17 to -0.23; 40 participants; Analysis 5.1), but this was not the case for the lay panel (MD -0.30, 95% CI -0.84 to 0.24; 40 participants; Analysis 5.2).

Brands: different implant manufacturing companies

No study dealt with this comparison.

Implant generation: fifth versus previous generations

No study dealt with this comparison.

ADDITIONAL SUMMARY OF FINDINGS [Explanation]

Silicone-filled versus saline-filled implants for reconstructive breast surgery

Patient or population: women having reconstructive breast surgery
Settings: cancer centre
Intervention: silicone-filled implants
Comparison: saline-filled implants

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Saline-filled	Silicone-filled				
Capsular contracture Number of women with capsular contracture Follow-up: mean 6 years	**Study population**		**RR 3.25** (1.24 to 8.51)	60 (1 study)	⊕◯◯◯ **very low**[1,2]	
	154 per 1000	**500 per 1000** (191 to 1000)				
	Moderate					
	154 per 1000	**500 per 1000** (191 to 1000)				
Patient satisfaction for consistency Number of women satisfied Follow-up: mean 6 years	**Study population**		**RR 0.60** (0.41 to 0.88)	58 (1 study)	⊕◯◯◯ **very low**[1,2]	
	833 per 1000	**500 per 1000** (342 to 733)				
	Moderate					
	833 per 1000	**500 per 1000** (342 to 733)				

Reintervention Number of women with reintervention Follow-up: mean 6 years	**Study population**		**OR 0.08** (0.01 to 0.43)	60 (1 study)	⊕○○○ **very low**[1,2]
	231 per 1000	**23 per 1000** (3 to 114)			
	Moderate				
	231 per 1000	**23 per 1000** (3 to 114)			

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (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; **RR:** risk ratio; **OR:** odds ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]We downgraded twice based on unclear risk of selection and performance bias, high risk of attrition and detection bias.
[2]We downgraded once on the basis that there was only one study with 65 participants. Different numbers of participants have been analysed for each outcome.

PVP-hydrogel-filled versus saline-filled implants for reconstructive breast surgery

Patient or population: women having reconstructive breast surgery
Settings: cancer centre
Intervention: PVP-hydrogel-filled implants
Comparison: saline-filled implants

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Saline-filled implants	PVP-hydrogel-filled implants				
Capsular contracture Number of women with capsular contracture Follow-up: mean 12 months	**Study population**		**RR 3.50** (0.83 to 14.83)	40 (1 study)	⊕◯◯◯ **very low**[1,2]	
	100 per 1000	**350 per 1000** (83 to 1000)				
	Moderate					
	100 per 1000	**350 per 1000** (83 to 1000)				
Short-term complications Number of women with at least one short-term complication Follow-up: mean 12 months	**Study population**		**RR 2.10** (0.21 to 21.39)	41 (1 study)	⊕◯◯◯ **very low**[1,2]	
	48 per 1000	**100 per 1000** (10 to 1000)				
	Moderate					
	48 per 1000	**100 per 1000** (10 to 1000)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (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; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]We downgraded twice based on unclear risk of selection, performance and detection bias.
[2]We downgraded once on the basis that there was only one study with 41 women.

Anatomical versus round implants for reconstructive breast surgery

Patient or population: women having reconstructive breast surgery
Settings: cancer centre
Intervention: anatomical implants
Comparison: round implants

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Round implants	Anatomical implants				
Capsular contracture Number of women with capsular contracture Follow-up: mean 30 months	**Study population**		**RR 2.00** (0.2 to 20.15)	36 (1 study)	⊕○○○ **very low**[1,2]	
	56 per 1000	**111 per 1000** (11 to 1000)				
	Moderate					
	56 per 1000	**111 per 1000** (11 to 1000)				
Short-term complications Number of women with at least one short-term complication Follow-up: mean 30 months	**Study population**		**RR 2.00** (0.42 to 9.58)	36 (1 study)	⊕○○○ **very low**[1,2]	
	111 per 1000	**222 per 1000** (47 to 1000)				
	Moderate					
	111 per 1000	**222 per 1000** (47 to 1000)				

Reintervention Number of women with reintervention Follow-up: mean 30 months	**Study population**		**RR 1.50** (0.51 to 4.43)	36 (1 study)	⊕◯◯◯ **very low**[1,2]
	222 per 1000	**333 per 1000** (113 to 984)			
	Moderate				
	222 per 1000	**333 per 1000** (113 to 984)			

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (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; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]We downgraded twice based on unclear risk of selection and performance bias and high risk of attrition bias.
[2]We downgraded once on the basis that there was only one study with 36 participants.

Variable- versus fixed-volume implants for reconstructive breast surgery

Patient or population: women having reconstructive breast surgery
Settings: cancer centres
Intervention: one-stage variable-volume implants
Control: two-stage fixed-volume implants

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Two-stage fixed volume implants	One-stage variable volume implants				
Patient satisfaction: correspondence to expectations Number of women reporting correspondence with expectation Follow-up: mean 3.5 years	**Study population**		**RR 0.25** (0.10 to 0.62)	40 (1 study)	⊕◯◯◯ **very low**[1,2]	
	800 per 1000	**200 per 1000** (80 to 496)				
	Moderate					
	800 per 1000	**200 per 1000** (80 to 496)				
Patient satisfaction: aesthetic results Rating scale from 1 to 6 (1 being very bad and 6 being very good) Follow-up: mean 3.5 years	The mean patient satisfaction, aesthetic results in the control group was **4.2 score**	The mean patient satisfaction, aesthetic results in the intervention groups was **1.1 lower** (1.59 lower to 0.61)		40 (1 study)	⊕◯◯◯ **very low**[1,2]	

Reintervention Number of women with re intervention Follow-up: mean 3.5 years	**Study population**		**RR 7.0** (1.82 to 26.89)	40 (1 study)	⊕◯◯◯ **very low**[1,2]
	100 per 1000	**700 per 1000** (182 to 1000)			
	Moderate				
	100 per 1000	**700 per 1000** (182 to 1000)			

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (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; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]We downgraded twice based on unclear risk of selection and performance bias and high risk of attrition bias.
[2]We downgraded once on the basis that there was only one study with 40 participants.

DISCUSSION

Summary of main results

The aim of this review was to assess the effects of different types of breast implants on capsular contracture, surgical short- and long-term complications, cosmetic outcomes, postoperative satisfaction level and quality of life in women who have undergone reconstructive breast surgery after mastectomy. We included five heterogeneous randomised controlled trials, involving a total of 202 women who underwent mastectomy for breast cancer (four studies) or as a risk-reducing procedure (one study). Trials reported data about different comparisons: texturised silicone versus smooth silicone implants, silicone versus saline-filled implants, poly(N-vinyl-2-pyrrolidone) (PVP)-hydrogel- versus saline-filled implants, anatomically versus round implants (in the risk-reducing setting), and one-stage variable-volume implants versus two-stage fixed-volume implants. The majority of studies explored submuscular placements of the implants instead of subcutaneous placements. Only two of these comparisons showed a significant difference for some of the outcomes considered. The comparison of silicone- versus saline-filled implants favoured saline-filled implants for some outcomes, specifically, fewer severe capsular contractures, and a higher number of women satisfied with their reconstructed breast, however, there was a lower reintervention rate in the silicone-filled group. In addition, the comparison of one-stage variable-volume implants versus two-stage fixed-volume implants favoured the fixed-volume implants with significantly higher satisfaction levels in women and significantly lower reintervention rates. The better results in terms of satisfaction level and reintervention rates in the fixed-volume group could be attributable to the different surgical approach (a two-stage surgical process instead of a one-stage process). The small number of women included in each study did not allow us to draw any definitive conclusions about all the considered outcomes.

Overall completeness and applicability of evidence

Despite breast cancer surgery being one of the most commonly performed procedures in surgical oncology, the number of women involved in randomised controlled trials investigating implant breast reconstruction is extremely low. This 'under-randomisation' is common in surgical research, and is caused by the challenges of conducting surgical trials, and also by surgeons' rejection and limited understanding of trial methodology (Potter 2014).

Outcomes reported in each study were often reported using scales that were not standardised. The patient-reported outcome measures (PROMs) were often reported according to study-specific, non-validated scales. The recent definition of a core outcome set in reconstructive breast surgery will allow researchers to choose appropriate and standardised outcomes when conducting clinical trials, thus eliminating reporting bias and facilitating data synthesis (Potter 2015).

Only two studies included women who underwent postmastectomy radiotherapy (PMRT). The effect of PMRT on reconstructive surgical outcomes cannot be predicted, and no conclusions can be drawn for women who have had radiotherapy.

Even though only one trial included women undergoing breast reconstruction following risk-reducing mastectomy (Gahm 2010), we can assume that the overall clinical results could be applied to this group of women as well, given that the surgical technique is the same in women with operable breast cancer. However, other outcomes such as PROMs might differ. Women undergoing risk-reducing mastectomy are significantly different in terms of their psychological background and we suppose that the PROMs could not be extended from women with operable cancer to women who undergo a risk-reducing mastectomy.

Although all of the included trials have been conducted in a well-defined area of Northern Europe, we do not have major concerns related to the generalisability of the clinical outcome results. The baseline characteristics of the women seem to represent the general breast cancer population well. Concerns exist around the representativeness of the aesthetic outcomes, meaning that there might be plausible differences in aesthetic appreciation of beauty across different cultural settings.

Quality of the evidence

All of the included trials had methodological shortcomings that placed them at high or unclear risk of bias for most risk of bias domains.

Based on the high risk of bias of the included trials and the imprecision of the results, we conclude that the evidence for all primary outcomes is of very low quality, which means that we are very uncertain about the reported results.

Moreover the quality of the reporting was very low: none of the studies followed the CONSORT 2010 guidelines, which often led to difficulty when interpreting the results. Although we are not surprised that our surgical colleagues did not follow the reporting guidelines strictly (Ahmed 2013), we were disappointed by the number of inaccuracies and incompleteness of data.

Potential biases in the review process

We conducted extensive searches and were careful and systematic in our screening processes, but it is possible that we may have failed to identify studies, especially those that are unpublished. We were unsuccessful in our attempts to obtain further information and data on the included trials from the trial authors. The poor reporting of included trials may have affected our data extraction

process, and frequently led to an assessment of unclear for the risk of bias.

Agreements and disagreements with other studies or reviews

To our knowledge there have been no previous systematic reviews directly comparing different types of implants in breast reconstructive surgery. Other systematic reviews have compared the effects of different types of implants on capsular contracture in breast augmentation (Wong 2006), suggesting that textured implants reduce the risks of early capsular contracture compared with smooth implants.

The assessment of cosmetic outcomes and PROMs after breast reconstructive surgery have been investigated in systematic reviews and they have highlighted the lack of consistency and methodological rigour in outcome reporting (Chen 2010; Lee 2009; Potter 2011a; Potter 2011b).

Evidence about patient satisfaction and health-related quality of life following breast reconstruction (using the BREAST-Q questionnaire) derived from small observational studies that compared different types of implants showed higher satisfaction with silicone-filled implants than with saline-filled implants (Macadam 2010). Further observational research showed no differences in terms of satisfaction with outcomes when anatomical silicone-filled implants were compared with round implants (Macadam 2013).

The largest amount of evidence about breast implants comes from the US Food and Drug Administration (FDA) postapproval studies that are referred to as core studies. These prospective observational studies investigated complication profiles for the FDA-approved implant manufacturers, which the FDA required after the temporary moratorium on silicone breast implants in the USA between 1992 and 2006. These studies now provide results with 10 year follow-up (FDA). The Allergan core study (Maxwell 2012) and the Mentor core study (Hammond 2012) reported 10.7% and 10.1% capsular contracture rates, respectively, after primary breast reconstruction at six years of follow-up. Most of the studies included in our review reported significantly higher capsular contracture rates when compared with data derived from these core studies, which was probably due to the use of older generation implants and obsolete surgical techniques in the included RCTs.

AUTHORS' CONCLUSIONS

Implications for practice

The available evidence is too weak to draw conclusions about which is the best implant to use in breast reconstructive surgery. The current trend in breast reconstructive surgery is driven by studies with a low level of evidence. This issue should be discussed when informing women about the benefits, risks and complications of surgery for breast reconstruction. Recommendations regarding options for different implant-based breast reconstruction seem to be based on expert opinions or anecdotic experience at best. The lack of high-quality evidence and the underlying uncertainty about different types of approaches might reduce the outcomes expected by women from this type of treatment and reduce their willingness to resort to surgery.

Implications for research

Considering the high incidence of breast cancer, its strong social implications and the low quality of evidence available on breast reconstructive surgery, new high-quality randomised controlled trials that include a higher number of women and that compare different types of implants appear to be needed deeply. Women with breast cancer are cared for and monitored in specialist breast units, often connected to national or international networks (e.g. European Society of Breast Cancer Specialists - EUSOMA) to ensure quality of service. Parts of these breast cancer centres could easily be connected in a research network to take on this surgical research challenge. From this perspective, a large multicentre clinical trial is possible.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Benediktsson 2000

Methods	Randomised controlled trial
Participants	41 women (mean age 55 years) undergoing modified radical mastectomy and immediate one-stage reconstruction for breast cancer
Interventions	20 women undergoing subcutaneous positioning of textured PVP-hydrogel-filled implant versus 21 women undergoing subcutaneous positioning of textured saline-filled implant
Outcomes	Capsular contracture rate and severity at 1 year (Baker's classification (Palmer 1992) considering significant capsular contracture as Baker $\geq$ 2 or differences in applanation tonometry operative/postoperative ratio of $\leq$ 0.75); data on 40 patients Short-term complications: infection rate; data on 41 patients
Notes	Follow-up: 12 months Source of support: this research was supported by the Ryan Hill Research Foundation and by the Serafimer Hospital Foundation Competing interests: information not reported 41 women randomised; 40 women analysed for capsular contracture; 41 women analysed for short-term complications

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not reported
Allocation concealment (selection bias)	Unclear risk	Method not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Information not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Expert panel (3 surgeons and 1 nurse). Information about blinding of the panel not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Two of the Misti Gold implants and one of the saline-filled type were removed because of infection."; few dropouts, balanced between groups
Selective reporting (reporting bias)	Low risk	No protocol available, but outcomes listed in the Methods section were reported in the Results

Benediktsson 2000 (*Continued*)

Other bias	Unclear risk	Insufficient baseline characteristics; competing interests not reported

Eriksen 2012

Methods	Randomised controlled trial
Participants	70 women (mean age 50 years) undergoing modified radical mastectomy and immediate one- or two-stage reconstruction for breast cancer Note: a total of 40 participants were included in the analysis
Interventions	35 one-stage submuscular positioning of textured round permanent expander Becker implant versus 35 two-stage submuscular positioning of textured crescent-shaped expanders, later replaced by textured silicone-filled implants Note: 20 participants from each group were included in the analysis
Outcomes	Participant-reported outcomes: quality of life (QoL; evaluated preoperatively and postoperatively with SF-36) and satisfaction level using a study-specific questionnaire (scale ranging from 1, 'very bad' to 6, 'very good') about aesthetic outcomes (shape, size, scars, nipple-areola complex, symmetry and overall aesthetic results), expectations reached (scale from 1 to 6, being 1-2 'not at all', 3-4 'some' and 5-6 'very much') and recommendations to other women (scale from 1 to 6, being 1-2 'never', 3-4 'probably', 5-6 'definitely'); Reintervention rate; Cosmetic outcome not reported by participants: two panels composed of experts (6 plastic surgeons) and lay people (6 people with no connection to the medical profession) scored the categories (upper pole fullness, projection, ptosis, inframammary fold, symmetry, shape, volume, scars, nipple-areola complex and overall aesthetic results) from unidentified photographs using a scale from 1 ('very bad') to 6 ('very good')
Notes	Follow-up: median 3.5 years (range 1.5 to 5 years) Financial support: this study was supported by grants from the Swedish Breast Cancer Association Competing interests: "The authors have no financial interest to declare in relation to the content of this article." 70 women randomised; 40 women analysed for each outcome

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not reported
Allocation concealment (selection bias)	Low risk	Quote: "Presealed envelopes ordered from the state pharmacy company"

Eriksen 2012 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Information not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Two panels, 6 experts (plastic surgeons) and 6 lay people, evaluated standard photographic documentation
Incomplete outcome data (attrition bias) All outcomes	High risk	43% dropout after randomisation, balanced between groups and no intention-to-treat analyses
Selective reporting (reporting bias)	Low risk	No protocol available, but outcomes listed in the Methods section were reported in the Rsesults
Other bias	Unclear risk	Insufficient baseline characteristics;

Gahm 2010

Methods	Randomised controlled trial
Participants	36 women (mean age 38 years) undergoing bilateral risk-reducing mastectomy and immediate reconstruction
Interventions	18 women undergoing bilateral one-stage submuscular positioning of textured anatomically-shaped permanent expander implants versus 18 women undergoing bilateral submuscular positioning of textured round permanent expander implants
Outcomes	Capsular contracture rate and severity at 30 months (Baker classification) Participant-reported outcomes: satisfaction level (study-specific questionnaire addressing aesthetic and lifestyle issues with a scale ranging from 1 ('not at all [satisfied]') to 7 ('absolutely [satisfied]')); Short-term complications: infection, haematoma, implant malpositioning; Long-term complications: pain; Reintervention rate; Cosmetic outcome not reported by participants: a blinded expert panel (3 plastic surgeons not involved in the surgical procedure and a specially educated nurse) evaluated 4 standardised digital photographs of each breast. The assessed categories for each single breast were: appearance of the upper pole, projection, inframammary fold, natural look, implant edges and shape. Appearance of cleavage, symmetry in shape, scar tissue and overall aesthetic results were assessed for both breasts. Each category was scored using a scale ranging from 1 ('not at all [satisfied]') to 7 ('absolutely [satisfied]') and a mean was calculated as a final score for each category
Notes	Follow-up: average 30 months (range 24 to 49 months) Financial support: this research was supported in part by grants from the Capio Research Foundation. The Capio Research Foundation had no involvement in the study design, materials and methods, or manuscript process Competing interests: none of the authors of this article had a conflict of interest to declare

Gahm 2010 (*Continued*)

	36 women randomised; 36 women analysed for each outcome

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not reported
Allocation concealment (selection bias)	Unclear risk	Method not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Information not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded expert panel (3 plastic surgeons not involved in the surgical procedures and a nurse specially educated in patient undergoing breast reconstruction) that evaluated 4 standardised digital photographs of each breast
Incomplete outcome data (attrition bias) All outcomes	High risk	Significant exclusion from analyses (10 participants excluded from the aesthetic evaluation because they received a reimplant)
Selective reporting (reporting bias)	Low risk	No protocol available, but outcomes listed in the Methods section were reported in the Results
Other bias	Unclear risk	Insufficient baseline characteristics provided. Information about competing interests not reported

Gylbert 1990

Methods	Randomised controlled trial
Participants	65 women (mean age 49 years) undergoing modified radical mastectomy and immediate reconstruction for breast cancer
Interventions	32 women had submuscular positioning of smooth silicone-filled implants versus 33 women who had submuscular positioning of smooth saline-filled implants
Outcomes	Capsular contracture rate and severity at 6 years of follow-up according to the breast augmentation classification (BAC) which is a modification of Baker's classification (Gylbert 1989); data on 60 patients; Participant-reported outcomes: satisfaction level (study-specific questionnaire about consistency of the breast, tenderness of the reconstruction areas, wrinkles on the prosthesis, sound from the prosthesis, changes in size of reconstructed breast); data on 58 patients; Long-term complications: implant deflation; data on 58 patients; Reintervention rate; data on 60 patients.

Gylbert 1990 (*Continued*)

Notes	Follow-up: mean 6 years (range: 5.5 to 7.5 years) Financial support: information not reported Competing interests: information not reported 65 women randomised; 60 women analysed for capsular contracture and reintervention rate; 58 women analysed for participant-reported outcomes and long-term complications

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not reported
Allocation concealment (selection bias)	Unclear risk	Method not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Information not reported
Blinding of outcome assessment (detection bias) All outcomes	High risk	Independent plastic surgeon unaware of the type of prosthesis used for reconstruction, but not strictly blinded because in 80% of patients the doctors could tell what type of implant had been employed
Incomplete outcome data (attrition bias) All outcomes	High risk	28% drop out rate, reasons reported, unbalanced across groups
Selective reporting (reporting bias)	Low risk	No protocol available, but outcomes listed in the Methods section were reported in the Results
Other bias	Unclear risk	Insufficient baseline characteristics. No information reported about competing interests or funding

Thuesen 1995

Methods	Randomised controlled trial
Participants	20 women (mean age 50 years) undergoing modified radical mastectomy for breast cancer and immediate reconstruction
Interventions	11 two-stage reconstructions with submuscular positioning of expander later replaced by textured silicone-filled implants versus 9 two-stage reconstructions with submuscular positioning of expander later replaced by smooth silicone-filled implants
Outcomes	Capsular contracture rate and severity at a median follow-up of 3 years (Baker classification); Participant-reported outcomes: satisfaction level (data not extractable); Reintervention rate

Thuesen 1995 (*Continued*)

Notes	Follow-up: mean 3 years (range 1 to 4 years) Financial support: information not reported Competing interests: information not reported 20 women randomised; 20 women analysed for each outcome

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not reported
Allocation concealment (selection bias)	Unclear risk	Method not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Information not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Information not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss at follow-up
Selective reporting (reporting bias)	Low risk	No protocol available, but outcomes listed in the Methods section were reported in the Results
Other bias	Unclear risk	Insufficient baseline characteristics. No information reported about competing interests or funding

BAC: breast augmentation classification
PVP-hydrogel: poly(N-vinyl-2-pyrrolidone) hydrogel
QoL: quality of life

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

Study	Reason for exclusion
Benediktsson 2006	Not an RCT study design
Hammerstad 1996	Not an RCT study design
Macadam 2010	Not an RCT study design

(*Continued*)

Macadam 2013	Not an RCT study design

DATA AND ANALYSES

Comparison 1. Capsular contracture

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Textured vs smooth implants	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2 Silicone-filled vs saline-filled implants	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3 PVP-hydrogel-filled vs saline-filled implants	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4 Anatomical vs round implants	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Comparison 2. Patient satisfaction

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Silicone-filled vs saline-filled implants: patient satisfaction for consistency	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2 Silicone-filled vs saline-filled implants: size decrease	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3 Variable- vs fixed-volume implants: patient satisfaction, aesthetic results	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4 Variable- vs fixed-volume implants: patient satisfaction, correspondence to expectations	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5 Variable- vs fixed-volume implants: patient satisfaction, recommending to others	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Comparison 3. Short-term complications

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 PVP-hydrogel-filled vs saline-filled implants	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2 Anatomical vs round implants	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Comparison 4. Reintervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Textured vs smooth implants	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2 Silicone-filled vs saline-filled implants	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Totals not selected
3 Anatomical vs round implants	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4 Variable-volume vs fixed-volume implants	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Comparison 5. Cosmetic outcomes not reported by participants

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Variable- vs fixed-volume implants: cosmetic outcomes according to expert panel	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Variable- vs fixed-volume implants: cosmetic outcomes according to lay panel	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1 Capsular contracture, Outcome 1 Textured vs smooth implants.

Review: Different types of implants for reconstructive breast surgery

Comparison: 1 Capsular contracture

Outcome: 1 Textured vs smooth implants

Study or subgroup	Textured implants n/N	Smooth implants n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Thuesen 1995	2/11	2/9		0.82 [0.14, 4.71]

Analysis 1.2. Comparison 1 Capsular contracture, Outcome 2 Silicone-filled vs saline-filled implants.

Review: Different types of implants for reconstructive breast surgery

Comparison: 1 Capsular contracture

Outcome: 2 Silicone-filled vs saline-filled implants

Study or subgroup	Silicone-filled n/N	Saline-filled n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Gylbert 1990	17/34	4/26		3.25 [1.24, 8.51]

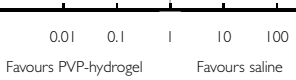
Analysis 1.3. Comparison 1 Capsular contracture, Outcome 3 PVP-hydrogel-filled vs saline-filled implants.

Review: Different types of implants for reconstructive breast surgery

Comparison: 1 Capsular contracture

Outcome: 3 PVP-hydrogel-filled vs saline-filled implants

Study or subgroup	PVP-hydrogel-filled n/N	Saline-filled n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Benediktsson 2000	7/20	2/20		3.50 [0.83, 14.83]



Analysis 1.4. Comparison 1 Capsular contracture, Outcome 4 Anatomical vs round implants.

Review: Different types of implants for reconstructive breast surgery

Comparison: 1 Capsular contracture

Outcome: 4 Anatomical vs round implants

Study or subgroup	Anatomical implant n/N	Round implant n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Gahm 2010	2/18	1/18		2.00 [0.20, 20.15]

Analysis 2.1. Comparison 2 Patient satisfaction, Outcome 1 Silicone-filled vs saline-filled implants: patient satisfaction for consistency.

Review: Different types of implants for reconstructive breast surgery

Comparison: 2 Patient satisfaction

Outcome: 1 Silicone-filled vs saline-filled implants: patient satisfaction for consistency

Study or subgroup	Silicone-filled n/N	Saline-filled n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Gylbert 1990	17/34	20/24		0.60 [0.41, 0.88]

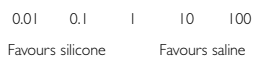
Analysis 2.2. Comparison 2 Patient satisfaction, Outcome 2 Silicone-filled vs saline-filled implants: size decrease.

Review: Different types of implants for reconstructive breast surgery

Comparison: 2 Patient satisfaction

Outcome: 2 Silicone-filled vs saline-filled implants: size decrease

Study or subgroup	Silicone-filled n/N	Saline-filled n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Gylbert 1990	7/34	9/24		0.55 [0.24, 1.27]



Analysis 2.3. Comparison 2 Patient satisfaction, Outcome 3 Variable- vs fixed-volume implants: patient satisfaction, aesthetic results.

Review: Different types of implants for reconstructive breast surgery

Comparison: 2 Patient satisfaction

Outcome: 3 Variable- vs fixed-volume implants: patient satisfaction, aesthetic results

Study or subgroup	Variable-volume N	Mean(SD)	Fixed-volume N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Eriksen 2012	20	4.2 (1)	20	5.3 (0.5)		-1.10 [-1.59, -0.61]

Analysis 2.4. Comparison 2 Patient satisfaction, Outcome 4 Variable- vs fixed-volume implants: patient satisfaction, correspondence to expectations.

Review: Different types of implants for reconstructive breast surgery

Comparison: 2 Patient satisfaction

Outcome: 4 Variable- vs fixed-volume implants: patient satisfaction, correspondence to expectations

Study or subgroup	Variable-volume n/N	Fixed-volume n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Eriksen 2012	4/20	16/20		0.25 [0.10, 0.62]

Analysis 2.5. Comparison 2 Patient satisfaction, Outcome 5 Variable- vs fixed-volume implants: patient satisfaction, recommending to others.

Review: Different types of implants for reconstructive breast surgery

Comparison: 2 Patient satisfaction

Outcome: 5 Variable- vs fixed-volume implants: patient satisfaction, recommending to others

Study or subgroup	Variable-volume n/N	Fixed-volume n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Eriksen 2012	15/20	20/20		0.76 [0.58, 0.98]

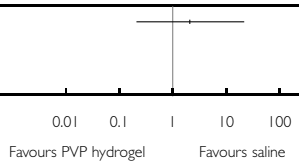
Analysis 3.1. Comparison 3 Short-term complications, Outcome 1 PVP-hydrogel-filled vs saline-filled implants.

Review: Different types of implants for reconstructive breast surgery

Comparison: 3 Short-term complications

Outcome: 1 PVP-hydrogel-filled vs saline-filled implants

Study or subgroup	PVP-hydrogel-filled n/N	saline-filled n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Benediktsson 2000	2/20	1/21		2.10 [0.21, 21.39]



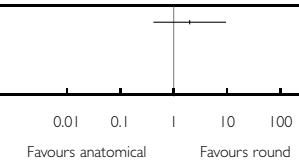
Analysis 3.2. Comparison 3 Short-term complications, Outcome 2 Anatomical vs round implants.

Review: Different types of implants for reconstructive breast surgery

Comparison: 3 Short-term complications

Outcome: 2 Anatomical vs round implants

Study or subgroup	Anatomical implant n/N	Round implant n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Gahm 2010	4/18	2/18		2.00 [0.42, 9.58]



Analysis 4.1. Comparison 4 Reintervention, Outcome 1 Textured vs smooth implants.

Review: Different types of implants for reconstructive breast surgery

Comparison: 4 Reintervention

Outcome: 1 Textured vs smooth implants

Study or subgroup	Textured implants n/N	Smooth implants n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Thuesen 1995	2/11	2/9		0.82 [0.14, 4.71]

Analysis 4.2. Comparison 4 Reintervention, Outcome 2 Silicone-filled vs saline-filled implants.

Review: Different types of implants for reconstructive breast surgery

Comparison: 4 Reintervention

Outcome: 2 Silicone-filled vs saline-filled implants

Study or subgroup	Silicone-filled n/N	Saline-filled n/N	Peto Odds Ratio Peto,Fixed,95% CI	Peto Odds Ratio Peto,Fixed,95% CI
Gylbert 1990	0/34	6/26		0.08 [0.01, 0.43]

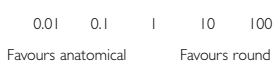
Analysis 4.3. Comparison 4 Reintervention, Outcome 3 Anatomical vs round implants.

Review: Different types of implants for reconstructive breast surgery

Comparison: 4 Reintervention

Outcome: 3 Anatomical vs round implants

Study or subgroup	Anatomical implant n/N	Round implant n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Gahm 2010	6/18	4/18		1.50 [0.51, 4.43]



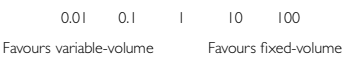
Analysis 4.4. Comparison 4 Reintervention, Outcome 4 Variable-volume vs fixed-volume implants.

Review: Different types of implants for reconstructive breast surgery

Comparison: 4 Reintervention

Outcome: 4 Variable-volume vs fixed-volume implants

Study or subgroup	Variable-volume n/N	Fixed-volume n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Eriksen 2012	14/20	2/20		7.00 [1.82, 26.89]



Analysis 5.1. Comparison 5 Cosmetic outcomes not reported by participants, Outcome 1 Variable- vs fixed-volume implants: cosmetic outcomes according to expert panel.

Review: Different types of implants for reconstructive breast surgery

Comparison: 5 Cosmetic outcomes not reported by participants

Outcome: 1 Variable- vs fixed-volume implants: cosmetic outcomes according to expert panel

Study or subgroup	Variable-volume		Fixed-volume		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI	IV,Fixed,95% CI
Eriksen 2012	20	4 (0.87)	20	4.7 (0.62)		-0.70 [-1.17, -0.23]

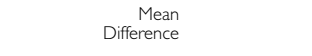
Analysis 5.2. Comparison 5 Cosmetic outcomes not reported by participants, Outcome 2 Variable- vs fixed-volume implants: cosmetic outcomes according to lay panel.

Review: Different types of implants for reconstructive breast surgery

Comparison: 5 Cosmetic outcomes not reported by participants

Outcome: 2 Variable- vs fixed-volume implants: cosmetic outcomes according to lay panel

Study or subgroup	Variable-volume		Fixed-volume		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI	IV,Fixed,95% CI
Eriksen 2012	20	3.2 (1.02)	20	3.5 (0.7)		-0.30 [-0.84, 0.24]



APPENDICES

Appendix 1. MEDLINE

#	Searches
1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	randomized.ab.
4	placebo.ab.
5	drug therapy.fs.
6	randomly.ab.
7	trial.ab.
8	groups.ab.
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10	cohort studies/
11	longitudinal studies/
12	follow-up studies/
13	prospective studies/
14	retrospective studies/
15	cohort.ti,ab.
16	longitudinal.ti,ab.
17	prospective.ti,ab.
18	retrospective.ti,ab.
19	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20	Case-Control Studies/
21	Control Groups/
22	Matched-Pair Analysis/

(*Continued*)

23	retrospective studies/
24	((case* adj5 control*) or (case adj3 comparison*) or control group*).ti,ab
25	20 or 21 or 22 or 23 or 24
26	exp Breast Neoplasms/
27	(breast adj6 cancer$).mp.
28	(breast adj6 neoplasm$).mp.
29	(breast adj6 carcinoma$).mp.
30	(breast adj6 tumour$).mp.
31	(breast adj6 tumor$).mp.
32	26 or 27 or 28 or 29 or 30 or 31
33	exp Mammaplasty/
34	exp Reconstructive Surgical Procedures/
35	exp Surgery, Plastic/
36	exp *Breast Implants/
37	mammoplasty.mp.
38	mammaplasty.mp.
39	mammoplast*.mp.
40	mammaplast*.mp.
41	breast reconstruction$.mp.
42	breast reconstructive surger$.mp.
43	implant-based breast reconstruction$.mp.
44	exp Silicone Gels/
45	silicone breast implant$.mp.
46	saline breast implant$.mp.

(*Continued*)

47	saline-filled breast implant$.mp.
48	texturi#ed implant.mp.
49	smooth implant.mp.
50	implant envelope surface.mp.
51	variable volume implant.mp.
52	fixed volume implant.mp.
53	texturi#ation.mp.
54	(implant$ adj5 breast reconstruction).mp.
55	(implant$ adj5 breast reconstructive surger$).mp.
56	(silicone adj5 breast implant$).mp.
57	(saline adj5 breast implant$).mp.
58	(texturi#ed adj5 implant$).mp.
59	(smooth adj5 implant$).mp.
60	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 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59
61	32 and 60
62	autologous tissue breast reconstruction.mp.
63	autologous tissue-based breast reconstruction.mp.
64	(autologous tissue adj5 breast reconstruct*).mp.
65	autologous reconstruction.mp.
66	Breast reconstruction with autologous tissue.mp.
67	autogenous tissue breast reconstruction.mp.
68	(autogenous tissues adj5 breast reconstruct*).mp.
69	autologous fat graft*.mp.

(*Continued*)

70	(autologous adj5 fat graft*).mp.
71	autogenous fat graft*.mp.
72	(autogenous adj5 fat graft*).mp.
73	autologous fat transplant*.mp.
74	(autologous adj5 fat transplant*).mp.
75	autogenous fat transplant*.mp.
76	(autogenous adj5 fat transplant*).mp.
77	latissimus dorsi musculocutaneous flap.mp.
78	Transverse Rectus Abdominis Myocutaneous flap.mp.
79	TRAM flap.mp.
80	DIEP.mp.
81	SIEP.mp.
82	TRAM.mp.
83	deep inferior epigastric perforator flap.mp.
84	62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83
85	61 not 84
86	Animals/ not Humans/
87	85 not 86
88	9 and 87
89	19 and 87
90	25 and 87

Appendix 2. EMBASE

1. **random*** OR **factorial*** OR **crossover*** OR **cross** NEXT/1 **over*** OR **placebo*** OR (**doubl*** AND **blind***) OR (**singl*** AND **blind***) OR **assign***AND **allocat*** OR **volunteer*** OR **'crossover procedure'**/exp OR **'double blind procedure'**/exp OR **'randomized controlled trial'**/exp OR**'single blind procedure'**/exp
2. (**cohort** OR **concurrent** OR **incidence** OR **longitudinal** OR **followup** OR **'follow up'** OR **prospective** OR **retrospective**) NEXT/1 (**analys***OR **design*** OR **evaluation*** OR **research** OR **stud*** OR **survey*** OR **trial***) OR **'prospective method'**/exp OR **'retrospective study'**/syn
3. **'case control study'**/syn OR (**'case control'** OR **'case base'** OR **'case matched'** OR **retrospective**) NEXT/3 (**analys*** OR **design*** OR**evaluation*** OR **research** OR **stud*** OR **survey*** OR **trial***)
4. **'breast'**/exp OR **'breast disease'**/exp AND **'neoplasm'**/exp OR **'breast tumor'**/exp OR (**breast*** NEAR/5 **neoplas***):ab,ti OR (**breast*** NEAR/5**cancer***):ab,ti OR (**breast*** NEAR/5 **carcin***):ab,ti OR (**breast*** NEAR/5 **tumo***):ab,ti OR (**breast*** NEAR/5 **metasta***):ab,ti OR (**breast*** NEAR/5**malig***):ab,ti
5. **'breast reconstruction'**/exp OR **'breast reconstruction'**
6. **'mammaplasty'**/exp OR **mammaplasty**
7. **'mammoplasty'**/exp OR **mammoplasty**
8. **'plastic surgery'**/exp OR **'plastic surgery'**
9. **'breast implant'**/exp OR **'breast implant'**
10. **'breast reconstructive surgery'**
11. **'implant-based breast reconstruction'**
12. **'silicone gel'**/exp OR **'silicone gel'**
13. **'silicone breast implant'**/exp OR **'silicone breast implant'**
14. **'saline breast implant'**
15. **'saline-filled breast implant'**
16. **'texturized implant'**
17. **'texturised implant'**
18. **'smooth implant'**
19. **'implant envelope surface'**
20. **'variable volume implant'**
21. **'fixed volume implant'**
22. **texturization**
23. **texturisation**
24. **implant** NEAR/5 **'breast reconstruction'**
25. **implant** NEAR/5 **'breast reconstructive surgery'**
26. **silicone** NEAR/5 **'breast implant'**
27. **saline** NEAR/5 **'breast implant'**
28. **texturized** NEAR/5 **implant**
29. **texturised** NEAR/5 **implant**
30. **smooth** NEAR/5 **implant**
31. **#5** OR **#6** OR **#7** OR **#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**
32. **#4** AND **#31**
33. **'autologous tissue breast reconstruction'**
34. **'autologous tissue-based breast reconstruction'**
35. **'autologous tissue'** NEAR/5 **'breast reconstruction'**
36. **'autologous reconstruction'**
37. **'breast reconstruction with autologous tissue'**
38. **'autogenous tissue breast reconstruction'**
39. **'autogenous tissues'** NEAR/5 **'breast reconstruction'**
40. **'autologous fat graft'**
41. **autologous** NEAR/5 **'fat graft'**
42. **'autogenous fat graft'**
43. **autogenous** NEAR/5 **'fat graft'**

44. **'autologous fat transplant'**
45. **autologous** NEAR/5 **'fat transplant'**
46. **'autogenous fat transplant'**
47. **autogenous** NEAR/5 **'fat transplant'**
48. **'latissimus dorsi musculocutaneous flap'**/exp OR **'latissimus dorsi musculocutaneous flap'**
49. **'transverse rectus abdominis myocutaneous flap'**/exp OR **'transverse rectus abdominis myocutaneous flap'**
50. **'tram flap'**/exp OR **'tram flap'**
51. **diep**
52. **siep**
53. **'deep inferior epigastric perforator flap'**/exp OR **'deep inferior epigastric perforator flap'**
54. **#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** OR **#48** OR **#49** OR**#50** OR **#51** OR **#52** OR **#53** OR **#54**
55. **#32** NOT **#55**
56. **#56** NOT ([animals]/lim NOT [humans]/lim)
57. **#1** AND **#57**
58. **#2** AND **#57**
59. **#3** AND **#57**

Appendix 3. CENTRAL

#1 MeSH descriptor: [Breast Neoplasms] explode all trees
#2 breast cancer* or breast neoplasm*
#3 #1 or #2
#4 MeSH descriptor: [Mammaplasty] explode all trees
#5 MeSH descriptor: [Reconstructive Surgical Procedures] explode all trees
#6 MeSH descriptor: [Surgery, Plastic] explode all trees
#7 MeSH descriptor: [Prostheses and Implants] explode all trees
#8 mammoplast*
#9 mammaplast*
#10 breast reconstruction*
#11 breast reconstructive surger*
#12 implant-based breast reconstruction*
#13 MeSH descriptor: [Breast Implants] explode all trees
#14 MeSH descriptor: [Silicone Gels] explode all trees
#15 silicone breast implant*
#16 saline breast implant*
#17 saline-filled breast implant*
#18 texturised implant or texturized implant
#19 smooth implant
#20 implant envelope surface
#21 variable volume implant
#22 fixed volume implant
#23 implant and breast reconstruct*
#24 #4 or #5 or #6 or #7 or #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
#25 #3 and #24

Appendix 4. WHO ICTRP search portal

Basic Searches:
1. Different types of implants for reconstructive breast surgery
2. breast cancer AND implant
3. reconstructive breast surgery AND implant
4. breast reconstruction and implant
5. mammoplasty AND breast implant
6. mammaplasty AND breast implant

Advanced Searches:
1. Title: Different types of implants for reconstructive breast surgery
Recruitment Status: ALL
2. Condition: breast cancer
Intervention: implant AND (reconstructive breast surgery OR breast reconstruction)
Recruitment Status: ALL
3. Condition: breast cancer
Intervention: (silicone OR saline) AND breast implant
Recruitment Status: ALL
4. Condition: breast cancer
Intervention: implant-based breast reconstruction OR mammoplasty OR mammaplasty
Recruitment Status: ALL

Appendix 5. Clinicaltrials.gov

Basic Searches:
1. Different types of implants for reconstructive breast surgery
2. breast cancer AND implant
3. reconstructive breast surgery AND implant
4. breast reconstruction and implant
5. mammoplasty AND breast implant
6. mammaplasty AND breast implant

Advanced Searches:
1. Title: Different types of implants for reconstructive breast surgery
Recruitment Status: All Studies
Study Results: All Studies
Study Type: All Studies
Gender: All Studies
2. Condition: breast cancer
Intervention: implant AND (reconstructive breast surgery OR breast reconstruction)
Recruitment Status: All Studies
Study Results: All Studies
Study Type: All Studies
Gender: All Studies
3. Condition: breast cancer
Intervention: (silicone OR saline) AND breast implant
Recruitment Status: All Studies
Study Results: All Studies
Study Type: All Studies
Gender: All Studies
4. Condition: breast cancer
Intervention: implant-based breast reconstruction OR mammoplasty OR mammaplasty
Recruitment Status: All Studies
Study Results: All Studies

Study Type: All Studies
Gender: All Studies

CONTRIBUTIONS OF AUTHORS

Drafting of the protocol: NR, CR, BA, AA

Study selection: NR, CR, LI, MBN

Disagreement resolution: NR, ST, LI

Data analysis: CR, LM, AS, GC

DECLARATIONS OF INTEREST

N Rocco: none known

C Rispoli: none known

L Moja: none known

B Amato: none known

L Iannone: none known

S Testa: none known

A Spano: none known

G Catanuto: none known

A Accurso: none known

MB Nava: none known

SOURCES OF SUPPORT

Internal sources

- No sources of support, Other.

External sources

- No sources of support, Other.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Two comparisons have been added in this review since publication of the protocol:

1. Implant filler material: PVP-hydrogel-filled versus saline-filled implants
2. Implant shape: anatomical versus round.

We used odds ratios to report estimates effect size for one comparison (silicone- versus saline-filled implants for the outcome reintervention) instead of relative risk due to the presence of zero events in one group.

In line with Cochrane conduct standards, the GRADE approach was used to assess the quality of evidence for the outcomes reported. Summary of Findings tables were created using GRADEproGDT software.

INDEX TERMS

Medical Subject Headings (MeSH)

*Mammaplasty; Breast Implants [*classification]; Breast Neoplasms [*surgery]; Hydrogels; Mastectomy; Patient Satisfaction; Prophylactic Surgical Procedures; Prosthesis Failure; Randomized Controlled Trials as Topic; Silicone Gels; Sodium Chloride

MeSH check words

Female; Humans; Middle Aged