Evidence report for Evidence report for pre- vs. subpectoral breast reconstruction after mastectomy

Prepared by EBSCO Health Innovations and EBM Development Department:

Brian S. Alper, MD, MSPH, FAAFP, Vice President

Marty Mayer, DMSc, MS, PA-C, Clinical Evidence Synthesizer

Eric Manheimer, PhD, EBM Editor

Table of Contents

*Note that each *section* of the report also has *section-specific* page numbering at the bottom-right corner of the page. The above page numbers refer to the *report-specific* page number, which appears in bolded and italicized font in the top-right corner of the page.

Evidence report for pre- vs. subpectoral breast reconstruction after mastectomy

Part 1 - Scoping

Prepared by EBSCO Information Services

September 12, 2019

Prepared by EBSCO Health Innovations and EBM Development Department:

Brian S. Alper, MD, MSPH, FAAFP, Vice President

Martin Mayer, DMSc, MS, PA-C, Clinical Evidence Synthesizer

Eric Manheimer, PhD, EBM Editor

Abbreviations

General abbreviations that may appear in this report

CI – confidence interval
CrI – credible interval
HR – hazard ratio
IQR – interquartile range
MA – meta-analysis
MD – mean difference
NA, N/A – not applicable
NR – not reported
OR – odds ratio
RCT – randomized, controlled trial
RR – risk ratio, relative risk
RtR – rate ratio
SMD – standardized mean difference
SR – systematic review
SRMA – systematic review and meta-analysis

Abbreviations specific to this report that may appear in this report

ADM – acellular dermal matrix
IBBR – implant-based breast reconstruction
TE – tissue expander

Note about terminology surrounding reconstructive surgery after mastectomy:

When a woman has a mastectomy and ultimately decides to have reconstructive surgery, she may have reconstructive surgery starting at the time of mastectomy or at some later time (this delay may be due either to an intentional delay in anticipation of needing additional treatment or because the woman wants time to consider whether she wants reconstructive surgery). The standard terminology used to describe this is "immediate" or "delayed" reconstruction. Additionally, reconstructive surgery can occur in one-stage (sometimes also called a "direct-to-implant" approach) or in two-stages (where the insertion of the permanent implant is preceded by insertion of a tissue expander). Although these terms are not used with perfect consistency, one-staged reconstruction is not necessarily the same as immediate reconstruction; for instance, there are immediate two-staged reconstructions.[1,2] Therefore, in this report, we use the phrase "immediate" reconstruction in line with the definition stated at the beginning of this paragraph, and do not consider it to indicate whether a woman undergoes a one-staged or two-staged approach to reconstruction.

Methods

Using an established, structured template that delineates key elements for scoping (i.e., the population, interventions, and key outcomes to consider), we collaboratively agreed with UKSH on the scope of the present evidence report. Scoping was completed on September 16, 2019.

Results – Criteria Selection for Critical Appraisal

Population:

Inclusion criteria

Patients with breast cancer with an indication for mastectomy who wish to have an implant-based immediate surgical reconstruction

Exclusion criteria

Skin involvement (e.g., inflammatory breast cancer or preservation of the skin not possible)

Relative exclusion criteria: planned post-mastectomy radiation, breast radiation in history, severe smoking, severe diabetes, severe overweight.

Intervention and Comparator:

Subpectoral placement of the implant

The comparator is prepectoral placement of the implant.

Prepectoral placement of the implant

The comparator is subpectoral placement of the implant.

Note: Preliminary scoping suggested interest in subpectoral placement + mesh vs. prepectoral placement ± mesh. However, evidence appears very limited for this specific comparison. For instance, in a 2019 systematic review comparing pre- vs. subpectoral implant placement after mastectomy, only 2 of the 16 studies specified use of mesh (titanium-coated poly propylene mesh in Bernini 2015 and sling/mesh in Kanesalingam 2017). The vast majority of the remaining studies used acellular dermal matrices.[3] If subgroup analyses are presented based on use of mesh vs. acellular dermal matrices, we will incorporate those findings into this report; otherwise, we will present results for the comparison of subpectoral vs. prepectoral placement of the implant irrespective of the use of mesh or an acellular dermal matrix.

Outcomes:

Where outcomes will be answered with systematic evidence searches, critical appraisal, and evidence synthesis, we will state the intended approach after we state the outcome(s) of interest for that FAQ (e.g., "The outcome of interest is all-cause mortality. We will obtain effect estimates from systematic reviews and meta-analyses of randomized, controlled trials or from individual trials if systematic reviews do not exist or meta-analysis is not the most appropriate method of synthesis."). Otherwise, where we say: "We will include a description of", we will answer the FAQ with descriptive responses, which do not involve systematic evidence searches, critical appraisal, or evidence synthesis.

FAQ 1: What does the treatment involve?

We will include a description of the treatment or procedure, including length of stay.

FAQ 2: Will the surgery make my breast look and feel natural?

We will include a description of how the breast should look and feel after the surgery, including things like surface density and structure, final breast contour, whether the implant will be apparent, and whether there may be loss of sensation.

FAQ 3: Will the surgery have an effect on my quality of life?

The outcome of interest is quality of life, and we will give preference to quality of life assessed via breast reconstruction-specific modalities that include measures of psychological and sexual well-being after reconstruction (e.g., BREAST-Q), even if these specific domains are not reported as subscales.

Data from randomized, controlled trials are lacking for this comparison. We will obtain estimates from systematic reviews of observational studies.

FAQ 4: Will I need to have another surgery?

The outcome of interest is reoperation.

Data from randomized, controlled trials are lacking for this comparison. We will obtain estimates from systematic reviews of observational studies.

FAQ 5: What are the risks?

The outcomes of interest are implant loss, nipple or skin flap necrosis, hematoma, wound or skin infection, wound dehiscence, "rippling", and capsular contraction.

Data from randomized, controlled trials are lacking for this comparison. We will obtain estimates from systematic reviews of observational studies.

FAQ 6: What are the side effects?

The outcomes of interest are postoperative pain, seroma, and scar formation.

Data from randomized, controlled trials are lacking for this comparison. We will obtain estimates for these outcomes from systematic reviews of observational studies used to answer the above FAQs; if these outcomes are not addressed in those evidence sources, then descriptive responses are acceptable.

FAQ 7: When will I recover?

We will include a description of any restrictions in daily physical activity and time to return to usual activity, including work.

---

[1] Davila AA, Mioton LM, Chow G, Wang E, Merkow RP, Bilimoria KY, Fine N, Kim JY. Immediate two-stage tissue expander breast reconstruction compared with one-stage permanent implant breast reconstruction: a multi-institutional comparison of short-term complications. J Plast Surg Hand Surg. 2013 Oct;47(5):344-9. doi: 10.3109/2000656X.2013.767202. Epub 2013 Apr 3.
[2] Lam TC, Borotkanics R, Hsieh F, Salinas J, Boyages J. Immediate Two-Stage Prosthetic Breast Reconstruction Failure: Radiation Is Not the Only Culprit. Plast Reconstr Surg. 2018 Jun;141(6):1315-1324. doi: 10.1097/PRS.0000000000004358.
[3] Li L, Su Y, Xiu B, Huang X, Chi W, Hou J, Zhang Y, Tian J, Wang J, Wu J. Comparison of prepectoral and subpectoral breast reconstruction after mastectomies: A systematic review and meta analysis. Eur J Surg Oncol. 2019 Sep;45(9):1542-1550. doi: 10.1016/j.ejso.2019.05.015. Epub 2019 May 14.

Evidence report for pre- vs. subpectoral breast reconstruction after mastectomy

Part 4 - Evidence Synthesis

Prepared by EBSCO Information Services

October 2, 2019

Prepared by EBSCO Health Innovations and EBM Development Department:

Brian S. Alper, MD, MSPH, FAAFP, Vice President

Martin Mayer, DMSc, MS, PA-C, Clinical Evidence Synthesizer

Eric Manheimer, PhD, EBM Editor

Methods

General statements about methods

Where evidence is very limited, or the FAQ is scoped as a descriptive response, such that no evidence synthesis or processing is applied, the descriptive summary/-ies will be given.

For each FAQ for which evidence synthesis or processing is considered, the key concepts (results and factors affecting certainty of the results) from the included studies that are most relevant to evidence synthesis will be summarized in Evidence Review Tables. For each outcome, Evidence Synthesis Process tables will then articulate the method selected for evidence synthesis and justification of that method. We will do this for the effect estimate (i.e., answering the question "Is there a difference between the intervention and comparator?") and results will be presented with GRADE-based certainty of evidence ratings related to the certainty of effect estimates. For FAQs which require noncomparative/option-specific responses (i.e., the FAQ is "What will happen with this option?" rather than "How do things change with this option?") the Evidence Synthesis Process tables will be extended to include the method to produce noncomparative responses.

For summary statements representing a plain language summary of evidence appraisal and synthesis

We will include the following 2 items immediately after the summary statement as a parenthetical, regardless of whether they occur in the Summary of Findings section or the individual FAQs in the body of the Evidence Synthesis document:

- our certainty in the summary statement (categorized as High, Moderate, Low, or Very low), and
- the number and type of studies informing the statement, as well as a label for the studies in "[Author] [Year]" format.

If the study informing the summary statement is a systematic review and meta-analysis, then unless there are compelling reasons to proceed in a different manner, we will cite the systematic review and meta-analysis as the source. We will do this even if the result on which our summary statement is based comes from a subset of studies in that systematic review and meta-analysis (e.g., a meta-analysis of 5 out of 10 studies, because only 5 of the 10 reported on the outcome of interest). If EBSCO Information Services conducts its own meta-analysis of studies to inform a summary statement, we will list the individual studies.

For summary statements representing a plain language summary of descriptive sources

Certainty rating and provision of details about contributing studies do not apply. Accordingly, we will not include a parenthetical at the end of the summary statement. However, when descriptive summaries appear in the Summary of Findings section, we will include a general parenthetical citation of the references we consulted. We will place this at the end of the relevant FAQ in the Summary of Findings section. For summary statements occurring in the body of the Evidence Synthesis document, we will provide this general parenthetical citation as part of the longer descriptive summary component that precedes the simplified summary statement.

Statements specific to methods in this report

Although there was interest in presenting subgroup findings – if possible – based on the use of mesh vs. acellular dermal matrices, data were insufficient to permit any such subgroup analysis. As stated in Scoping, we therefore present results for the comparison of pre- vs. subpectoral implant irrespective of the use of mesh or acellular dermal matrix.

Abbreviations

General abbreviations that may appear in this report

CI – confidence interval
CrI – credible interval
HR – hazard ratio
IQR – interquartile range
MA – meta-analysis
MD – mean difference
NA, N/A – not applicable
NR – not reported
OR – odds ratio
RCT – randomized, controlled trial
RR – risk ratio, relative risk
RtR – rate ratio
SMD – standardized mean difference
SR – systematic review
SRMA – systematic review and meta-analysis

Abbreviations specific to this report that may appear in this report

ADM – acellular dermal matrix
IBBR – implant-based breast reconstruction
TE – tissue expander

Results – Summary of Findings

FAQ 1: What does the treatment involve?

The surgery may last from 1 to 6 hours depending on the specific needs of the woman. When a woman gets an implant below her chest muscle (often called a “subpectoral” implant), the surgeon has to cut or stretch the chest muscle. When a woman gets an implant above her chest muscle (often called a “prepectoral” implant), the surgeon does not have to do this, so the surgery may be somewhat shorter. Women may be in the hospital for about 3 days or more if they have the mastectomy and implant surgery are done at the same time. Women may be sent home with tubing coming out of the area where the surgery was done to help the area heal. When the area has healed enough, the tubing will be removed. Some women have the implant surgery done in two parts. In this case, the first part stretches the skin so there is enough to cover the implant, and the second part inserts the implant. When this is done, the second part often takes an hour, and the woman usually will not need to stay in the hospital.

(References consulted for this descriptive summary include: American Cancer Society 2017, American Society of Plastic Surgeons nd, Bernini 2015, Breastcancer.org 2019, Davila 2013, Douglas 2018, Lam 2018, Li 2019, Mayo Clinic 2019, Memorial Sloan Kettering Cancer Center nd, Pittman 2017, Susan G. Komen Foundation 2019, Tutt 2017, and WebMD Medical Reference 2017.)

FAQ 2: Will the surgery make my breast look and feel natural?

Regardless of whether a woman receives the implant above or below the chest muscle:
A woman can expect to lose some feeling in her breast. Although the feeling in her breast may get better over time for some women, it is unlikely to regain completely normal feeling in her breast.

Swelling and bruising is expected for 2 to 3 weeks, and it may take up to 8 weeks to go away completely.

As her breast heals, the shape of her breast often gets better as well.

There will be scarring from where the surgery was done, but this may get better over 1 to 2 years. The scarring is not usually visible during normal daily activities, even if a woman is wearing a bathing suit or low-cut blouse.

With placement of the implant above the chest muscle:
There is a small chance of the implant turning, which can make the breasts look different from each other. In bad cases, the breast with the implant may have an "upside down" appearance, and this may result in needing more surgery.

In about 3 out of 100 women (3%), the breast may feel too hard or have issues with the shape, such as looking too round or having a nipple that is not shaped normally. (Low certainty evidence from a meta-analysis conducted by EBSCO Information Services that included data from 5 cohort studies [Bernini 2015, Chandarana 2018, Chopra 2016, Sbitany 2017, and Sinnott 2018])

More women may be unhappy with rippling (where folds in the implant can be seen or felt) compared to women who have an implant under the chest muscle. (Very low certainty evidence from 1 cohort study [Baker 2018])

With placement of the implant below the chest muscle:

The implant may move upward when the chest muscles are used and back to the normal position when the chest muscles are relaxed. This is often called “animation of the implant” or “dynamic distortion”.

When a woman uses her chest muscles, the muscle fibers may be more visible through the skin, kind of like when a bodybuilder flexes his or her chest muscles. Doing things like pushing something across a counter or pressing yourself up from the ground or the bed use the chest muscles.

The breast may look somewhat less round than if the implant had been placed above the chest muscle

The implant may not position correctly, which can make the breasts look different from each other.

In about 8 out of 100 women (8%), the breast may feel too hard or have issues with the shape, such as looking too round or having a nipple that doesn't have a normal shape. (Low certainty evidence from a meta-analysis conducted by EBSCO Information Services that included data from 5 cohort studies [Bernini 2015, Chandarana 2018, Chopra 2016, Sbitany 2017, and Sinnott 2018])

Fewer women may be unhappy with rippling (where folds in the implant can be seen or felt) compared to women who have an implant above the chest muscle. (Very low certainty evidence from 1 cohort study [Baker 2018])

(References consulted for the descriptive summaries above include: American Cancer Society 2017, American Society of Plastic Surgeons nd, Bernini 2015, Breastcancer.org 2019, Davila 2013, Douglas 2018, Lam 2018, Li 2019, Mayo Clinic 2019, Memorial Sloan Kettering Cancer Center nd, Pittman 2017, Susan G. Komen Foundation 2019, Tutt 2017, and WebMD Medical Reference 2017.)

FAQ 3: Will the surgery have an effect on my quality of life?

Women who have the implant above the chest muscle may have better overall satisfaction and quality of life related to their breast reconstruction than women who have the implant below the chest muscle. However, this is uncertain and the difference may be small. (Very low certainty evidence from 4 cohort studies [Baker 2018, Bernini 2015, Cattelani 2017, and Walia 2018])

FAQ 4: Will I need to have another surgery?

The placement of the implant does not clearly change a woman’s risk for needing more surgery. (Very low certainty evidence from 1 systematic review and meta-analysis of cohort studies [Li 2019] and 2 of the cohort studies that were included in that systematic review and meta-analysis [Bernini 2015, Chandarana 2018])

FAQ 5: What are the risks?

Risks of getting an implant include:

- infection
- bleeding
- skin over the implant dying and needing to be removed
- the area where the surgery was done opening back up after being closed by the surgeon
- needing to remove the implant

Where the implant is placed does not clearly change these risks. (Very low certainty evidence from 1 systematic review and meta-analysis of cohort studies [Li 2019] and 6 of the cohort studies included in that systematic review and meta-analysis [Bernini 2015, Bettinger 2017, Chandarana 2018, Chopra 2016, Sbitany 2017, Sinnott 2018])

FAQ 6: What are the side effects?

Some women may get a collection of fluid at the area where the surgery was done, but this may be uncommon. Where the implant is placed does not clearly change the chance of this happening. (Very low certainty evidence from 1 systematic review and meta-analysis of cohort studies [Li 2019])

Women may have less pain after surgery if they have the implant above the muscle instead of below the muscle. (Very low certainty evidence from 1 systematic review and meta-analysis of cohort studies [Li 2019])

FAQ 7: When will I recover?

It is normal to feel tired after implant surgery, and this may last for a week or two. Women may need to take 3 to 4 weeks off from work. Women should do any exercises prescribed by the surgical team. They may be advised to avoid activities that put a lot of stress on the body, especially in the area where the surgery was done. This may include avoiding sex for 4 to 6 weeks after implant surgery. It may be possible for women to return to normal activities within 6 weeks of having implant surgery. If the implant surgery is done in two parts, the recovery time for the second part may only take about 2 weeks. When a woman has implant surgery and mastectomy at the same time or close together, it can be hard to tell the difference between recovering from the implant surgery and recovering from the mastectomy. Some women may not feel completely normal until a year or two after mastectomy.

(References consulted for this descriptive summary include: American Cancer Society 2017, American Society of Plastic Surgeons nd, Bernini 2015, Breastcancer.org 2019, Davila 2013, Douglas 2018, Lam 2018, Li 2019, Mayo Clinic 2019, Memorial Sloan Kettering Cancer Center nd, Pittman 2017, Susan G. Komen Foundation 2019, Tutt 2017, and WebMD Medical Reference 2017.)

Search Summary

Number of articles screened and selected

	Screened	Selected*
1st-round (DynaMed)	Not applicable	
2nd-round (Systematic review searches)	4	1
3rd-round (Study tracing)	16	10
4th-round (Original article searches)	Not applicable	
Total	*20*	*11*

* Number shown is after deduplication

	Articles selected for evaluation (Author Year)
Systematic reviews	1 – Li 2019 (systematic review of observational studies)
Randomized, controlled trials	Not applicable (no randomized, controlled trials available for this comparison)
Other article types (e.g., observational studies, guidelines)	10 – Baker 2018, Bernini 2015, Bettinger 2017, Catellani 2017, Chandarana 2018, Chopra 2016, Cox 2018, Sbitany 2017, Sinnott 2018, Walia 2018 (all observational studies obtained from tracing Li 2019)

Results – Synthesis Details

FAQ 1: What does the treatment involve?

One descriptive summary is presented below for efficiency, with delineation of differences where relevant.

Subpectoral or prepectoral placement

Descriptive Summary (pre-synthesis and synthesis efforts not applicable for descriptive summaries)

The population of interest specified in Part 1 Scoping is women seeking immediate reconstruction, but breast reconstruction with an implant can occur during the same time as mastectomy (immediate reconstruction), at a later time (delayed reconstruction), or partially during mastectomy and partially later (delayed-immediate reconstruction). In any of these approaches, it is not uncommon for a woman to need multiple operations for reconstruction. The implant may be placed either in a two-staged approach (with the first stage involving a tissue expander being placed) or in a one-staged approach (which may be called a "direct-to-implant" approach). Sometimes, immediate reconstruction is also called direct-to-implant reconstruction, but there is some inconsistency in terminology, and there are, for instance, two-staged immediate reconstructions. The preferred terminology may therefore separate the notion of immediate, delayed, and immediate-delayed reconstruction from one-stage and two-stage reconstruction. The woman and her surgeon can decide whether a one- or two-staged approach is best for her, but it will also depend on how much skin was removed during the mastectomy.

In subpectoral implant placement (which might also be referred to as "traditional", "submuscular", or "retropectoral" reconstruction/placement), the implant is placed under the pectoralis major muscle. This requires cutting and/or stretching some of that muscle to allow insertion of the implant. In prepectoral implant placement (which might also be referred to as "epipectoral" or "subglandular" reconstruction/placement), the implant is placed above the pectoralis major muscle, and the muscle is not disturbed.

The procedure may take anywhere from 1 to 6 hours, but all other things being equal, the procedure duration may be shorter for prepectoral placement because there is no manipulation of the pectoral muscle when placing the implant. Women may be in the hospital for 1 to 2 days on average when having reconstruction alone and 3 days or less on average when having mastectomy alone; when these are done together, women may be in the hospital a little longer than if they had mastectomy alone. Women may be discharged from the hospital with one or more drains at the area where the surgery was done to help with fluid drainage; the healthcare team will monitor this and inform women when the drains can be removed. For women having a two-staged reconstruction, the second stage is typically done as an outpatient procedure, and the procedure may take about an hour. However, the woman should still plan on receiving general anesthesia, so she should have someone else drive her home.

(American Cancer Society 2017, American Society of Plastic Surgeons nd, Bernini 2015, Breastcancer.org 2019, Davila 2013, Douglas 2018, Lam 2018, Li 2019, Mayo Clinic 2019, Memorial Sloan Kettering Cancer Center nd, Pittman 2017, Susan G. Komen Foundation 2019, Tutt 2017, WebMD Medical Reference 2017)

Descriptive Summary Results for FAQ 1

The surgery may last from 1 to 6 hours depending on the specific needs of the woman. When a woman gets an implant below her chest muscle, the surgeon has to cut or stretch the chest muscle. When a woman gets an implant above her chest muscle, the surgeon does not have to do this, so the surgery may be somewhat shorter. Women may be in the hospital for about 3 days or more if they have the mastectomy and implant surgery are done at the same time. Women may be sent home with tubing coming out of the area where the surgery was done to help the area heal. When the area has healed enough, the tubing will be removed. If a woman has the implant surgery done in two parts, the second part often takes an hour, and the woman usually will not need to stay in the hospital.

FAQ 2: Will the surgery make my breast look and feel natural?

One descriptive summary is presented below for efficiency, with delineation of differences where relevant.

Subpectoral or prepectoral placement

Descriptive Summary (pre-synthesis and synthesis efforts not applicable for descriptive summaries)
Implants come in numerous sizes, are either round or shaped like a teardrop, and can be either saline (silicone shell with saline filling) or silicone (both shell and filling are silicone). The woman and surgeon can decide which shape is a better match to mimic the contour of the contralateral breast, or, in the case of double mastectomy, which shape the woman prefers. Additionally, some surgeons may prefer working with a specific shape; the woman can discuss this with the surgeon before having reconstruction. The implant may be smooth or have a slightly rough texture. The woman and/or her partner may feel "wrinkles" or the texture of the implant if s/he rubs his/her hand over the reconstructed breast, especially at the lower part of the breast. Saline implants tend to have a firmer texture than silicone implants and also tend to have more wrinkling that can be felt. Some women think silicone implants feel more like breast tissue than saline implants do. For women having unilateral mastectomies, depending on the characteristics of the contralateral breast, the surgeon may recommend surgery on the contralateral breast as well to help make the reconstructed breast and contralateral breast match each other better.

Any reconstructed breast will lose at least some of its normal sensation, though some sensation may come back with time. Still, women should not expect their reconstructed breast(s) to have normal sensation like a normal breast. Swelling and bruising is expected for at least 2 to 3 weeks, but it can take up to 8 weeks for swelling and bruising from the surgery to go away completely. As the reconstructed breast heals, its shape often gradually improves as well. Regardless of the type of reconstructive surgery a woman has for her breast(s), there will be scars in the breast area. Although these may become less prominent with time (even up to 1 to 2 years after surgery), women should expect to have some scarring in the breast area. However, these scars are often not visible during day-to-day activities, even if wearing something like a bathing suit or low-cut blouse.

Key differences in the appearance or possible appearance of the breast with a prepectoral versus subpectoral implant have to do with where the muscle and skin are in relation to the implant.

With subpectoral implantation, because the skin and pectoralis major muscle are closer to each other (compared to a prepectoral implant) and the implant is under the pectoralis major muscle:

- women may experience something known as "dynamic distortion" or "animation of the implant", where the implant tends to move upward when the chest muscles are contracted back into its original position when the chest muscles are relaxed;
- when a woman is using her chest muscles, the muscle fibers may be visible through the skin, somewhat like a bodybuilder flexing his/her chest muscles;
- the contour of the breast may appear flatter; and
- there may be a greater chance of the breast feeling too firm or having an abnormal appearance such as being overly round or the nipple being misshaped (see "FAQ 5: What are the risks?")

There is also a possibility of implant malposition, which can lead to an asymmetric appearance in the breasts.

With prepectoral implantation, because the skin and implant are closer to each other (compared to a subpectoral implant) and the implant is over the pectoralis major muscle:

- rippling or wrinkling may be more common (see "FAQ 5: What are the risks?"), and
- there is a small chance of the implant rotating, which can give an asymmetric or even an "upside down" appearance to the implant.

(See FAQ1 for references.)

In addition to the descriptive summary above, we also considered that two outcomes, namely rippling and capsular contracture, would be better placed within FAQ 2 given their impact on the appearance of the breast despite these outcomes originally scoped as part of "FAQ 5: What are the risks?". We present below the evidence for these outcomes.

Evidence Review Tables for FAQ 2

All evidence for all outcomes comes from Li 2019 – a systematic review of observational studies – or individual observational studies included in Li 2019 (all other named studies).

Capsular contracture

Source	No of breasts	Prepectoral event rate (%)	Subpectoral group event rate (%)	Combined groups event rate (%)	Difference	Certainty
Li 2019 meta-analysis	1,123 in 5 studies	3.65% (23/630)	6.69% (33/493)	4.99% (56/1,123)	odds ratio 0.37 (95% CI 0.21 to 0.65)	Low[1]
Meta-analysis by EBSCO Information Services from extracted data	1,119 (130 as patients, not breasts) in 5 studies	3.83% (24/626)	7.91% (39/493)	5.63% (63/1,119)	relative risk 0.36 (95% CI 0.21 to 0.63)	
Bernini 2015						
as summarized in Li 2019	73	0% (0/39)	11.76% (4/34)	5.48% (4/73)	Not significant	Invalid (for outcome of any capsular contracture)
directly summarized	69				$p < 0.01$ (for comparison of distribution of 4 grades between two groups)	
any capsular contracture (grades II, III, or IV)		0% (0/35)	23.53% (8/34)			Very low[1,2]
moderate to severe contracture (grades III or IV)		0% (0/35)	11.76% (4/34)			Very low[1,2]

Chandarana 2018						
as summarized in Li 2019	154 breasts, 130 patients	1.64% (1/61)	7.25% (5/69)	4.62% (6/130)	Not significant	Very low[1,2]
directly summarized	154 breasts, 130 patients	1.64% (1/61)	7.25% (5/69)	4.62% (6/130)	p-value not reported	Very low[1,2]
Chopra 2016						
as summarized in Li 2019	558	0% (0/20)	17.1% (7/41)	11.48% (7/61)	Not significant	Very low[1,2]
directly summarized	61	0% (0/20)	17.1% (7/41)	11.48% (7/61)	p = 0.049	Very low[1,2]
Sbitany 2017						
as summarized in Li 2019 (tissue expander subgroup)	270	0% (0/84)	0.54% (1/186)	0.37% (1/270)	Not significant	Invalid
directly summarized	270	1.19% (1/84)	1.61% (3/186)	1.48% (4/270)	Not significant	Very low[1,2]
Sinnott 2018						
as summarized in Li 2019	589	5.2% (22/426)	9.8% (16/163)	6.45% (38/589)	p = 0.04	Very low[1,2]
directly summarized	589	5.2% (22/426)	9.8% (16/163)	6.45% (38/589)	p = 0.0588	Very low[1,2]

1 Very serious concern for risk of bias
2 Serious concern for imprecision

Rippling

Source	Definition of rippling	No of breasts or patients	Prepectoral event rate (%)	Subpectoral group event rate (%)	Combined groups event rate (%)	Difference	Certainty
Li 2019 meta-analysis	Not clearly defined	Li 2019 only discussed these results narratively, saying there were "similar results" in breast rippling in both groups in 3 studies (Sinnott 2018, Bernini 2015, Cox 2018), but that there was "significantly more" dissatisfaction with the amount of rippling in the prepectoral group in 1 study (Baker 2018). Li 2019 also reported a low rate of rippling in 1 study (Sinnott 2018; 0.5% in prepectoral group and none in subpectoral group) but did not provide quantified estimates for the other studies.					Very low[1-3]
Baker 2018							
	"very dissatisfied or dissatisfied with the amount of rippling... that could be **seen**" (patient-reported outcome)	30 patients	53.85% (7/13)	11.76% (2/17)	30% (9/30)	p = 0.02	Very low[1-3]
	"very dissatisfied or dissatisfied with the amount of rippling...that could be...**felt**" (patient-reported outcome)	30 patients	53.85% (7/13)	17.65% (3/17)	33.33% (10/30)	p = 0.06	Very low[1-3]
Cox 2018	"rate of rippling" (not further defined)	20 patients	40% (4/10)	0% (0/10)	20% (4/20)	p = 0.08	Very low[1,2]
Bernini 2015	"Rippling: fairly or very evident" (evaluated by surgeons)	69 breasts	8.57% (3/35)	14.71% (5/34)	11.59% (8/69)	Not significant	Very low[1,2]
Sinnott 2018	"rippling" (not further defined)	589 breasts	0.47% (2/426)	0% (0/163)	0.34% (2/589)	Not significant	Very low[1,2]

1 Very serious concern for risk of bias
2 Serious concern for imprecision
3 Serious concern for inconsistency

Evidence Synthesis for FAQ 2

Outcome	Approach taken and justification: measure of comparative effect	Results: measure of comparative effect	Approach taken and justification: option-specific measure	Results: option-specific measure
Capsular contracture	**Meta-analysis created from results**. Despite the concerns we have with Li 2019's methods, there appeared to be a signal for a possibly-meaningful difference in capsular contracture, so we extracted the data from all 5 studies identified by Li 2019 as reporting this outcome to redo the meta-analysis. We utilized the same methods as Li 2019 aside from correcting data errors and computing a relative risk instead of an odds ratio (the relative risk is more useful and there is no reason to compute an odds ratio here).	**RR 0.36 (95% CI 0.21 to 0.63) favoring prepectoral group** (Low certainty)	**Meta-analysis created from results.** The pooled risk in the subpectoral group = 7.9% (39/493). Therefore, the estimated risk in the prepectoral group is 0.36*(39/493) = 2.8%.	**About 8% in subpectoral group and about 3% in prepectoral group**
Rippling	**Use of single study, qualitative summarization.** Only 1 study (Baker 2018) reported patient-reported outcome related to rippling. The study had such a small sample size that quantitative estimates have high imprecision.	**Prepectoral placement may increase risk for dissatisfaction with rippling.** (Low certainty)	**Inability to provide a meaningful result.** The rates reported in the single available study are limited by very small sample size and inconsistency within the study (large difference in dissatisfaction with rippling yet no difference in overall satisfaction).	**Not sufficiently valid to report**

Descriptive Summary and Evidence Synthesis Results for FAQ 2

Regardless of whether a woman receives the implant above or below the chest muscle:

A woman can expect to lose some feeling in her breast. Although the feeling in her breast may get better over time for some women, it is unlikely to regain completely normal feeling in her breast.

Swelling and bruising is expected for 2 to 3 weeks, and it may take up to 8 weeks to go away completely.

As her breast heals, the shape of her breast often gets better as well.

There will be scarring from where the surgery was done, but this may get better over 1 to 2 years. The scarring is not usually visible during normal daily activities, even if a woman is wearing a bathing suit or low-cut blouse.

With placement of the implant above the chest muscle:

There is a small chance of the implant turning, which can make the breasts look different from each other. In bad cases, the breast with the implant may have an "upside down" appearance, and this may result in needing more surgery.

In about 3 out of 100 women (3%), the breast may feel too hard or have issues with the shape, such as looking too round or having a nipple that is not shaped normally. (Low certainty evidence from a meta-analysis conducted by EBSCO Information Services that included data from 5 cohort studies [Bernini 2015, Chandarana 2018, Chopra 2016, Sbitany 2017, and Sinnott 2018])

More women may be unhappy with rippling (where folds in the implant can be seen or felt) compared to women who have an implant under the chest muscle. (Very low certainty evidence from 1 cohort study [Baker 2018])

With placement of the implant below the chest muscle:

The implant may move upward when the chest muscles are used and back to the normal position when the chest muscles are relaxed. This is often called “animation of the implant” or “dynamic distortion”.

When a woman uses her chest muscles, the muscle fibers may be more visible through the skin, kind of like when a bodybuilder flexes his or her chest muscles.

The breast may look somewhat less round than if the implant had been placed above the chest muscle

The implant may not position correctly, which can make the breasts look different from each other.

In about 8 out of 100 women (8%), the breast may feel too hard or have issues with the shape, such as looking too round or having a nipple that doesn't have a normal shape. (Low certainty evidence from a meta-analysis conducted by EBSCO Information Services that included data from 5 cohort studies [Bernini 2015, Chandarana 2018, Chopra 2016, Sbitany 2017, and Sinnott 2018])

Fewer women may be unhappy with rippling (where folds in the implant can be seen or felt) compared to women who have an implant above the chest muscle. (Very low certainty evidence from 1 cohort study [Baker 2018])

FAQ 3: Will the surgery have an effect on my quality of life?

All evidence for all outcomes comes from Li 2019 – a systematic review of observational studies – or individual observational studies included in Li 2019 (all other named studies).

Prepectoral vs. subpectoral placement of the implant

Evidence Review Table for FAQ 3

BREAST-Q scores (0-100 with higher being better; assesses the domains of psychosocial, physical, and sexual well-being and satisfaction with breasts, overall outcome, and care received)

Source	No of patients	Findings	Certainty
Li 2019	Not reported	Li 2019 stated there were "similar" mean global scores in BREAST-Q at 3 months postoperatively in both groups in 2 studies (Walia 2018, Baker 2018) and "statistically better" psychosocial well-being and satisfaction in the prepectoral group in 1 study (Cattelani 2017), but did not provide quantified estimates for any of these studies.	Very low[1-3]
Baker 2018	31	Mean BREAST-Q score in pre- and subpectoral groups: 72 and 71 (p = 0.81). There were no significant differences in any individual BREAST-Q domain reported (satisfaction with breasts, satisfaction with outcome, psychosocial well-being, sexual well-being, or physical well-being: chest).	Very low[1,2]
Bernini 2015 (*missed by Li 2019*)	59	As assessed by BREAST-Q, there were no significant differences in satisfaction with breasts, psychosocial well-being, physical well-being, or sexual well-being. Prepectoral group associated with significant improvement in "satisfaction with outcome" (p = 0.03): • mean (SD): prepectoral, 98 (9); subpectoral, 84 (28) • median: prepectoral, 100; subpectoral, 100 • lower bound of calculated CI for the mean difference (using t distribution given small amount of data) includes possibility of a mean difference as small as about 3 points, which is of questionable clinical relevance	Very low[1,2]

Cattelani 2017	84	BREAST-Q score: • prepectoral (n = 39 patients): mean 92.91 (SD 9.03, 95% CI 89.28 to 95.13), median 94 • subpectoral (n = 45 patients): mean 76.07 (SD 14.55, 95% CI 71.70 to 80.44), median 79 • calculated CI for the mean difference (using t distribution given small amount of data): 11.5 to 22.0 "[P]sychosocial well-being and aesthetic outcome satisfaction, as analyzed by the BREAST-Q, were statistically better with [prepectoral group]"	Low[1]
Walia 2018	135 (but response rate only 50%)	No significant differences in any BREAST-Q domain, but 6 of the 7 favored prepectoral (all but satisfaction with surgeon, which had identical median values)	Very low[2,4]

1 Very serious concern for risk of bias
2 Serious concern for imprecision
3 Serious concern for inconsistency
4 Critical concern for risk of bias

Evidence Synthesis Process for FAQ 3

The four studies reporting BREAST-Q data were not consistent in how they reported the data (e.g., global score, domain-specific score, etc.); however, the pattern of the data suggests there may be a benefit for prepectoral implantation versus subpectoral implantation, though this is uncertain and the effect may be small.

Evidence Synthesis Result for FAQ 3

Women who have the implant above the chest muscle may have better overall satisfaction and quality of life related to their breast reconstruction than women who have the implant below the chest muscle. However, this is uncertain and the difference may be small. (Very low certainty evidence from 4 cohort studies [Baker 2018, Bernini 2015, Cattelani 2017, and Walia 2018])

FAQ 4: Will I need to have another surgery?

All evidence for all outcomes comes from Li 2019 – a systematic review of observational studies – or individual observational studies included in Li 2019 (all other named studies).

Prepectoral vs. subpectoral placement of the implant

Evidence Review Table for FAQ 4

Reoperation

Source	No of breasts or patients	Prepectoral event rate (%)	Subpectoral group event rate (%)	Combined groups event rate (%)	Difference	Certainty
Li 2019 meta-analysis	1,048 patients in 5 studies	4.64% (16/345)	4.13% (29/703)	4.29% (45/1,048)	odds ratio 0.93 (0.48 to 1.82)	Very low[1,2]
Bernini 2015						
as summarized in Li 2019	73 breasts	2.56% (1/39)	0% (0/34)	1.37% (1/73)	Not significant	Very low[1,2]
directly summarized	73 breasts	2.56% (1/39)	0% (0/34)	1.37% (1/73)	Not significant	Very low[1,2]
Chandarana 2018						
as summarized in Li 2019	130 patients	18.03% (11/61)	20.29% (14/69)	19.23% (25/130)	Not significant	Very low[1,2]
directly summarized	130 patients	18.03% (11/61)	20.29% (14/69)	19.23% (25/130)	Not significant	Very low[1,2]
Chopra 2016						
as summarized in Li 2019	558	1.24% (2/161)	1.01% (4/397)	1.08% (6/558)	Not significant	Invalid
directly summarized	Chopra 2016 did not report this outcome. Li 2019 appears to obtain their numerators from Chopra 2016's outcome of 30-day readmission; however, being readmitted to the hospital does not necessarily mean that readmission resulted in another operation. Additionally, Li 2019 uses incorrect denominators for the readmission outcome in prepectoral versus subpectoral group (161 vs. 397) compared to Chopra 2016 (20 vs. 41).					

1 Very serious concern for risk of bias
2 Serious concern for imprecision

Evidence Synthesis Process for FAQ 4

Outcome	Approach taken and justification: measure of comparative effect	Results: measure of comparative effect	Approach taken and justification: option-specific measure	Results: option-specific measure
Reoperation rate	**Preponderance of evidence, qualitative summarization.** The meta-analysis has erroneous data but the meta-analysis, all 5 cohorts as reported in the meta-analysis, and the studies we checked that reported on this outcome have consistent findings of no significant effect.	**No clear effect** (Very low certainty)	**Inability to provide a meaningful result.** If pooling across both options (given no clear difference), the individual estimates from the 2 sampled studies with the relevant outcome ranged from 1% to 20%. The pooled estimate from the meta-analysis is also inaccurate for risk estimates due to serious data errors and inclusion of mismatched outcomes.	**Not sufficiently valid to report**

Evidence Synthesis Result for FAQ 4

The placement of the implant does not clearly change a woman's risk for needing more surgery. (Very low certainty evidence from 1 systematic review and meta-analysis of cohort studies [Li 2019] and 2 of the cohort studies that were included in that systematic review and meta-analysis [Bernini 2015, Chandarana 2018])

FAQ 5: What are the risks?

All evidence for all outcomes comes from Li 2019 – a systematic review of observational studies – or individual observational studies included in Li 2019 (all other named studies).

Prepectoral vs. subpectoral placement of the implant

Evidence Review Table for FAQ 5

Overall complications

Source	No of breasts	Prepectoral event rate (%)	Subpectoral group event rate (%)	Combined groups event rate (%)	Difference	Certainty
Li 2019 meta-analysis	2,101 in 11 studies	11.70% (95/812)	11.56% (149/1,289)	11.61% (244/2,101)	odds ratio 0.97 (95% CI 0.72 to 1.29)	Very low[1,2]
Bernini 2015 (early [within 1 year] complications)						
as summarized in Li 2019	73	7.69% (3/39)	8.82% (3/34)	8.22% (6/73)	Not significant	Very low[1,2]
directly summarized	73	7.69% (3/39)	8.82% (3/34)	8.22% (6/73)	Not significant	Very low[1,2]
Bettinger 2017 (any complication)						
after expander placement						
as summarized in Li 2019 (tissue expander subgroup)	294	13.33% (22/165)	13.95% (18/129)	13.61% (40/294)	Not significant	Very low[1,2]
directly summarized	294	13.33% (22/165)	13.95% (18/129)	13.61% (40/294)	Not significant	Very low[1,2]
after implant placement						
as summarized in Li 2019 (implant subgroup)	222	5.88% (7/119)	3.88% (4/103)	4.95% (11/222)	Not significant	Very low[1,2]
directly summarized	222	5.88% (7/119)	3.88% (4/103)	4.95% (11/222)	Not significant	Very low[1,2]

Chandarana 2018						
as summarized in Li 2019	154 breasts, 130 patients	34.43% (21/61)	30.43% (21/69)	32.31% (42/130)	Not significant	Very low[1,2] (also possible double-counting)
directly summarized	154 breasts, 130 patients					
major implant-related complications		11.48% (7/61)	13.04% (9/69)	12.31% (16/130)	Not significant	Very low[1,2]
early (< 90 day) complications total		22.95% (14/61)	21.74% (15/69)	22.31% (29/130)	Not significant	Very low[1,2]
delayed (91 days to 1 year) complications total		11.48% (7/61)	8.70% (6/69)	10.00% (13/130)	Not significant	Very low[1,2]
Chopra 2016						
as summarized in Li 2019	558	1.86% (3/161)	2.52% (10/397)	2.33% (13/558)	Not significant	Invalid
directly summarized	61					
complications		15.00% (3/20)	24.39% (10/41)	21.31% (13/61)	Not significant	Very low[1,2]
complication requiring explantation or exchange		15.00% (3/20)	21.95% (9/41)	19.67% (12/61)	Not significant	Very low[1,2]
Sbitany 2017						
as summarized in Li 2019 (tissue expander subgroup)	270	17.86% (15/84)	18.82% (35/186)	18.52% (50/270)	Not significant	Very low[1,2]
directly summarized (reported to be assessed "during TE stage")	270	17.86% (15/84)	18.82% (35/186)	18.52% (50/270)	Not significant	Very low[1,2]

1 Very serious concern for risk of bias

2 Serious concern for imprecision

Implant loss

Source	No of breasts	Prepectoral event rate (%)	Subpectoral group event rate (%)	Combined groups event rate (%)	Difference	Certainty
Li 2019 meta-analysis	2,630 in 11 studies	4.20% (53/1,263)	4.46% (61/1,367)	4.33% (114/2,630)	odds ratio 0.84 (95% CI 0.56 to 1.25)	Very low[1,2]
Bernini 2015						
as summarized in Li 2019	73	8% (3/39)	0% (0/34)	4.11% (3/73)	Not significant	Very low[1,2]
directly summarized	73	8% (3/39)	0% (0/34)	4.11% (3/73)	Not significant	Very low[1,2]
Bettinger 2017						
after expander placement						
as summarized in Li 2019 (tissue expander subgroup)	294	8.48% (14/165)	7.75% (10/129)	8.16% (24/294)	Not significant	Very low[1,2]
directly summarized	294	8.48% (14/165)	7.75% (10/129)	8.16% (24/294)	Not significant	Very low[1,2]
after implant placement						
as summarized in Li 2019 (implant subgroup)	222	4.20% (5/119)	1.94% (2/103)	3.15% (7/222)	Not significant	Very low[1,2]
directly summarized	222	4.20% (5/119)	1.94% (2/103)	3.15% (7/222)	Not significant	Very low[1,2]
Chandarana 2018						
as summarized in Li 2019	154 breasts, 130 patients	4.2% (3/71)	10.8% (9/83)	6.49% (10/154)	Not significant	Very low[1,2]
directly summarized	154 breasts, 130 patients	4.2% (3/71)	10.8% (9/83)	6.49% (10/154)	p-values not reported	Very low[1,2]

Chopra 2016						
as summarized in Li 2019	558	1.86% (3/161)*	2.27% (9/397)*	2.15% (12/558)*	Not significant	Invalid
directly summarized	61	15.00% (3/20)*	21.95% (9/41)*	19.67% (12/61)*	Not significant	Very low[1,2]
Sbitany 2017 (tissue expander explantation)						
as summarized in Li 2019 (tissue expander subgroup)	270	2.38% (2/84)*	6.45% (12/186)*	5.19% (14/270)*	Not significant	Invalid
directly summarized	270	1.19% (1/84)*	4.30% (8/186)*	3.33% (9/270)*	Not significant	Very low[1,2]
Sinnott 2018						
as summarized in Li 2019	589	3.99% (17/426)	4.29% (7/163)	4.07% (24/589)	Not significant	Very low[1,2]
directly summarized	589	3.99% (17/426)	4.29% (7/163)	4.07% (24/589)	Not significant	Very low[1,2]

* These data extraction errors in Li 2019 are considered problematic for the sake of accuracy in data extraction, but given the erroneous extraction in Li 2019 and the correct figures from the cited source both fail to find a clear difference between the two groups, the overall conclusion of no clear difference between the groups is considered unlikely to be affected. Additionally, given our reluctance to report univariate estimates from these data, the differences between what Li 2019 reports and what the cited source actually reports do not have any material impact on evidence synthesis statements.

1 Very serious concern for risk of bias

2 Serious concern for imprecision

Nipple or skin flap necrosis

Source	No of breasts	Prepectoral event rate (%)	Subpectoral group event rate (%)	Combined groups event rate (%)	Difference	Certainty
Li 2019 meta-analysis	2,788 in 12 studies	2.86% (37/1,294)	3.61% (54/1,494)	3.26% (91/2,788)	odds ratio 0.80 (95% CI 0.51 to 1.25)	Very low[1-3]
Bernini 2015						
as summarized in Li 2019	73	2.56% (1/39)	0% (0/34)	1.37% (1/73)	Not significant	Very low[1,2]
directly summarized	73	2.56% (1/39)	0% (0/34)	1.37% (1/73)	Not significant	Very low[1,2]
Bettinger 2017						
after expander placement						
as summarized in Li 2019 (tissue expander subgroup)	294	5.45% (9/165)	8.53% (11/129)	6.80% (20/294)	Not significant	Very low[1,2]
directly summarized	294	5.45% (9/165)	8.53% (11/129)	6.80% (20/294)	Not significant	Very low[1,2]
after implant placement						
as summarized in Li 2019 (implant subgroup)	222	2.52% (3/119)	1.94% (2/103)	2.25% (5/222)	Not significant	Very low[1,2]
directly summarized	222	2.52% (3/119)	1.94% (2/103)	2.25% (5/222)	Not significant	Very low[1,2]

Chandarana 2018						
as summarized in Li 2019	154 breasts, 130 patients	9.84% (6/61)	5.78% (4/69)	7.69% (10/130)	Not significant	Invalid
directly summarized	154 breasts, 130 patients					
early (< 90 day)		0% (0/61)	5.80% (4/69)	3.08% (4/130)	p-value not reported	Very low[1,2]
delayed (91 days to 1 year)		4.92% (3/61)	0% (0/69)	2.31% (3/130)	Not significant	Very low[1,2]
Chopra 2016						
as summarized in Li 2019	558	0.62% (1/161)*	0.50% (2/397)*	0.54% (3/558)*	Not significant	Invalid
directly summarized	61	5.00% (1/20)*	4.88% (2/41)*	4.92% (3/61)*	Not significant	Very low[1,2]
Sbitany 2017						
as summarized in Li 2019 (tissue expander subgroup)	270	1.19% (1/84)*	4.84% (9/186)*	3.70% (10/270)*	Not significant	Invalid
directly summarized	270	1.19% (1/84)*	4.30% (8/186)*	3.33% (9/270)*	Not significant	Very low[1,2]
Sinnott 2018						
as summarized in Li 2019	589	1.1% (5/426)	1.2% (2/163)	1.19% (7/589)	Not significant	Very low[1,2]
directly summarized	589	1.1% (5/426)	1.2% (2/163)	1.19% (7/589)	Not significant	Very low[1,2]

* These data extraction errors in Li 2019 are considered problematic for the sake of accuracy in data extraction, but given the erroneous extraction in Li 2019 and the correct figures from the cited source both fail to find a clear difference between the two groups, the overall conclusion of no clear difference between the groups is considered unlikely to be affected. Additionally, given our reluctance to report univariate estimates from these data, the differences between what Li 2019 reports and what the cited source actually reports do not have any material impact on evidence synthesis statements.

1 Very serious concern for risk of bias

2 Serious concern for imprecision

3 Serious concern for inconsistency

Wound-skin infection

Source	No of breasts	Prepectoral event rate (%)	Subpectoral group event rate (%)	Combined groups event rate (%)	Difference	Certainty
Li 2019 meta-analysis	2,922 in 13 studies	3.36% (45/1,338)	3.72% (59/1,584)	3.56% (104/2,922)	odds ratio 0.96 (95% CI 0.64 to 1.45)	Very low[1,2]

1 Very serious concern for risk of bias
2 Serious concern for imprecision

Hematoma

Source	No of breasts	Prepectoral event rate (%)	Subpectoral group event rate (%)	Combined groups event rate (%)	Difference	Certainty
Li 2019 meta-analysis	697 in 5 studies	4.02% (10/249)	2.68% (12/448)	3.16% (22/697)	odds ratio 1.19 (95% CI 0.52 to 2.70)	Very low[1,2]

1 Very serious concern for risk of bias
2 Serious concern for imprecision

Wound dehiscence

Source	No of breasts	Prepectoral event rate (%)	Subpectoral group event rate (%)	Combined groups event rate (%)	Difference	Certainty
Li 2019 meta-analysis	1,485 in 5 studies	0.98% (7/713)	0.78% (6/772)	0.88% (13/1,485)	odds ratio 1.16 (95% CI 0.40 to 3.33)	Very low[1,2]

1 Very serious concern for risk of bias
2 Serious concern for imprecision

Evidence Synthesis Process for FAQ 5

Outcome	Approach taken and justification: measure of comparative effect	Results: measure of comparative effect	Approach taken and justification: option-specific measure	Results: option-specific measure
Overall complications	**Preponderance of evidence, qualitative summarization.** The meta-analysis has erroneous data but the meta-analysis, all 11 cohorts as reported in the meta-analysis, and all 5 studies we checked have consistent findings of no significant effect.	**No clear effect** (Very low certainty)	**Inability to provide a meaningful result.** If pooling across both options (given no clear difference), the individual estimates from the 5 sampled studies ranged from 5% to 22% (or 32% if adding early and late complications is not counting the same patients twice). The pooled estimate from the meta-analysis is also inaccurate for risk estimates due to serious data errors.	**Not sufficiently valid to report**
Implant loss	**Preponderance of evidence, qualitative summarization.** The meta-analysis has erroneous data but the meta-analysis, all 11 cohorts as reported in the meta-analysis, and all 6 studies we checked have consistent findings of no significant effect.	**No clear effect** (Very low certainty)	**Inability to provide a meaningful result.** If pooling across both options (given no clear difference), the individual estimates from the 6 sampled studies ranged from 3% to 20%. The pooled estimate from the meta-analysis is also inaccurate for risk estimates due to serious data errors.	**Not sufficiently valid to report**

Nipple or skin flap necrosis	**Preponderance of evidence, qualitative summarization.** The meta-analysis has erroneous data and includes a study in patients receiving flap-based reconstruction (instead of implant-based reconstruction), but the meta-analysis, all 12 cohorts as reported in the meta-analysis, and all 6 studies we checked have consistent findings of no significant effect.	**No clear effect** (Very low certainty)	**Inability to provide a meaningful result.** If pooling across both options (given no clear difference), the individual estimates from the 6 sampled studies ranged from 1% to 7%, but this represents only 6 of the 12 cohorts summarized above and one of the cohorts in the Li meta-analysis had rates up to 12%. The pooled estimate from the meta-analysis also inaccurate for risk estimates due to serious data errors.	**Not sufficiently valid to report**
Other complications	**Drop from further synthesis.** Other complications were not suggested to be different in meta-analysis and are generally included in the 'Overall complications' outcome.	**Not applicable**		

Evidence Synthesis Results for FAQ 5

Risks of getting an implant include:

- **infection**
- **bleeding**
- **skin over the implant dying and needing to be removed**
- **the area where the surgery was done opening back up after being closed by the surgeon**
- **needing to remove the implant**

Where the implant is placed does not clearly change these risks. (Very low certainty evidence from 1 systematic review and meta-analysis of cohort studies [Li 2019] and 6 of the cohort studies included in that systematic review and meta-analysis [Bernini 2015, Bettinger 2017, Chandarana 2018, Chopra 2016, Sbitany 2017, Sinnott 2018])

FAQ 6: What are the side effects?

All evidence for all outcomes comes from Li 2019 – a systematic review of observational studies – or individual observational studies included in Li 2019 (all other named studies).

Evidence synthesis does not apply for scarring, and we considered this outcome to be better addressed as part of responding to "FAQ 2: Will the surgery make my breast look and feel normal?" (please see that FAQ for answers regarding scarring).

Prepectoral vs. subpectoral placement of the implant

Evidence Review Table for FAQ 6

Seroma

Source	No of breasts	Prepectoral event rate (%)	Subpectoral group event rate (%)	Combined groups event rate (%)	Difference	Certainty
Li 2019 meta-analysis	in 10 studies 2,715 patients	2.23% (28/1255)	2.88% (42/1460)	2.58% (70/2,715)	odds ratio 0.88 (95% CI 0.53 to 1.47)	Very low[1,2]

1 Very serious concern for risk of bias
2 Serious concern for imprecision

Postoperative pain

Source	Findings	Certainty
Li 2019	Li 2019 only described findings pertaining to postoperative pain narratively without any meta-analysis. <u>Pain scores</u> • "significantly lower" in the prepectoral group within the first 7 days in 2 studies (Walia 2018, Cattelani 2017), at 30 days in 1 study (Walia 2018), and at 3 months in 1 study (Schaeffer 2018) • "no significant difference" between groups at 3 months in 1 study (Baker 2018) <u>Postoperative analgesic requirement</u> • "33% fewer days on opioid analgesic medication" and "66% less likely to require opioid prescription refills" in the prepectoral group in 1 study (Copeland-Halperin 2019) • post-operative opioid use of 19.81 morphine-equivalents in prepectoral group and 27.12 in subpectoral group (p = 0.05) 1 study (Myers 2018) • "no difference in analgesia requirements" between groups in 1 study (Kanesalingam 2017)	Very low[1,2]

1 Very serious concern for risk of bias
2 Serious concern for imprecision

Evidence Synthesis Process for FAQ6

Outcome	Approach taken and justification: measure of comparative effect	Results: measure of comparative effect	Approach taken and justification: option-specific measure	Results: option-specific measure
Seroma	**Meta-analysis already done.**	**No clear effect** (Very low certainty)	**Qualitative representation of range of risk estimates across the studies.** Risk estimates across the studies range up to 7%. With limited certainty in expressing quantified results this can be presented as being an uncommon side effect.	**Not common**
Postoperative pain	**Preponderance of evidence, qualitative summarization.** Although we have concerns about Li 2019's methods, the preponderance of results presented narratively suggests a signal of possible reduction in postoperative pain with prepectoral implantation.	**Possible reduction in postoperative pain with prepectoral implant** (Very low certainty)	**Inability to provide a meaningful result.** There are insufficient data to present option-specific estimates.	**Not sufficiently valid to report**

Evidence Synthesis Results for FAQ 6

Some women may get a collection of fluid at the area where the surgery was done, but this may be uncommon. Where the implant is placed does not clearly change the chance of this happening. (Very low certainty evidence from 1 systematic review and meta-analysis of cohort studies [Li 2019])

Women may have less pain after surgery if they have the implant above the muscle instead of below the muscle. (Very low certainty evidence from 1 systematic review and meta-analysis of cohort studies [Li 2019])

FAQ 7: When will I recover?

One descriptive summary is presented below for efficiency, with delineation of differences where relevant.

Subpectoral or prepectoral placement

Descriptive Summary (pre-synthesis and synthesis efforts not applicable for descriptive summaries)

Women typically feel tired after having implant surgery, and this usually lasts for about a week or two. Soreness, swelling, and bruising is common for the first 2 to 3 weeks, but as noted in "FAQ 2: Will the surgery make my breast look and feel natural?", it may take up to 8 weeks for swelling and bruising to subside completely. Your surgeon can prescribe medicine to help treat the pain.

Women may need to take 3 to 4 weeks off from work, and they might return to normal activities within 6 weeks of having implant surgery. In particular, women are often advised to avoid strenuous activity and may be advised to avoid sex for 4 to 6 weeks after reconstructive surgery. Because prepectoral implant surgery involves less disruption of normal tissue, woman having this type of implant may have quicker recovery, particularly for activities that involve the pectoralis major muscle or dependent or interacting muscles (e.g., things like pushing something across a counter or pressing yourself up from the ground or the bed use the chest muscles). All women should ask their healthcare team for timelines specific to their case.

Because immediate reconstruction more closely coincides with the time of the mastectomy, it may be hard to separate recovery from the implant surgery from recovery from the mastectomy. Some women may not feel completely normal for a year or two after mastectomy.

If a woman is given exercises to do, she should be sure to do them consistently to help with the recovery process. However, if drains are put in place, women might be advised to avoid exercises that might put strain on the drains (which may include overhead exercises or exercises using the chest wall) until the drains are removed. The health care team will give specifics. All women should ask their healthcare team for timelines specific to their case.

For women having two-stage procedures, the recovery time from the second stage is shorter given it is less complicated, usually taking about 2 weeks.

(See FAQ 1 for references.)

Descriptive Summary Results for FAQ 7

It is normal to feel tired after implant surgery, and this may last for a week or two. Women may need to take 3 to 4 weeks off from work. Women should do any exercises prescribed by the surgical team. They may be advised to avoid activities that put a lot of stress on the body, especially in the area where the surgery was done. This may include avoiding sex for 4 to 6 weeks after implant surgery. It may be possible for women to return to normal activities within 6 weeks of having implant surgery. If the implant surgery is done in two parts, the recovery time for the second part may only take about 2 weeks. When a woman has implant surgery and mastectomy at the same time or close together, it can be hard to tell the difference between recovering from the implant surgery and recovering from the mastectomy. Some women may not feel completely normal until a year or two after mastectomy.

Evidence report for pre- vs. subpectoral breast reconstruction after mastectomy

Part 2 - Search and Selection

Prepared by EBSCO Information Services

September 25, 2019

Prepared by EBSCO Health Innovations and EBM Development Department:

Brian S. Alper, MD, MSPH, FAAFP, Vice President

Martin Mayer, DMSc, MS, PA-C, Clinical Evidence Synthesizer

Eric Manheimer, PhD, EBM Editor

Abbreviations

General abbreviations that may appear in this report

CI – confidence interval
CrI – credible interval
HR – hazard ratio
IQR – interquartile range
MA – meta-analysis
MD – mean difference
NA, N/A – not applicable
NR – not reported
OR – odds ratio
RCT – randomized, controlled trial
RR – risk ratio, relative risk
RtR – rate ratio
SMD – standardized mean difference
SR – systematic review
SRMA – systematic review and meta-analysis

Abbreviations specific to this report that may appear in this report

ADM – acellular dermal matrix
IBBR – implant-based breast reconstruction
TE – tissue expander

Methods

First-round searching will consist of searching DynaMed Plus summaries pertinent to the topic. The search starts with DynaMed Plus because DynaMed Plus content is based on a thorough, systematic search and active literature surveillance system.

> Systematic literature surveillance (SLS) has been a cornerstone of creating DynaMed content since its inception. Currently, the SLS team works closely with members of McMaster University's Department of Health Research Methods, Evidence, and Impact to define and refine optimal search strategies, utilizing search terms for methodology and for clinical concepts (especially diagnosis and treatment) for each journal. These filters for PubMed searches are derived from PubMed Clinical Queries, McMaster University Hedges system, and DynaMed search filters and were found to capture >95% of relevant valid articles for use in DynaMed.[1]
> [1]Alper BS, Iorio A. Optimising search filters for active literature surveillance: a concordance study. Global Evidence Summit. Cape Town, South Africa; September 2017.
>
> The SLS team, in collaboration with McMaster University, continually evaluates and improves these filters to keep abreast of the ever-changing medical literature landscape. PubMed searches are performed daily. Each article is assessed by an external screener for clinical relevance, then reviewed by internal staff for both clinical relevance and validity. Any disagreements are settled by the Deputy Editor of the SLS team.
> In addition, the SLS team continually monitors the Journal source list against the list of journals catalogued in MEDLINE and existing DynaMed content to determine the set of journals that provide the highest yield for valid, clinically relevant content. As of November 2018, 507 Journals are systematically searched (see http://dynamed.com/home/content/content-sources). The journal selection threshold leads to routine adjustments to the number of journals selected.

Second-round searching will involve PubMed/MEDLINE® searches for intervention-specific systematic reviews or guidelines that involve a systematic review that are more recent than those identified in first-round searching.

Third-round searching will involve original study tracing from systematic reviews, guidelines or other relevant sources. This may be done to identify additional evidence sources if the results from the first two rounds of searching are insufficient.

Fourth-round searching will involve searches for original evidence reports. Such searching will be limited to areas considered insufficiently addressed by earlier searches, such as focused concepts published after search dates in systematic reviews.

Additional selective searching, such as tracing citations from articles found or seeking related articles, may be done for additional concepts discovered.

Additional evidence updates may also be added continuously from feedback from any source.

FAQ Summary

Results

First-round searching – DynaMed:

DynaMed subsection	Number of article citations	Number of unique references included
DynaMed did not have relevant content for this evidence report.		

Second-round searching – searches for intervention-specific systematic reviews:

Database	Search string	Number of search results	Number of references included
PubMed September 25, 2019	(prepect* OR pre-pect* OR epipect* OR epi-pect* OR subgland* OR sub-gland*) AND (subpect* OR sub-pect* OR submusc* OR sub-musc* OR retropect* OR retro-pect*) AND (mastectom*[tiab] OR reconstruct*[tiab] OR postmastectom*[tiab] OR post-mastectom*[tiab]) AND (systematic[sb] OR meta-analysis[tiab] OR guideline[pt])	4	1 (Li 2019)

Third-round searching – study tracing from systematic reviews:

Source	Tracing	Number of search results	Number of references included
Li 2019	Sampling of included studies for key outcomes and for checking of report quality	16	10 (Baker 2018, Bernini 2015, Bettinger 2017, Catellani 2017, Chandarana 2018, Chopra 2016, Cox 2018, Sbitany 2017, Sinnott 2018, Walia 2018)

Fourth-round searching – searches for original evidence reports:

Database	Search string	Number of search results	Number of references included
Not applicable			

Search summary:

Number of articles screened and selected

	Screened	Selected*
1st-round (DynaMed)	Not applicable	
2nd-round (Systematic review searches)	4	1
3rd-round (Study tracing)	16	10
4th-round (Original article searches)	Not applicable	
Total	*20*	*11*

* Number shown is after deduplication

	Articles selected for evaluation (Author Year)
Systematic reviews	1 – Li 2019 (systematic review of observational studies)
Randomized, controlled trials	Not applicable (no randomized, controlled trials available for this comparison)
Other article types (e.g., observational studies, guidelines)	10 – Baker 2018, Bernini 2015, Bettinger 2017, Catellani 2017, Chandarana 2018, Chopra 2016, Cox 2018, Sbitany 2017, Sinnott 2018, Walia 2018 (all observational studies obtained from tracing Li 2019)

Evidence report for pre- vs. subpectoral breast reconstruction after mastectomy

Part 3 - Critical Appraisal of Evidence Reports

Prepared by EBSCO Information Services

September 20, 2019

Prepared by EBSCO Health Innovations and EBM Development Department:

Brian S. Alper, MD, MSPH, FAAFP, Vice President

Martin Mayer, DMSc, MS, PA-C, Clinical Evidence Synthesizer

Eric Manheimer, PhD, EBM Editor

Abbreviations

General abbreviations that may appear in this report

CI – confidence interval
CrI – credible interval
HR – hazard ratio
IQR – interquartile range
MA – meta-analysis
MD – mean difference
NA, N/A – not applicable
NR – not reported
OR – odds ratio
RCT – randomized, controlled trial
RR – risk ratio, relative risk
RtR – rate ratio
SMD – standardized mean difference
SR – systematic review
SRMA – systematic review and meta-analysis

Abbreviations specific to this report that may appear in this report

ADM – acellular dermal matrix
IBBR – implant-based breast reconstruction
TE – tissue expander

Methods

For each study selected for critical appraisal, we assessed for criteria needed for Level 1 [likely reliable] evidence ratings in DynaMed's Levels of Evidence criteria in which evidence quality is labeled in 1 of 3 levels:

- **(level 1 [likely reliable] evidence)** for studies with clinical outcomes and minimal risk of bias;
- **(level 2 [mid-level] evidence)** for studies with clinical outcomes and significant methodological or statistical limitations; and
- **(level 3 [lacking direct] evidence)** for reports that do not include scientific analysis of clinical outcomes or for study types that do not include comparisons between groups.

The specific concepts we critically assessed are fully mapped to cover all the criteria used in GRADE. We summarized key concerns identified that reduce the certainty of evidence in categories used for GRADE methods (i.e., risks of bias, indirectness, imprecision, inconsistency, and other considerations if relevant). In the study-level summaries inconsistency assessment was applied to consistency of within-study results – this applies to consistency across related outcomes for both original studies and for systematic reviews, and also applies to consistency across studies when applied to systematic reviews.

FAQ Summary

Results

Characteristics and Results of Critically Appraised Studies/Sources

Below is a template for study summaries. At each major level, the intended content is a high-level statement (e.g., "Systematic review and meta-analysis of randomized controlled trials" for the item "Study design"). If there is a need to indicate additional relevant information, do so with a sub-bullet under the parent item. For instance, if downgrading once for "Risk of bias", one would comment "Serious concern" for the "Risk of bias" domain, and then using sub-bullets under the "Risk of bias" item, one would comment on the limitations that resulted in the serious concern. A template is included below, followed by an example summary.

BAKER 2018
Baker BG, Irri R, MacCallum V, Chattopadhyay R, Murphy J, Harvey JR. A Prospective Comparison of Short-Term Outcomes of Subpectoral and Prepectoral Strattice-Based Immediate Breast Reconstruction. Plast Reconstr Surg. 2018 May;141(5):1077-1084. PubMed

Relevant to FAQs 3 and 5 (quality of life and rippling outcome only) – only the abstract was assessed to confirm statements in Li 2019 systematic review that "Significantly more patients in the prepectoral group were either very dissatisfied or dissatisfied with the amount of rippling of the implant, who underwent DTI reconstructions" and BREAST-Q scores were "similar".

Baker 2018 was a prospective cohort study with 40 women having either prepectoral or subpectoral implant-based breast reconstruction. It reports the following results on the rippling outcome: "When analyzing outcomes from individual questions of the BREAST-Q, significantly more patients in the prepectoral group were either very dissatisfied or dissatisfied with the amount of rippling of the implant that could be seen (prepectoral, seven of 13; subpectoral, two of 17; p = 0.02) and felt (prepectoral, seven of 13; subpectoral, three of 17; p = 0.06)." The calculated confidence interval for being very dissatisfied or dissatisfied with the rippling *seen* yields an absolute risk difference of 8.6% to 66.5%. BREAST-Q scores (from 31 returned questionnaires) were similar between the prepectoral and subpectoral groups (72 and 71, respectively, p = 0.81). There were no significant differences in satisfaction with breasts, satisfaction with outcome, psychosocial well-being, sexual well-being, or physical well-being: chest.

Certainty: Very low for implant rippling (two downgrades for risk of bias due to observational study, downgrade for imprecision, downgrade for inconsistency with BREAST-Q scores [which should be correlated], upgrade for large effect), Very low for BREAST-Q scores (downgrades for risk of bias and imprecision).

BERNINI 2015
Bernini M, Calabrese C, Cecconi L, Santi C, Gjondedaj U, Roselli J, Nori J, Fausto A, Orzalesi L, Casella D. Subcutaneous Direct-to-Implant Breast Reconstruction: Surgical, Functional, and Aesthetic Results after Long-Term Follow-Up. Plast Reconstr Surg Glob Open. 2016 Jan 7;3(12):e574. doi: 10.1097/GOX.0000000000000533. eCollection 2015 Dec. PubMed

Relevant to FAQ2, FAQ3, FAQ4, FAQ5, FAQ6

- **Study design:** observational study
- **Population:** women having mastectomy with direct-to-implant reconstructions

- **Intervention:** prepectoral approach
- **Comparison:** subpectoral approach

- **Number of participants:** 63 patients; 73 breasts
  - 34 patients and 39 breasts in prepectoral group
  - 29 patients and 34 breasts in subpectoral group
- **Duration of follow-up:**
  - long-term follow-up outcomes
    - 25 months median overall
      - 25 months median in prepectoral group
      - 26 months median in subpectoral group
  - short-term follow-up outcomes (the durations below were not reported in Bernini 2015 and were found by checking abstract of earlier study [Casella 2014 25339795] of which Bernini 2015 is a follow-up; Bernini 2015 reports both the short-term outcomes in Casella 2014 plus additional longer-term outcomes)
    - 12 months median in prepectoral group
    - 13 months median in prepectoral group

- **Certainty: Very Low**
  - Risk of bias: Very serious concern (observational study, no randomization)
  - Imprecision: Serious concern (for all outcomes; though a few outcomes were statistically significant, they failed to provide confidence intervals, so we assigned a downgrade for imprecision for these outcomes as well)
  - Inconsistency: No concerns
  - Indirectness: No concerns
- **Results:**

Risks of 1-year outcomes*

Outcome	Prepectoral (n = 39 breasts) (%)	Subpectoral (n = 34 breasts) (%)	P-value if statistically significant; combined groups proportion if not (n = 73 breasts) (%)
early overall complications†	3 (8%)	3 (9%)	8.22% (6/73)
implant loss or removal‡	3 (8%)	0 (0%)	4.11% (3/73)
skin–nipple necrosis	1 (3%)	0 (0%)	1.37% (1/73)
seroma	0 (0%)	0 (0%)	0% (0/73)
wound dehiscence	0 (0%)	1 (3%)	1.37% (1/73)
wound-skin infection	0 (0%)	2 (6%)	2.74% (2/73)
hematoma	1 (3%)	0 (0%)	1.37% (1/73)
reoperation	1 (3%)	0 (0%)	1.37% (1/73)

*No statistically significant differences.
† Measure of overall early complications included the following specific complications: implant loss, skin–nipple necrosis, seroma, wound dehiscence, wound-skin infection, hematoma, atopic reaction versus prosthesis, and reoperation.
‡This outcome includes 1-year and 2-year outcomes

Risk of 2-year outcomes

Rippling and capsular contracture outcomes

Outcomes	Prepectoral (n = 35 breasts) (%)	Subpectoral (n = 34 breasts) (%)	P-value if statistically significant; combined groups proportion if not (n = 69 breasts) (%)
capsular contracture*			p < 0.01 (for comparison of distribution of 4 grades between two groups)
any capsular contracture (grades II, III, or IV)	0 (0%)	24% (8/34)	
moderate to severe contracture (grades III or IV)	0 (0%)	12% (4/34)	
rippling (fairly or very evident) (*as evaluated by surgeons*)†	9% (3/35)	15% (5/34)	11.59% (8/69)
visible implant: fairly or very evident	6% (2/35)	18% (6/34)	11.59% (8/69)
palpable implant: fairly or very evident	9% (3/35)	15% (5/34)	11.59% (8/69)
aesthetic result: "agree or strongly agree with an excellent aesthetic outcome" (*as assessed by surgeons*)	91% (32/35)	65% (22/34)	p < 0.01

* Capsular contractures were graded using the Baker scale, which has 4 grades: grade 1 - normally soft breast with a nonpalpable implant; grade II - breast slightly firm to touch that appears normal; grade III - breast firm to touch that appears distorted; grade IV - breast hard and painful to touch that appears distorted.
† In Methods, rippling was described as assessed as follows: "The form was structured as follows: a, ...; b, registration of signs of rippling, using a 5-grade Likert scale (score: 1, strongly disagree; 2, disagree; 3, undecided; 4, agree; 5, strongly agree) to judge the statement 'this case has no signs at all of rippling'". However, Results (Table 2) reported the outcome as "Rippling: fairly or very evident (%)".

BREAST-Q scores at 2 years (evaluated in 59 patients, 30 prepectoral and 29 subpectoral)

- no significant differences in
  - satisfaction with breasts
  - psychosocial well-being
  - physical well-being
  - sexual well-being
- prepectoral group associated with significant improvement in satisfaction with outcome (p = 0.03)
  - mean (SD): prepectoral, 98 (9); subpectoral, 84 (28)
  - median: prepectoral, 100; subpectoral, 100

- **Other considerations:**
  - Discrepancies compared to Li 2019
    - capsular contracture
      - Li 2019 Fig 4 has 0/39 in prepectoral and 4/34 in subpectoral
      - Bernini 2015 Table 2 has 0/35 in prepectoral and 8/34 in subpectoral
    - BREAST-Q scores and other appearance-related outcomes (except rippling and capsular contraction) were not reported for Bernini 2015 in Li 2019 Results text

BETTINGER 2017
Bettinger LN, Waters LM, Reese SW, Kutner SE, Jacobs DI. Comparative Study of Prepectoral and Subpectoral Expander-Based Breast Reconstruction and Clavien IIIb Score Outcomes. Plast Reconstr Surg Glob Open. 2017 Jul 26;5(7):e1433. PubMed

Relevant to FAQ5

- **Study design:** observational study
    - complications measured twice, first after expander placement and again after implant placement
- **Population:** women having mastectomy with two-staged expander breast reconstructions
- **Intervention:** prepectoral approach with acellular dermal matrix
- **Comparison:** subpectoral approach
    - included 2 groups, one with and the other without acellular dermal matrix; these were pooled into single subpectoral group for the Li 2019 systematic review meta-analyses and we also pooled them for reporting in table below

- **Study inclusion criteria:** 6-month minimum follow-up

- **Number of studies:** not applicable
- **Number of participants:**
    - patients
        - 110 in prepectoral group
        - 103 patients in the combined ("Classic" and "No ADM [acellular dermal matrix]") subpectoral group
    - breasts (unit of analysis at expander stage and implant stage)
        - 294 at expander stage
            - 165 in prepectoral group
            - 129 in combined subpectoral groups
        - 222 at implant stage
            - 119 in prepectoral group
            - 103 in combined subpectoral groups
- **Duration of follow-up:** 6 months after expander placement for expander complications and 6 months after implant placement for implant complications

- **Certainty: Very Low**
    - Risk of bias: Very serious concern (observational study, no randomization)
    - Imprecision: Serious concern (for all outcomes)
    - Inconsistency: No concerns
    - Indirectness: No concern

- **Results:**

Risks of surgery-related complications in prepectoral and subpectoral breast reconstruction groups at 180 days*

Outcome	**Prepectoral**	**Subpectoral**	**Combined prepectoral and subpectoral groups**
EXPANDER	**(n = 165 breasts) (%)**	**both subpectoral groups pooled (n = 129 breasts) (%)**	**(n = 294 breasts) (%)**
any expander complications†	22 (13.33%)	18 (13.95%)	40 (13.61%)
loss			
expander	14 (8.48%)	10 (7.75%)	24 (8.16%)
deflation	2 (1.21%)	0 (0%)	2 (0.68%)
seroma	5 (3.03%)	8 (6.20%)	13 (4.42%)
hematoma	2 (1.21%)	1 (0.78%)	3 (1.02%)
infection	11 (6.67%)	9 (6.98%)	20 (6.80%)
nipple or skin necrosis	9 (5.45%)	11 (8.53%)	20 (6.80%)
IMPLANT	**(n = 119 breasts) (%)**	**both subpectoral groups pooled (n = 103 breasts) (%)**	**(n = 222 breasts) (%)**
any implant complications†	7 (5.88%)	4 (3.88%)	11 (4.95%)
implant loss	5 (4.20%)	2 (1.94%)	7 (3.15%)
seroma	5 (4.20%)	1 (0.97%)	6 (2.70%)
hematoma	0 (0%)	1 (0.97%)	1 (0.45%)
infection	4 (3.36%)	1 (0.97%)	5 (2.25%)
nipple or skin necrosis	3 (2.52%)	2 (1.94%)	5 (2.25%)

* Table 2 reports these complications in each of the 3 groups along with p-values comparing the 3 groups. However, because we pooled the two subpectoral groups for our analyses to compare prepectoral vs. subpectoral, the p-values reported in the table were not relevant to us. Comparisons between the two groups show no significant differences so we have reported the proportion with the outcome in the combined analysis of prepectoral and subpectoral.

† Measure of overall complications was not defined, although specific complications assessed included (each limited to grade IIIb Clavien score) seroma, infection, hematoma, skin and nipple necrosis, expander deflation, and expander or implant loss.

CATTELANI 2017
Cattelani L, Polotto S, Arcuri MF, Pedrazzi G, Linguadoca C, Bonati E. One-Step Prepectoral Breast Reconstruction With Dermal Matrix-Covered Implant Compared to Submuscular Implantation: Functional and Cost Evaluation. Clin Breast Cancer. 2018 Aug;18(4):e703-e711. doi: 10.1016/j.clbc.2017.11.015. Epub 2017 Dec 2. PubMed

Relevant to FAQ3 (quality of life) only. We present an abbreviated summary of the BREAST-Q results below, which we prepared to verify Li 2019's statement of "statistically better" psychosocial well-being and satisfaction in the prepectoral group.

"[P]sychosocial well-being and aesthetic outcome satisfaction, as analyzed by the BREAST-Q were statistically better" with prepectoral (it is not further specified why they used this phrasing, but the presentation in the table suggests their report of BREAST-Q is for the global score):

- prepectoral (n = 39 patients): mean 92.91 (SD 9.03, 95% CI 89.28 to 95.13), median 94
- subpectoral (n = 45 patients): mean 76.07 (SD 14.55, 95% CI 71.70 to 80.44), median 79
- calculated CI for the mean difference (using t distribution given small amount of data): 11.5 or 11.6 to 22.0 or 22.2 (depending on whether one assumes homo- or heteroscedasticity)

Certainty: Low (downgrade due to risk of bias due to observational evidence)

CHANDARANA 2018
Chandarana MN, Jafferbhoy S, Marla S, Soumian S, Narayanan S. Acellular dermal matrix in implant based immediate breast reconstructions: a comparison of prepectoral and subpectoral approach. Gland Surg. 2018 Aug;7(Suppl 1):S64-S69. PubMed

Relevant to FAQ4, FAQ5

- **Study design:** observational study
- **Population:** women having mastectomy with single-stage implant-based immediate breast reconstruction in single breast unit
- **Intervention:** prepectoral approach
- **Comparison:** subpectoral approach

- **Study inclusion criteria:** women who had procedure from January 2015 to May 2017

- **Number of studies:** not applicable
- **Number of participants:** 130 patients; 154 breasts
- **Duration of follow-up:** 11.8 months median
    - 9.8 months for prepectoral group
    - 19.6 months for subpectoral group

- **Certainty: Very Low**
    - Risk of bias: Very serious concern (observational study; possible impact of differential follow-up [see "Other considerations" below])
    - Imprecision: Serious concern (for all outcomes)
    - Inconsistency: No concerns
    - Indirectness: No concerns

- **Results:**

Risks of surgery-related complications in prepectoral and subpectoral breast reconstruction groups

Outcome *†	Prepectoral (n=61 patients) (%)	Subpectoral (n=69 patients) (%)	Combined groups (n=130 patients) (%)
Major implant-related complications ‡	7 (11.48%)	9 (13.04%)	16 (12.31%)
Early (≤ 90 day) complications total §	14 (22.95%)	15 (21.74%)	29 (22.31%)
hematoma	7 (11.48%)	5 (7.25%)	12 (9.23%)
surgical site infection	4 (6.56%)	5 (7.25%)	9 (6.92%)
skin necrosis	0 (0%)	4 (5.80%)	4 (3.08%)
wound dehiscence	1 (1.64%)	0 (0%)	1 (0.77%)
Delayed (91 days to 1 year) complications total¶	7 (11.48%)	6 (8.70%)	13 (10.00%)
capsular contracture	1 (1.64%)	5 (7.25%)	6 (4.62%)
skin necrosis	3 (4.92%)	0 (0%)	3 (2.31%)
wound dehiscence	1 (1.64%)	0 (0%)	1 (0.77%%)
surgical site infection	0 (0%)	1 (1.45%)	1 (0.77%%)

* p-values comparing individual complications between groups was not reported.
† All complication outcomes below use number of patients as denominator (61 for prepectoral and 69 for subpectoral).
‡ Defined as Clavien-Dindo grade III or higher
§ Includes the following early complications: hematoma, surgical site infection, skin necrosis, seroma, wound dehiscence, redness, and pulmonary embolism. The four specific early complications scoped are included below.
¶: Includes the following delayed complications: capsular contracture, skin necrosis, skin redness, wound dehiscence, and surgical site infection. The four specific delayed complications scoped are included below.

Return to theater in 18% (11/61) of patients in prepectoral group vs. 20.3% (14/69) of patients in subpectoral group (p = 0.825)

Implant loss in 4.2% (3/71) of breasts in prepectoral group vs. 10.8% (9/83) of breasts in subpectoral group (p = 0.29) (5 of the 12 patients were noted to have bilateral procedures, although the number with bilateral procedures in each of the two groups was not reported)

- **Other considerations:**
    - The pre- and subpectoral implant groups had different median follow-up times: 9.8 months for the prepectoral group and 19.6 months for the subpectoral group. This raises the possibility that the reported complications in the prepectoral group measured between 91 days and 1 year could be spuriously low, which could have the following impact:
        - For outcomes where the risk in the prepectoral group is reported to be numerically lower than the risk in the subpectoral group
            - the risks could actually be more similar between the groups, or
            - the prepectoral group could actually have a higher risk than the subpectoral group.
        - For outcomes where the risk in the prepectoral group is reported to be numerically similar to the risk in the subpectoral group, the prepectoral group could actually have an increased risk compared to the subpectoral group.

        - For outcomes where the risk in the prepectoral group is reported to be numerically higher than the subpectoral group, there could be an even greater increased risk in the prepectoral group compared to the subpectoral group.
        - To the extent that outcomes measured between 91 days and 1 year contributed to the composite outcome of major implant-related complications (defined as implant-related complications with a Clavien-Dindo grade III or higher), the same concerns about a possible spurious lowering of risk in the prepectoral group would apply.
    - Discrepancies compared to Li 2019:
        - Overall complications outcome as summarized in Li 2019 Figure 1 (overall complications) reports the pooled results of "early" and "delayed". This could result in double-counting for the totals (because some patients may have had both early and delayed).
        - "nipple or skin flap necrosis" outcome in Li 2019
            - Li 2019 Fig 3 has 6/61 in prepectoral and 4/69 in subpectoral for outcome defined as "nipple or skin flap necrosis"
            - Chandarana 2018 (defines outcome as 'skin necrosis')
                - reports separately by follow-up time
                    - early (< 90 day) has 0/61 in prepectoral and 4/69 in subpectoral
                    - delayed (91 days to 1 year) has 3/61 in prepectoral and 0/69 in subpectoral

CHOPRA 2016
Chopra K, Houssock C, Cai SS, et al. Submuscular versus prepectoral immediate implant based breast reconstruction. Northeastern Society of Plastic Surgeons 33rd Annual Meeting abstracts. Available at http://meeting.nesps.org/abstracts/2016/57.cgi.
Relevant to FAQ5, FAQ6

- **Study design:** observational study
    - retrospective review of experience of single surgeon
- **Population:** women having mastectomy with single-stage direct-to-implant breast reconstruction with acellular dermal matrix between 2011 and 2015
- **Intervention:** prepectoral
- **Comparison:** subpectoral

- **Number of participants:** 38 patients; 61 breasts
    - 13 patients and 20 breasts in prepectoral group
    - 25 patients and 41 breasts in subpectoral group
- **Duration of follow-up:** 283 days median
    - 397 days in subpectoral group vs. 161 days in prepectoral group (p = 0.031)

- **Certainty: Very Low**
    - Risk of bias: Very serious concern (observational study; possible impact of differential follow-up [see "Other considerations" below])
    - Imprecision: Serious concern (for all outcomes)
    - Inconsistency: No concerns
    - Indirectness: No concerns

- **Results:**

Risks of surgery-related complications in prepectoral and subpectoral breast reconstruction groups*

Outcome	Prepectoral (n = 20 breasts) (%)	Subpectoral (n = 41 breasts) (%)	P-value if statistically significant; combined groups proportion if not (n = 61) (%)
incidence of complications (not further defined) (% per breast)	3 (15.0%)	10 (24.4%)	13 (21.31%)
dehiscence	1 (5.0%)	1 (2.4%)	2 (3.28%)
infection	1 (5.0%)	3 (7.3%)	4 (6.56%)
necrosis	1 (5.0%)	2 (4.9%)	3 (4.92%)
seroma	2 (10.0%)	2 (4.9%)	4 (6.56%)
capsular contracture	0 (0%)	7 (17.1%)	p = 0.049
complication requiring explantation or exchange	3 (15.0%)	9 (21.9%)	12 (19.67%)

*p-values comparing groups were reported, and only the capsular contraction outcome showed a significant difference between groups (p = 0.049).

No significant difference in readmission within 30 days (2/13 women in prepectoral group [15.4%] vs. 4/25 women in supectoral group [16%]; p = 0.961)

- **Other considerations:**
  - The pre- and subpectoral implant groups had different median follow-up times: 161 days for the prepectoral group and 397 days for the subpectoral group. The authors report complications data at the overall median of 283 days. This raises the possibility that the reported complications in the prepectoral group could be spuriously low. Accordingly, because all outcomes were numerically lower in the prepectoral group or were numerically similar between the two groups, this raises the following possibilities:
    - For outcomes where the risk in the prepectoral group is reported to be numerically lower than the risk in the subpectoral group
      - the risks could actually be more similar between the groups, or
      - the prepectoral group could actually have a higher risk than the subpectoral group.
    - For outcomes where the risk in the prepectoral group is reported to be numerically similar to the risk in the subpectoral group, the prepectoral group could actually have an increased risk compared to the subpectoral group.
  - Discrepancies compared to Li 2019:
    - Overall complications: Li 2019 uses incorrect denominators in prepectoral versus subpectoral group (3/161 vs. 10/397) compared to Chopra 2016 (3/20 vs. 10/41)
    - Implant loss: Li 2019 uses incorrect denominators in prepectoral versus subpectoral group (3/161 vs. 9/397) compared to Chopra 2016 (3/20 vs. 9/41)

- Necrosis: Li 2019 uses incorrect denominators in prepectoral versus subpectoral group (1/161 vs. 2/397) compared to Chopra 2016 (1/20 vs. 2/41)
- Seroma: Li 2019 uses incorrect denominators in prepectoral versus subpectoral group (2/161 vs. 2/397) compared to Chopra 2016 (2/20 vs. 2/41)
- Infection: Li 2019 uses incorrect denominators in prepectoral versus subpectoral group (1/161 vs. 3/397) compared to Chopra 2016 (1/20 vs. 3/41)
- Reoperation: Chopra 2016 did not report this outcome. Li 2019 appears to obtain their numerators from Chopra 2016's outcome of 30-day readmission, but being readmitted to the hospital does not necessarily mean that readmission resulted in another operation. Additionally, Li 2019 uses incorrect denominators in prepectoral versus subpectoral group (161 vs. 397) compared to Chopra 2016 (20 vs. 41).
- Wound dehiscence: Li 2019 uses incorrect denominators in prepectoral versus subpectoral group (1/161 vs. 1/397) compared to Chopra 2016 (1/20 vs. 1/41)

COX 2018

Cox S, Bozzuto L, Bartholomew A, et al. Prepectoral versus retropectoral implant-based reconstruction following nipple-sparing mastectomy and adjuvant radiation therapy. Ann Surg Oncol 2018;25(2):357e8. (Available as abstract in conference book on pg 357-8 at https://www.breastsurgeons.org/docs/resources/old_meetings/2018_Official_Proceedings_ASBrS.pdf)

Relevant to FAQ5 (rippling outcome only) – this abstract was assessed only to confirm statement in Li 2019 systematic review that there were "similar results in breast rippling in each group". The Cox 2018 study was a retrospective chart review comparing results in 10 patients with prepectoral vs. 10 patients with subpectoral. It reports the following on rippling outcome:

- Results: "There was an increased trend of breast rippling in the prepectoral group (40% vs. 0%, p=0.08)." It was not reported whether rippling was clinician-assessed or patient-assessed. However, because all other outcomes included in this retrospective review are typically assessed by physician, it is assumed that rippling was probably also clinician-assessed.
- Conclusions: "Prepectoral implant-based reconstruction following NSM [nipple-sparing mastectomy] and adjuvant radiation therapy is associated with increased levels of implant rippling, but lower rates of grade 3 and 4 contracture, and reduced rates of overall surgical complications compared to retropectoral implant-based reconstruction."
- Certainty: Very low (despite not appraising in full, these results would start at Low certainty per GRADE standards given they are observational, and they also suffer from imprecision)

LI 2019

Li L, Su Y, Xiu B, Huang X, Chi W, Hou J, Zhang Y, Tian J, Wang J, Wu J. Comparison of prepectoral and subpectoral breast reconstruction after mastectomies: A systematic review and meta analysis. Eur J Surg Oncol. 2019 Sep;45(9):1542-1550. Epub 2019 May 14. PubMed

Relevant to FAQ3, FAQ4, FAQ5, FAQ6

- **Study design:** systematic review of observational studies
- **Population:** women having mastectomy (prophylactic and/or therapeutic)
- **Intervention:** prepectoral breast reconstruction
- **Comparison:** subpectoral breast reconstruction
- **Number of studies:** 16
    - 12 articles and 4 abstracts
    - 4 prospective and 12 retrospective
    - 13 studies included for meta-analyses
    - all studies used either acellular dermal matrix or titanium-coated poly propylene mesh as prosthetic coverage material, and most used acellular dermal matrix, no subgroups reported
- **Number of participants:** summed number in all 16 studies not reported; number per outcome meta-analyzed included in table below
- **Duration of follow-up:** 2 to 34 months
- **Results and Certainty:**
    - All outcomes are considered to have critical risk of bias resulting in Very low certainty due to being comprised solely of observational studies *and* our concerns about the quality of systematic review methods (see “Other considerations” below). We note these concerns simply as “risk of bias” when discussing the reason(s) for downgrading a given outcome. Where inconsistency and/or imprecision also apply, this is also noted.

Effects of prepectoral vs. subpectoral breast reconstruction on surgery-related complications

Outcome	No of patients (studies)	Odds ratio (95% CI)	Prepectoral event rate (%)	Subpectoral group event rate (%)	Combined groups event rate (%)	Certainty (reason for downgrade)
overall complications	2,101 (11)	0.97 (95% CI 0.72 to 1.29)	11.70% (95/812)	11.56% (149/1,289)	11.61% (244/2,101)	Very low (risk of bias, imprecision)
implant loss	2,630 (11)	0.84 (95% CI 0.56 to 1.25)	4.20% (53/1,263)	4.46% (61/1,367)	4.33% (114/2,630)	Very low (risk of bias, imprecision)
nipple or skin flap necrosis (overall analysis)	2,788 (12)	0.80 (95% CI 0.51 to 1.25)	2.86% (37/1,294)	3.61% (54/1,494)	3.26% (91/2,788)	Very low (risk of bias, imprecision, inconsistency)
hematoma	697 (5)	1.19 (95% CI 0.52 to 2.70)	4.02% (10/249)	2.68% (12/448)	3.16% (22/697)	Very low (risk of bias, imprecision)
wound or skin infection	2,922 (13)	0.96 (95% CI 0.64 to 1.45)	3.36% (45/1,338)	3.72% (59/1,584)	3.56% (104/2,922)	Very low (risk of bias, imprecision)
wound dehiscence	1,485 (5)	1.16 (95% CI 0.40 to 3.33)	0.98% (7/713)	0.78% (6/772)	0.88% (13/1,485)	Very low (risk of bias, imprecision)
capsular contracture	1,123 (5)	0.37 (95% CI 0.21 to 0.65)	3.65% (23/630)	6.69% (33/493)	4.99% (56/1,123)	Low (risk of bias)*
reoperation	1,048 (5)	0.93 (0.48 to 1.82)	4.64% (16/345)	4.13% (29/703)	4.29% (45/1,048)	Very low (risk of bias, imprecision)

*Despite our concerns about Li 2019's methods, there there appeared to be a strong signal for a possibly-meaningful difference in capsular contracture, so we extracted the data from all 5 studies identified by Li 2019 as reporting this outcome to redo the meta-analysis. We utilized the same methods as Li 2019 aside from correcting data errors and computing a relative risk instead of an odds ratio (the relative risk is more useful and there is no reason to compute an odds ratio here). This gives RR 0.36 (95% CI 0.21 to 0.63) and a pooled event rate in the subpectoral group of 7.9% (39/493). Therefore, we considered the capsular contracture outcome to have Low certainty instead of Very low certainty.

Additional outcomes not meta-analyzed

For the outcomes below, Li 2019 only presented results in a narrative format (no meta-analysis performed). Where Li 2019 reported numerical results, we report them as well. Because of the relative lack of detail provided, we often use Li 2019's exact phrasing, which appears in quotes.

rippling

- **Results**
  - "similar results" in breast rippling in both groups in 3 studies (Sinnott 2018, Bernini 2015, Cox 2018)
    - very low rate of rippling in the 1 study for which this was reported (0.5% in prepectoral group and none in subpectoral group)
  - "significantly more" dissatisfaction with the amount of rippling of the implant in prepectoral group in 1 study (Baker 2018)
- **Certainty/downgrade**: Very low (risk of bias, inconsistency, imprecision [inability to assess])

quality of life

- **Results**
  - "similar" mean global scores in BREAST-Q at 3 months postoperatively in both groups in 2 studies (Walia 2018, Baker 2018)
  - "statistically better" psychosocial well-being and satisfaction in prepectoral group in 1 study (Cattelani 2017)
- **Certainty/downgrade**: Very low (risk of bias, imprecision [inability to assess], inconsistency)

postoperative pain

- pain scores
  - **Results**
    - within first 7 days
      - "significantly lower" in prepectoral group in 2 studies (Walia 2018, Cattelani 2017)
    - at 30 days, "significantly lower" in prepectoral group in 1 study (Walia 2018)
    - at 3 months
      - "significantly lower" in prepectoral group in 1 study (Schaeffer 2018)
      - "no significant difference" between groups in 1 study (Baker 2018)
  - **Certainty/downgrade**: Very low (risk of bias, imprecision [inability to assess])

- postoperative analgesic requirement
  - **Results**
    - "33% fewer days on opioid analgesic medication" and "66% less likely to require opioid prescription refills" in prepectoral group in 1 study (Copeland-Halperin 2019)
    - post-operative opioid use of 19.81 morphine-equivalents in prepectoral group and 27.12 in subpectoral group ($p = 0.05$) in 1 study (Myers 2018)
    - "no difference in analgesia requirements" between groups in 1 study (Kanesalingam 2017)
  - **Certainty/downgrade**: Very low (risk of bias, imprecision [inability to assess])

Other considerations:

Although Li 2019 is a very current SR of evidence comparing prepectoral to subpectoral breast reconstruction (and apparently the only SR dedicated to this question), we found the quality of their methods and reporting to raise multiple concerns. We have briefly described some of our concerns below (this is not necessarily an exhaustive consideration of the matter):

- Types of prosthetic device used in studies and analyzed in subgroup analyses were not clear, and we have concerns about appropriate categorization of the studies. Li 2019 used categories of "tissue expander" (TE), "implant", and "other" (where "other" meant the study did not specify whether it used tissue expander, implant, or both), but it is not clear that the studies were categorized appropriately based on reviewing Table 1 and cross-checking some of the included studies. For instance, for the outcome of overall complications (Figure 1), Copeland-Halperin 2019 and Nahabedian 2017 are included in the subgroup analysis "other" (Analysis 1.1.3), but Table 1 lists them as being "Implant/TE-implant" and "TE-implant", respectively. Another example of this concern is discussed in the summary of Sinnott 2018.
- We also have concerns about incorrect data extraction or missed data extraction for numerous outcomes (e.g., see summaries for Bernini 2015, Chopra 2016, Sbitany 2017)

- Li 2019 also included a study that was not implant-based reconstruction (Zhu 2016), but rather, flap-based reconstruction. The inclusion of Zhu 2016 is of questionable appropriateness (as women pursuing flap-based reconstruction may be importantly different from women pursuing implant-based reconstruction), and its inclusion in certain subgroup analyses very likely influenced the results to reach statistical significance. The best example of this is perhaps the subgroup analysis for nipple or skin flap necrosis in the tissue expander subgroup (Figure 3, Analysis 1.5.1).

SBITANY 2017
Sbitany H, Piper M, Lentz R. Prepectoral Breast Reconstruction: A Safe Alternative to Submuscular Prosthetic Reconstruction following Nipple-Sparing Mastectomy. Plast Reconstr Surg. 2017 Sep;140(3):432-443. PubMed

Relevant to FAQ5

- **Study design:** observational study
- **Population:** women having nipple-sparing mastectomy with immediate prosthetic reconstruction; only 2-stage expander/implant reconstruction cases were included
- **Intervention:** prepectoral
    - with full acellular dermal matrix coverage for soft tissue support
- **Comparison:** subpectoral
    - partial subpectoral/partial acellular dermal matrix coverage (dual plane)
- **Number of participants:**
    - patients
        - 51 in prepectoral group
        - 115 in subpectoral group
    - breasts
        - 84 in prepectoral group
        - 186 in subpectoral group
- **Duration of follow-up:** mean 11.1 months in prepectoral cohort and mean 12.5 months in subpectoral cohort
- **Certainty: Very Low**
    - Risk of bias: Very serious concern (observational study)
    - Imprecision: Serious concern (for all outcomes)
    - Inconsistency: No concerns
    - Indirectness: No concerns

- **Results:**

Risks of surgery-related complications in prepectoral and subpectoral breast reconstruction groups during tissue expander stage *

Outcome	Prepectoral (n = 84 breasts) (%)	Subpectoral (n = 186 breasts) (%)	Combined prepectoral and subpectoral groups (n = 270 breasts) (%)
any complication during tissue expander stage (not further defined)	15 (17.9)	35 (18.8)	50 (18.52)
hematoma	2 (2.4)	2 (1.1)	4 (1.48)
seroma	3 (3.6)	12 (6.5)	15 (5.56)
major skin necrosis	1 (1.2)	8 (4.3)	9 (3.33)
infection requiring washout	2 (2.4)	11 (5.9)	13 (4.81)
capsular contractures †	1 (1.19)	3 (1.61)	4 (1.48)

* No statistically significant differences for any outcomes reported below

† All capsular contractures occurred in the subset of 24 breasts (17 in subpectoral group and 7 in prepectoral group) with postmastectomy radiation therapy; none occurred in non-irradiated breasts. Although the results text suggests these might be the number of capsular contractures per *patient*, the reported percentages match the percentage *per breast* (these results can also be seen in Table 4 as the combination of "Baker grade 2 encapsulation" and "Baker grade 3 encapsulation").

- **Other considerations:**
  - discrepancies compared to Li 2019
    - capsular contracture in Li 2019 Figure 4 uses incorrect numerators for the prepectoral and subpectoral groups (0/84 vs. 1/186, respectively) compared to Sbitany 2017 (1/84 vs. 3/186)
    - "nipple or skin flap necrosis" in Li 2019 Figure 3 vs. "Major skin necrosis" in Sbitany 2017 Table 3
      - Li 2019 Figure 3 has 1/84 in prepectoral group and 9/186 in subpectoral group
      - Sbitany 2017 Table 3 has 1/84 in prepectoral group and 8/186 in subpectoral group
    - "implant loss" in Li 2019 Figure 2 includes Sbitany 2017 in "tissue expander" subgroup and reports 2/84 losses in prepectoral group and 12/186 in subpectoral group but implant loss outcome not identified in in Sbitany 2017
      - "TE [tissue expander] explantation" is potentially related outcome in Sbitany 2017 Table 3, with 1/84 in prepectoral group and 8/186 in subpectoral group

SINNOTT 2018

Sinnott CJ, Persing SM, Pronovost M, Hodyl C, McConnell D, Ott Young A. Impact of Postmastectomy Radiation Therapy in Prepectoral Versus Subpectoral Implant-Based Breast Reconstruction. Ann Surg Oncol. 2018 Oct;25(10):2899-2908. PubMed

Relevant to FAQ5

- **Study design:** observational study
- **Population:** women having postmastectomy implant-based breast reconstruction
  - minority of women were exposed to postmastectomy radiation therapy
- **Intervention:** prepectoral implant-based breast reconstruction
  - about 97% performed as single-stage, direct-to-implant approach and remaining reconstructions as two-stage expander-to-implant procedures
- **Comparison:** subpectoral implant-based breast reconstruction
  - about 72% performed as single-stage, direct-to-implant approach and remaining reconstructions as two-stage expander-to-implant procedures
- **Study inclusion criteria:** no additional
- **Number of studies:** not applicable
- **Number of participants:** 374 patients; 589 breasts
  - 274 patients and 426 breasts in prepectoral group
  - 100 patients and 163 breasts in partial subpectoral group
- **Duration of follow-up: 32 months for subpectoral vs. 19 months for prepectoral (p = 0.0001)**
  - authors reported that reason for longer follow-up for subpectoral was because prepectoral had been adopted more recently
- **Certainty: Very Low**
  - Risk of bias: Very serious concern (observational study; possible impact of differential follow-up [see "Other considerations" below])
  - Imprecision: Serious concern (for all outcomes)
  - Inconsistency: No concerns
  - Indirectness: No concerns
- **Results:**

Risks of surgery-related complications in prepectoral and subpectoral breast reconstruction groups*

Outcome	Prepectoral (n = 426 breasts) (%)	Subpectoral (n = 163 breasts) (%)	Combined groups (n = 589) (%)
infection	12 (2.8)	2 (1.2)	14 (2.38%)
seroma	1 (0.2)	2 (1.2)	3 (0.51%)
hematoma	0	0	0
dehiscence	4 (0.9)	2 (1.2)	6 (1.02%)
necrosis	5 (1.1)	2 (1.2)	7 (1.19%)
capsular contracture	22 (5.2)	16 (9.8)	38 (6.45%)
rippling (not further defined)†	2 (0.5)	0	2 (0.34%)
implant loss	17 (4.0)	7 (4.3)	24 (4.07%)

* p-values comparing groups were reported, and only the capsular contracture outcome showed a close-to-significant difference between groups (p = 0.0588).

† It was not reported whether rippling was clinician-assessed or patient-assessed. Because all other complications described above are typically assessed by the clinician, it is assumed that rippling was probably also clinician-assessed.

- **Other considerations:**
  - The pre- and subpectoral implant groups had different mean follow-up times: 32 months for the subpectoral group vs. 19 months for the prepectoral group. This raises the possibility that the reported complications in the prepectoral group could be spuriously low, which could have the following impact:
    - For outcomes where the risk in the prepectoral group is reported to be numerically lower than the risk in the subpectoral group
      - the risks could actually be more similar between the groups, or
      - the prepectoral group could actually have a higher risk than the subpectoral group.
    - For outcomes where the risk in the prepectoral group is reported to be numerically similar to the risk in the subpectoral group, the prepectoral group could actually have an increased risk compared to the subpectoral group.
    - For outcomes where the risk in the prepectoral group is reported to be numerically higher than the subpectoral group, there could be an even greater increased risk in the prepectoral group compared to the subpectoral group.
  - Discrepancies compared to Li 2019
    - Sinnott 2018 was classified as an "Other" subgroup in Li 2019's forest plots (see summary of Li 2019 for details about "Other"). However, it appears Sinnott 2018 measured outcomes only after the implant and should have been classified in Li 2019's "implant" subgroup. A mention of time point for outcome measurement does not appear to have been explicitly mentioned in Sinnott 2018 identified, but the totality of the report makes it clear Sinnott 2018's data pertain to the post-implant stage:
      - it states its primary goal was to assess the outcomes of post-mastectomy radiation therapy "on outcomes after prepectoral versus subpectoral implant-based breast reconstruction",
      - its "Study design" states that it only included patients "who underwent pre- or subpectoral implant-based breast reconstruction in a single-stage, direct-to-implant approach or a two-stage approach with a tissue expander placed initially, followed by replacement with an implant"
      - the vast majority of implants were single-stage/direct-to-implant (97.2% for prepectoral and 72.4% for subpectoral, or 90.3% overall),
      - this study was a retrospective chart review, and the follow-up duration was well beyond the normal tissue-expander stage (19.0 months for prepectoral and 31.9 months for subpectoral), and
      - Sinnott 2018 includes loss of implant as an outcome, which by definition can only occur after the implant is put in place

WALIA 2018

Walia GS, Aston J, Bello R, Mackert GA, Pedreira RA, Cho BH, Carl HM, Rada EM, Rosson GD, Sacks JM. Prepectoral Versus Subpectoral Tissue Expander Placement: A Clinical and Quality of Life Outcomes Study. Plast Reconstr Surg Glob Open. 2018 Apr 20;6(4):e1731. doi: 10.1097/GOX.0000000000001731. eCollection 2018 Apr. PubMed

Relevant to FAQ3 (quality of life) only. An abbreviated summary of this study's results for BREAST-Q scores is presented below, which we prepared to verify Li 2019's statement that BREAST-Q scores were "similar" between the prepectoral and subpectoral groups.

Certainty: Very low (downgrades due to risk of bias from observational study and BREAST-Q survey response rate of 50%, imprecision)

Patient-reported BREAST-Q domains*

BREAST-Q domain	Prepectoral (n = unclear, but less than 26), median (IQR)	Subpectoral (n = unclear, but less than 109), median (IQR)	P value
Satisfaction with breasts	55 (38 to 78)	47 (40 to 58)	0.127
Psychosocial well-being	79 (50 to 100)	63 (50 to 82)	0.211
Sexual well-being	65 (28 to 100)	47 (34 to 60)	0.337
Physical well-being of the chest	79 (60 to 91)	71 (63 to 81)	0.326
Satisfaction with outcome	88 (63 to 100)	75 (61 to 100)	0.289
Satisfaction with information	85 (74 to 100)	71 (62 to 90)	0.082
Satisfaction with surgeon	100 (100 to 100)	100 (87 to 100)	0.147

* Walia 2018 does not clearly state in Table 3 that the values are median (IQR) but refers to some of the results in Table 3 within the results text as median (IQR), and these results correspond to the results in Table 3. We therefore included the labeling of median (IQR) in the column headers for the pre- and subpectoral groups. Additionally, although there were 26 women in the prepectoral implant group and 109 women in the subpectoral implant group in Walia 2018, Walia 2018 also noted only an approximate 50% BREAST-Q response rate. Walia 2018 also gives no indication of how that 50% was distributed between the two groups. Despite this, Walia 2018 lists the full sample size for each group in their tabulated results, which is clearly incorrect if there was only a 50% response rate. We therefore label the sample size as being unclear for each of the groups, but less than the overall sample size in each group.

Sample Decision Aid

Breast Reconstruction After Mastectomy: Subpectoral vs. Prepectoral Implant Placement

Patient Questions	Subpectoral placement (below the chest muscle)	Prepectoral placement (above the chest muscle)
What does the treatment involve?	You will have surgery to place an implant in your chest, below the chest muscle. The muscle will be cut or stretched.	You will have surgery to place an implant in your chest, above the chest muscle.
	The surgery may last from 1 to 6 hours. You may be in the hospital 3 days or longer if the implant surgery is done with the mastectomy. Tubes will come out of the area where the surgery was done to help it heal. Some women have the implant surgery in two parts. If this is done, the second surgery will take about an hour and you will likely go home the same day.	
Will the surgery make my breast look and feel natural?	The implant may move up when your chest muscles are used. It will return when the muscles are at rest. The breast may look less round than if the implant had been placed above the chest muscle. Your breasts may not look balanced. Some women can feel or see the folds of the implant. Fewer women may be unhappy about this compared to having an implant above the chest muscle. About 8 of 100 women (8%) who get an implant below the muscle may have a breast that feels hard or has an abnormal shape.	There is a small chance of the implant turning, which can make the breasts look different from each other. In bad cases, the breast may have an "upside down" appearance. This may lead to more surgery. Some women can feel or see the folds of the implant. More women may be unhappy about this compared to having an implant under the chest muscle. About 3 of 100 women (3%) who get an implant below the muscle may have a breast that feels hard or has an abnormal shape.
	You will likely have swelling and bruising for up to 3 weeks. There will be scars where the surgery was done, but it may get better in 1 to 2 years. The shape of the breast may improve as it heals. You may lose some feeling in your breast. This may get better over time, but it is unlikely that normal feeling will return.	
Will the surgery affect my quality of life?	Women who have the implant below the chest muscle may be a little less satisfied and have a slightly lower quality of life compared to women who have the implant above the chest muscle.	Women who have the implant above the chest muscle may be a little more satisfied and have a slightly better quality of life compared to women who have the implant below the chest muscle.

<table>
<tr><td>Will I need to have another surgery?</td><td colspan="2">Where the implant is placed may not change your risk for needing another surgery.</td></tr>
<tr><td>What are the risks?</td><td colspan="2">Risks of getting an implant include:
infection
bleeding
skin over the implant dying and needing to be removed
the wound opening again after surgery
needing to remove the implant
Where the implant is placed may not change these risks.</td></tr>
<tr><td rowspan="2">What are the side effects?</td><td>You may have more pain after surgery if you have the implant placed below the muscle instead of above the muscle.</td><td>You may have less pain after surgery if you have the implant placed above the muscle instead of below the muscle.</td></tr>
<tr><td colspan="2">Fluid may build up at the area where the surgery was done, but this may not be likely. Where the implant is placed may not change the chance of this happening.</td></tr>
<tr><td>When will I recover?</td><td colspan="2">It is normal to feel tired for up to 2 weeks.
You may need to take 3 to 4 weeks off from work after surgery, but this depends on the work you do.
You may be advised to avoid activities that put a lot of stress on your body, such as heavy lifting.
You may need to avoid sex for 4 to 6 weeks.
You may be able to return to all the things you normally do within 6 weeks.
You should do any exercises your surgeon gives you to help with recovery.
If the implant surgery is done in two parts, the recovery time for the second part may only take about 2 weeks.
Some women may not feel completely normal until a year or two after mastectomy.</td></tr>
</table>

Evidence report for pre- vs. subpectoral breast reconstruction after mastectomy

Reference list

Prepared by EBSCO Information Services

September 25, 2019

Prepared by EBSCO Health Innovations and EBM Development Department:

Brian S. Alper, MD, MSPH, FAAFP, Vice President

Martin Mayer, DMSc, MS, PA-C, Clinical Evidence Synthesizer

Eric Manheimer, PhD, EBM Editor

AMERICAN CANCER SOCIETY 2017
American Cancer Society. What to Expect After Breast Reconstruction Surgery. Last reviewed/modified September 12, 2017. Accessed September 20, 2019. Available at https://www.cancer.org/cancer/breast-cancer/reconstruction-surgery/what-to-expect-after-breast-reconstruction-surgery.html.

American Cancer Society. Breast Reconstruction Using Implants. Last reviewed/modified September 12, 2017. Accessed September 20, 2019. Available at https://www.cancer.org/cancer/breast-cancer/reconstruction-surgery/breast-reconstruction-options/breast-reconstruction-using-implants.html.

AMERICAN SOCIETY OF PLASTIC SURGEONS ND
American Society of Plastic Surgeons. What options are available for breast reconstruction? Date last reviewed/updated not stated. Accessed September 20, 2019. Available at https://www.plasticsurgery.org/reconstructive-procedures/breast-reconstruction/techniques.

American Society of Plastic Surgeons. What should I expect during my breast reconstruction recovery? Date last reviewed/updated not stated. Accessed September 20, 2019. Available at https://www.plasticsurgery.org/reconstructive-procedures/breast-reconstruction/recovery.

American Society of Plastic Surgeons. What results should I expect after breast reconstruction? Date last reviewed/updated not stated. Accessed September 20, 2019. Available at https://www.plasticsurgery.org/reconstructive-procedures/breast-reconstruction/results.

BAKER 2018
Baker BG, Irri R, MacCallum V, Chattopadhyay R, Murphy J, Harvey JR. A Prospective Comparison of Short-Term Outcomes of Subpectoral and Prepectoral Strattice-Based Immediate Breast Reconstruction. Plast Reconstr Surg. 2018 May;141(5):1077-1084. PubMed

BERNINI 2015
Bernini M, Calabrese C, Cecconi L, Santi C, Gjondedaj U, Roselli J, Nori J, Fausto A, Orzalesi L, Casella D. Subcutaneous Direct-to-Implant Breast Reconstruction: Surgical, Functional, and Aesthetic Results after Long-Term Follow-Up. Plast Reconstr Surg Glob Open. 2016 Jan 7;3(12):e574. doi: 10.1097/GOX.0000000000000533. eCollection 2015 Dec. PubMed

BETTINGER 2017
Bettinger LN, Waters LM, Reese SW, Kutner SE, Jacobs DI. Comparative Study of Prepectoral and Subpectoral Expander-Based Breast Reconstruction and Clavien IIIb Score Outcomes. Plast Reconstr Surg Glob Open. 2017 Jul 26;5(7):e1433. PubMed

BREASTCANCER.ORG 2019
Breastcancer.org. Dynamic Distortion. Last reviewed/modified Marcy 7, 2019. Accessed September 20, 2019. Available at https://www.breastcancer.org/treatment/surgery/reconstruction/corrective/dynamic-distortion.

Breastcancer.org. Implant Reconstruction. Last reviewed/modified August 29, 2019. Accessed September 20, 2019. Available at https://www.breastcancer.org/treatment/surgery/reconstruction/types/implants.

Breastcancer.org. Implant Reconstruction: What to Expect. Last reviewed/modified August 29, 2019. Accessed September 20, 2019. Available at https://www.breastcancer.org/treatment/surgery/reconstruction/types/implants/what-to-expect.

Breastcancer.org. Implant Surgery Risks. Last reviewed/modified August 8, 2019. Accessed September 20, 2019. Available at https://www.breastcancer.org/treatment/surgery/reconstruction/types/implants/risks.

Breastcancer.org. Mastectomy: What to Expect. Last reviewed/modified February 27, 2019. Accessed September 20, 2019. Available at https://www.breastcancer.org/treatment/surgery/mastectomy/expectations.

CATTELANI 2018
Cattelani L, Polotto S, Arcuri MF, Pedrazzi G, Linguadoca C, Bonati E. One-Step Prepectoral Breast Reconstruction With Dermal Matrix-Covered Implant Compared to Submuscular Implantation: Functional and Cost Evaluation. Clin Breast Cancer. 2018 Aug;18(4):e703-e711. doi: 10.1016/j.clbc.2017.11.015. Epub 2017 Dec 2. PubMed

CHANDARANA 2018
Chandarana MN, Jafferbhoy S, Marla S, Soumian S, Narayanan S. Acellular dermal matrix in implant based immediate breast reconstructions: a comparison of prepectoral and subpectoral approach. Gland Surg. 2018 Aug;7(Suppl 1):S64-S69. PubMed

CHOPRA 2016
Chopra K, Houssock C, Cai SS, et al. Submuscular versus prepectoral immediate implant based breast reconstruction. Northeastern Society of Plastic Surgeons 33rd Annual Meeting abstracts. Available at http://meeting.nesps.org/abstracts/2016/57.cgi.

COX 2018
Cox S, Bozzuto L, Bartholomew A, et al. Prepectoral versus retropectoral implant-based reconstruction following nipple-sparing mastectomy and adjuvant radiation therapy. Ann Surg Oncol 2018;25(2):357e8. (Available as abstract in conference book on pg 357-8 at https://www.breastsurgeons.org/docs/resources/old_meetings/2018_Official_Proceedings_ASBrS.pdf)

DAVILA 2013
Davila AA, Mioton LM, Chow G, Wang E, Merkow RP, Bilimoria KY, Fine N, Kim JY. Immediate two-stage tissue expander breast reconstruction compared with one-stage permanent implant breast reconstruction: a multi-institutional comparison of short-term complications. J Plast Surg Hand Surg. 2013 Oct;47(5):344-9. doi: 10.3109/2000656X.2013.767202. Epub 2013 Apr 3.

DOUGLAS 2018
Douglas BK. Subpectoral vs. Prepectoral Breast Reconstruction Surgery. Maurer Foundation. Last reviewed/updated August 13, 2018. Accessed September 20, 2019. Available at https://www.maurerfoundation.org/subpectoral-vs-prepectoral-breast-reconstruction-surgery/.

LAM 2018

Lam TC, Borotkanics R, Hsieh F, Salinas J, Boyages J. Immediate Two-Stage Prosthetic Breast Reconstruction Failure: Radiation Is Not the Only Culprit. Plast Reconstr Surg. 2018 Jun;141(6):1315-1324. doi: 10.1097/PRS.0000000000004358.

LI 2019
Li L, Su Y, Xiu B, Huang X, Chi W, Hou J, Zhang Y, Tian J, Wang J, Wu J. Comparison of prepectoral and subpectoral breast reconstruction after mastectomies: A systematic review and meta analysis. Eur J Surg Oncol. 2019 Sep;45(9):1542-1550. Epub 2019 May 14.

MAYO CLINIC 2019
Mayo Clinic. Breast Reconstruction with Implants. Last reviewed/updated January 3, 2019. Accessed September 20, 2019. Available at https://www.mayoclinic.org/tests-procedures/breast-reconstruction-implants/about/pac-20384934?p=1.

MEMORIAL SLOAN KETTERING CANCER CENTER ND
Memorial Sloan Kettering Cancer Center. Breast Reconstruction. Date last reviewed/updated not stated. Accessed September 20, 2019. Available at https://www.mskcc.org/cancer-care/types/breast/reconstruction-prosthesis#what-is-recovery-like-after-breast-reconstruction-.

PITTMAN 2017
Pittman T. What You Should Know About Pre-Pectoral Breast Reconstruction. MedStar Georgetown Cancer Institute. Last reviewed/updated January 6, 2017. Accessed September 20, 2019.

SBITANY 2017
Sbitany H, Piper M, Lentz R. Prepectoral Breast Reconstruction: A Safe Alternative to Submuscular Prosthetic Reconstruction following Nipple-Sparing Mastectomy. Plast Reconstr Surg. 2017 Sep;140(3):432-443. PubMed

SINNOTT 2018
Sinnott CJ, Persing SM, Pronovost M, Hodyl C, McConnell D, Ott Young A. Impact of Postmastectomy Radiation Therapy in Prepectoral Versus Subpectoral Implant-Based Breast Reconstruction. Ann Surg Oncol. 2018 Oct;25(10):2899-2908. PubMed

SUSAN G. KOMEN FOUNDATION 2019
Susan G. Komen Foundation. Breast Reconstruction. Last reviewed/updated June 7, 2019. Accessed September 20, 2019. Available at https://ww5.komen.org/BreastCancer/BreastReconstruction.html.

TUTT 2017
Tutt B. Advances in Breast Reconstruction. OncoLog, October 2017 (Volume 62, Issue 10), MD Anderson Cancer Center. Accessed September 20, 2019. Available at https://www.mdanderson.org/publications/oncolog/advances-in-breast-reconstruction.h19-1591413.html.

WALIA 2018
Walia GS, Aston J, Bello R, Mackert GA, Pedreira RA, Cho BH, Carl HM, Rada EM, Rosson GD, Sacks JM. Prepectoral Versus Subpectoral Tissue Expander Placement: A Clinical and Quality of Life Outcomes Study. Plast Reconstr Surg Glob Open. 2018 Apr 20;6(4):e1731. doi: 10.1097/GOX.0000000000001731. eCollection 2018 Apr. PubMed

WEBMD MEDICAL REFERENCE 2017
WebMD Medical Reference. Breast Reconstruction Surgery. Last reviewed/modified August 11, 2017. Accessed September 20, 2019. Available at https://www.webmd.com/breast-cancer/breast-reconstruction-after-mastectomy#1.