



## Topic Brief: Breast Reconstruction after Mastectomy

**Date:** 8/14/2019

**Nomination Number:** 0838

**Purpose:** This document summarizes the information addressing a nomination submitted on 1/28/2019 through the Effective Health Care Website. This information was used to inform the Evidence-based Practice Center (EPC) Program decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most suitable.

**Issue:** Breast cancer is the leading type of cancer affecting women with over a quarter million new cases of invasive breast cancer diagnosed in 2019<sup>1</sup>. Cancer treatment frequently requires a single or double mastectomy and nearly half of women undergoing a mastectomy choose to pursue breast reconstruction following mastectomy. As growing numbers of women elect breast reconstruction, this calls for development of more effective breast reconstruction options that are grounded in solid clinical evidence and allow for a patient centered decision-making process.

### Program Decision:

The EPC Program will develop a new systematic review based on this nomination. The scope of this topic will be further developed in the refinement phase. When key questions have been drafted, they will be posted on the AHRQ Web site and open for public comment. To sign up for notification when this and other Effective Health Care (EHC) Program topics are posted for public comment, please go to <https://effectivehealthcare.ahrq.gov/email-updates>.

### Key Findings

We found no systematic reviews pertaining to this nomination. We found sufficient evidence in primary studies for all questions but Question 3, for which there was only one primary study. A new evidence review would not be duplicative of an existing product (see Table 2, Systematic Reviews) and there is sufficient primary evidence for a new systematic review.

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### Background

Among women in the U.S., breast cancer is the most common cancer by new cancer diagnoses, and second highest cause of cancer deaths after lung and bronchus cancer<sup>2</sup>. Each year there are about 237,000 diagnoses in women and 41,000 deaths. While breast cancer is more common in women, breast cancer can also affect men. About 2,100 cases of breast cancer are diagnosed in men each year, and about 450 men die from it<sup>3</sup>. Age, family history, and being a carrier of certain genes such as BRCA1 and BRCA2 are risk factors associated with breast cancer<sup>4</sup>. Surgery is both an option to patients as a standard cancer treatment by removing cancerous tissue, and as a prophylactic measure for people who are at high-risk<sup>5</sup>. Surgical procedures include lumpectomy, where the cancer and surrounding tissue is removed but the breast remains intact, and mastectomy, where the entire breast is removed<sup>6</sup>.

Following a mastectomy, breast reconstruction is an option. According to the American Society of Plastic Surgeons (ASPS), about 106,000 women had breast reconstruction surgeries in 2017<sup>7</sup>. Furthermore, the Women's Health and Cancer Rights Act of 1998 requires that health insurance that covers mastectomies must also provide coverage for reconstruction<sup>8</sup>. While there is a variety of techniques and procedures that can be performed for reconstruction, these procedures fall under two main categories: implant-based or autologous tissue based<sup>9</sup>, with implant-based reconstruction being more popular<sup>10</sup>. Variation exists within implant-based reconstruction, including different textures of implants, shapes, materials, and volumes; and implant placement (sub vs. prepectoral), and use of acellular dermal matrix<sup>11</sup>. Prepectoral technique of implant-based breast reconstruction avoids many of the disadvantages of the traditional subpectoral technique including the need for pectoralis muscle dissection, animation deformity and a costly two stage reconstruction, however evidence regarding comparative effectiveness of these techniques is lacking. Acellular dermal matrix (ADM) has been extensively used in implant-based breast reconstruction because of improved aesthetic outcomes, decreased incidence of capsular contractures, reduced need for tissue expanders and other benefits predominantly reported from retrospective cohort studies and single surgeon experiences. However, data from several randomized controlled trials<sup>12-14</sup> have raised concerns regarding a higher incidence of postoperative complications associated with the use of ADM in implant-based breast reconstruction, necessitating reliable evidence based guidance regarding the safety and effectiveness of the use of ADM. Implant-based techniques can be one-stage direct-to-implant or two-stage where a tissue-expander is placed first, and the implant is placed in a separate follow-up procedure<sup>10</sup>.

Regardless of reconstruction modality after mastectomy, timing of the reconstruction also varies and can affect outcomes. Immediate reconstruction refers to a breast reconstruction procedure done at the time of mastectomy<sup>15</sup>. For the purposes of this brief, we define immediate reconstruction consistent with the literature to include both one stage or two-stage (if a tissue-expander is placed at that time). Delayed reconstruction refers to breast reconstruction performed any time after mastectomy<sup>15</sup>. Both immediate and delayed reconstruction have risks associated with them. Furthermore, adjuvant therapies such as chemotherapy or radiation may be done before or after reconstruction surgery, and can be associated with multiple complications such as infection, seroma formation, tissue necrosis, and capsular contracture<sup>16</sup>.

Decision-making on the type of reconstruction and timing of reconstruction and/or adjuvant therapies are complex and dependent on cancer type, prognosis, and patient preferences. Therefore, current guidelines for implant-based reconstruction are very important.

## **Nomination Summary**

The American Society of Plastic Surgeons (ASPS) nominated this topic for a systematic review to inform and update their 2013 guidelines on breast reconstruction with expanders and implants as well as the 2017 guideline on autologous breast reconstruction.

The initial topic nomination had a broad scope and included questions regarding immediate versus delayed implant-based breast reconstruction, screening for cancer after reconstruction, reconstruction with adjuvant chemotherapy, and comparing different autologous reconstruction surgical techniques. After clarifying the key areas of the nominator's interest, we narrowed the scope to focus on implant-based breast reconstruction with particular emphasis on the comparative effectiveness of a mediated versus delayed implant-based breast reconstruction (Question 1), the comparative effectiveness of immediate versus delayed timing of implant-based breast reconstruction with respect to radiation treatment (Question 2) and patient risk factors associated with requiring the repeat surgery (Question 3).

Our subsequent literature search identified that the evidence base was too small for systematic review, which was likely a consequence of the narrowly defined scope. We identified no relevant studies to address the Question 1, only a single retrospective study to address the Question 2 and 18 primary studies to address the Question 3.

We attempted to re-broaden the topic scope by revisiting our discussion with the nominator and by engaging input from an expert breast surgeon. Based on these discussions and identifying the areas of greatest need for evidence-based guidance, we then developed a revised set of six Questions. Five questions focused on various aspects of implant-based breast reconstruction (as further described in the next section) and the sixth question focused on the comparative effectiveness of different surgical techniques/flap types utilized in autologous breast reconstruction.

### **Scope**

- 1) For adult women undergoing a mastectomy for breast cancer, what is the comparative effectiveness of implant-based vs autologous breast reconstruction?
- 2) For adult women undergoing a mastectomy and requiring one or more of the following oncologic treatment(s) for breast cancer, what is the optimal time for implant-based breast reconstruction with respect to a) chemotherapy and b) radiation?
- 3) For adult women undergoing an implant-based breast reconstruction following a mastectomy, what is the comparative effectiveness of different types of implants (e.g., silicone, saline)?
- 4) For adult women undergoing an implant-based breast reconstruction following a mastectomy, what is the comparative effectiveness of prepectoral vs subpectoral implant placement technique?
- 5) For adult women undergoing an implant-based breast reconstruction following a mastectomy, what is the comparative effectiveness of implant-based breast reconstruction with vs without the use of an acellular dermal matrix (ADM) in the reconstruction procedure?
- 6) For adult women undergoing an autologous breast reconstruction following a mastectomy, what is the comparative effectiveness of different surgical techniques/flap types of autologous breast reconstruction?

**Table 1a.** Questions and PICO (population, intervention, comparator, outcome)

<b>Questions</b>	1) For adult women undergoing a mastectomy for breast cancer, what is the comparative effectiveness of implant-based vs autologous breast reconstruction?	2) What is the optimal time for implant-based breast reconstruction with respect to a) chemotherapy and b) radiation?	3) What is the comparative effectiveness of different types of implants (e.g., silicone, saline)?
<b>Population</b>	Adult women undergoing a mastectomy who are eligible for either implant-based or autologous breast reconstruction	Adult women undergoing a mastectomy and requiring an oncologic treatment for breast cancer who are eligible for an implant-based breast reconstruction	Adult women undergoing a mastectomy who are eligible for an implant-based breast reconstruction using different breast implant types
<b>Interventions</b>	Implant based breast reconstruction	Implant based breast reconstruction performed before either oncologic treatment	Implant based breast reconstruction with breast implants (e.g., silicone, saline etc.)
<b>Comparators</b>	Autologous breast reconstruction	Implant based breast reconstruction performed after oncologic treatment	Other implant types ((e.g., silicone, saline etc.)
<b>Outcomes</b>	<p>Benefits:</p> <ul style="list-style-type: none"> <li>- Patient satisfaction (e.g., aesthetics)</li> <li>- Health-related quality of life</li> </ul> <p>Harms:</p> <ul style="list-style-type: none"> <li>- Mortality</li> <li>- Repeat hospitalization</li> <li>- Any complication<sup>1</sup></li> <li>- Repeat surgery</li> </ul>	<p>Benefits:</p> <ul style="list-style-type: none"> <li>- Patient satisfaction (e.g., aesthetics)</li> <li>- Health-related quality of life</li> </ul> <p>Harms:</p> <ul style="list-style-type: none"> <li>- Mortality</li> <li>- Repeat hospitalization</li> <li>- Any complication</li> <li>- Repeat surgery</li> </ul>	<p>Benefits:</p> <ul style="list-style-type: none"> <li>- Patient satisfaction (e.g., aesthetics)</li> <li>- Health-related quality of life</li> </ul> <p>Harms:</p> <ul style="list-style-type: none"> <li>- Mortality</li> <li>- Repeat hospitalization</li> <li>- Any complication</li> <li>- Repeat surgery</li> </ul>

<sup>1</sup> Any complication is defined as an adverse postoperative surgery related event requiring additional treatment (infection, hematoma, wound dehiscence, skin necrosis, seroma, capsular contracture, implant malposition, acute partial flap necrosis, chronic fat necrosis, donor site - related complications, DVT, PE).

**Table 1b.** Questions and PICO (population, intervention, comparator, outcome)

<b>Questions</b>	4) What is the comparative effectiveness of prepectoral vs subpectoral implant placement technique?	5) What is the comparative effectiveness of implant-based breast reconstruction with vs without the use of an acellular dermal matrix (ADM) in the reconstruction procedure?	6) What is the comparative effectiveness of different surgical techniques/flap types of autologous breast reconstruction?
<b>Population</b>	Adult women undergoing a mastectomy who are eligible for an implant-based breast reconstruction using either prepectoral or subpectoral implant placement technique	Adult women undergoing a mastectomy who are eligible for an implant-based breast reconstruction that uses ADM in the reconstruction procedure	Adult women undergoing a mastectomy who are eligible for an autologous breast reconstruction using either type of surgical procedure/flap type
<b>Interventions</b>	Implant based breast reconstruction using prepectoral implant placement technique	Implant based breast reconstruction that uses an ADM in the reconstruction procedure	Autologous breast reconstruction using one of the following surgical techniques/flap types: <ol style="list-style-type: none"> <li>1) Pedicled transverse rectus abdominis myocutaneous (pTRAM) flap</li> <li>2) Free transverse rectus abdominis myocutaneous (fTRAM) flap</li> <li>3) Deep inferior epigastric perforator (DIEP) flap</li> <li>4) Latissimus dorsi (LD) flap</li> <li>5) Superficial inferior epigastric artery perforator (SIEA) flap</li> </ol>
<b>Comparators</b>	Implant based breast reconstruction using subpectoral implant placement technique	Implant based breast reconstruction that does not use an ADM in the reconstruction procedure	Other surgical technique/flap types specified under interventions
<b>Outcomes</b>	<p>Benefits:</p> <ul style="list-style-type: none"> <li>- Patient satisfaction (e.g., aesthetics)</li> <li>- Health-related quality of life</li> </ul> <p>Harms:</p> <ul style="list-style-type: none"> <li>- Mortality</li> <li>- Repeat hospitalization</li> <li>- Any complication</li> <li>- Repeat surgery</li> </ul>	<p>Benefits:</p> <ul style="list-style-type: none"> <li>- Patient satisfaction (e.g., aesthetics)</li> <li>- Health-related quality of life</li> </ul> <p>Harms:</p> <ul style="list-style-type: none"> <li>- Mortality</li> <li>- Repeat hospitalization</li> <li>- Any complication</li> <li>- Repeat surgery</li> </ul>	<p>Benefits:</p> <ul style="list-style-type: none"> <li>- Patient satisfaction (e.g., aesthetics)</li> <li>- Health-related quality of life</li> </ul> <p>Harms:</p> <ul style="list-style-type: none"> <li>- Mortality</li> <li>- Repeat hospitalization</li> <li>- Any complication</li> <li>- Repeat surgery</li> </ul>

## Assessment Methods

See Appendix A.

### Summary of Literature Findings

We identified no systematic reviews or protocols for completed or in-process systematic reviews that addressed the current nomination. We identified between 1 and 29 primary studies for each of the Questions 1 through 6 based on our targeted literature scan.

- For Question 1, we identified 26 primary studies<sup>17-38</sup>, including 1 RCT, evaluating the risks and benefits of implant-based compared to autologous forms of breast reconstruction. The identified studies assessed aesthetic outcomes of the implant base compared to autologous breast reconstruction and differences in healthcare resource utilization following each type of procedure, rates of postoperative complications, including reconstructive failures and required secondary breast surgeries within three years for each type of the two breast reconstruction procedures.
- For Question 2, we identified 24 primary studies<sup>12-14, 20, 39-58</sup> assessing the optimal timing of implant-based breast reconstruction with respect to either chemotherapy or radiation in women undergoing an implant-based breast reconstruction who would require oncologic treatment.
- For Question 3 we identified a single retrospective review<sup>59</sup> assessing the incidence of capsular contracture as a postoperative complication of using polyurethane-based implants in breast reconstruction following a mastectomy.
- For Question 4 we identified six primary studies<sup>60-65</sup>. One nonrandomized prospective study compared short-term postoperative outcomes, including postoperative pain and quality of life at three months among patients with subpectoral and prepectoral implant-based immediate breast reconstruction. Other retrospective studies assessed longer-term postoperative complications with subpectoral compared to prepectoral techniques of implant-based breast reconstruction including capsular contractures, other postoperative breast deformities and functional shoulder biomechanics.
- For Question 5 we identified 20 primary studies<sup>12-14, 30, 45, 46, 51, 66-78</sup> assessing the safety and effectiveness of acellular dermal matrix use in implant-based reconstruction. The identified studies evaluated postoperative outcomes such as rates of minor postoperative complications, including seroma, skin necrosis, wound dehiscence, wound inflammation and infection, major postoperative complications requiring a repeat operation and patient quality of life and satisfaction rates.
- For Question 6 we identified 29 primary studies<sup>18, 22, 26, 62, 79-102</sup> including numerous retrospective reviews comparing postoperative outcomes of autologous breast reconstruction using various surgical techniques, including perioperative and short-term postoperative outcomes such as prolonged operative times, length of stay and longer term postoperative outcomes such as patient physical well-being and breast satisfaction.

**Table 2.** Literature identified for each Question

	<b>Systematic reviews (7/2016-7/2019)</b>	<b>Primary studies (7/2014-7/2019)</b>
Question 1: For adult women undergoing a mastectomy for breast cancer, what is the comparative effectiveness of implant-based vs autologous breast reconstruction?	Total: 0	Total: 26 <ul style="list-style-type: none"> <li>• RCT: 1</li> <li>• Observational: 25</li> </ul> Clinicaltrials.gov <ul style="list-style-type: none"> <li>• Recruiting: 0</li> </ul>

	<b>Systematic reviews (7/2016-7/2019)</b>	<b>Primary studies (7/2014-7/2019)</b>
Question 2: For adult women undergoing implant-based breast reconstruction after mastectomy and requiring radiation for breast cancer treatment, what are the benefits and harms of immediate versus delayed reconstruction?	Total: 0	Total: 24 <ul style="list-style-type: none"> <li>• RCT: 2</li> <li>• Observational: 22</li> </ul> Clinicaltrials.gov <ul style="list-style-type: none"> <li>• Recruiting: 0</li> </ul>
Question 3: For adult women undergoing an implant-based breast reconstruction following a mastectomy, what is the comparative effectiveness of different types of implants (e.g., silicone, saline)?	Total: 0	Total: 1 <ul style="list-style-type: none"> <li>• RCT: 0</li> <li>• Observational: 1</li> </ul> Clinicaltrials.gov <ul style="list-style-type: none"> <li>• Recruiting: 0</li> </ul>
Question 4: For adult women undergoing an implant-based breast reconstruction following a mastectomy, what is the comparative effectiveness of prepectoral vs subpectoral implant placement technique?	Total: 0	Total: 6 <ul style="list-style-type: none"> <li>• RCT: 0</li> <li>• Observational: 6</li> </ul> Clinicaltrials.gov <ul style="list-style-type: none"> <li>• Recruiting: 0</li> </ul>
Question 5: For adult women undergoing an implant-based breast reconstruction following a mastectomy, what is the comparative effectiveness of implant-based breast reconstruction with vs without the use of an acellular dermal matrix (ADM) in the reconstruction procedure?	Total: 0	Total: 20 <ul style="list-style-type: none"> <li>• RCT: 4</li> <li>• Observational: 16</li> </ul> Clinicaltrials.gov <ul style="list-style-type: none"> <li>• Recruiting: 0</li> </ul>
Question 6: For adult women undergoing an autologous breast reconstruction following a mastectomy, what is the comparative effectiveness of different surgical techniques/flap types of autologous breast reconstruction?	Total: 0	Total: 29 <ul style="list-style-type: none"> <li>• RCT: 0</li> <li>• Observational: 29</li> </ul> Clinicaltrials.gov <ul style="list-style-type: none"> <li>• Recruiting: 0</li> </ul>

*Abbreviations:* RCT = randomized controlled trial.

See Appendix B for detailed assessments of all EPC selection criteria.

## Summary of Selection Criteria Assessment

We identified no systematic reviews to address any of the six Questions, however Question 1, Question 2, Question 4, Question 5 and Question 6 are largely covered by the identified primary studies.

## Related Resources

We identified one Cochrane database systematic review in our duplication search<sup>11</sup>. While this particular review did not meet our duplication search criteria having been conducted earlier than within the past three years, it may nevertheless be a valuable resource to the nominator as the review provides a high-quality assessment of comparative effectiveness of different types of breast implants used in implant-based breast reconstruction.

Additionally, we identified another good quality systematic review<sup>103</sup> that addressed the Question 1 for a subpopulation of obese women seeking breast reconstruction.

Finally, we found one small randomized study<sup>104</sup> assessing the effectiveness of a novel decision aid aimed to provide decision support and structured guidance for surgeon – patient led decision-making process in selecting either implant-based or autologous type of breast reconstruction surgery. The study evaluated the impact of using this decision aid on quality of life related outcomes as measured by the BREAST-Q and other postoperative patient surveys.

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## **Appendix A: Methods**

We assessed nomination for priority of a systematic review or other AHRQ Effective Health Care report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix B for detailed description of the criteria.

### **Appropriateness and Importance**

We assessed the nomination for appropriateness and importance.

### **Desirability of New Review/Absence of Duplication**

We searched for high-quality, completed or in-process evidence reviews published in the last three years from search date on July 9, 2019 on the questions of the nomination from these sources:

- AHRQ: Evidence reports and technology assessments
  - AHRQ Evidence Reports <https://www.ahrq.gov/research/findings/evidence-based-reports/index.html>
  - EHC Program <https://effectivehealthcare.ahrq.gov/>
  - AHRQ Technology Assessment Program <https://www.ahrq.gov/research/findings/ta/index.html>
- US Department of Veterans Affairs Products publications
  - Evidence Synthesis Program <https://www.hsrd.research.va.gov/publications/esp/>
  - VA/Department of Defense Evidence-Based Clinical Practice Guideline Program <https://www.healthquality.va.gov/>
- Cochrane Systematic Reviews <https://www.cochranelibrary.com/>
- PROSPERO Database (international prospective register of systematic reviews and protocols) <http://www.crd.york.ac.uk/prospéro/>
- PubMed <https://www.ncbi.nlm.nih.gov/pubmed/>
- Health Systems Evidence
- PDQ Evidence
- Epistemonikos

### **Impact of a New Evidence Review**

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

### **Feasibility of New Evidence Review**

We conducted a literature search in PubMed from the last five years from July 16, 2014 through July 16, 2019. We identified 42 abstracts for Question 1, 119 abstracts for Question 2, 14 abstracts for Question 3, 36 abstracts for Question 4, 58 abstracts for Question 5 and 52 abstracts for Question 6. We reviewed all identified abstracts for each Question for inclusion.

## Search strategy

### Question 1

**For adult women undergoing a mastectomy for breast cancer, what is the comparative effectiveness of implant-based vs autologous breast reconstruction?**

mastectomy	("Mastectomy"[Mesh]) OR (((Mastectomy[Title/Abstract] OR Mammectomies[Title/Abstract])) OR (Mastectomies[Title/Abstract] OR Mammectomy[Title/Abstract]))
breast reconstruction	("Mammaplasty"[Mesh]) OR ((((((Mammaplasties[Title/Abstract]) OR Mammoplasty[Title/Abstract]) OR Mammoplasties[Title/Abstract]) OR Breast Reconstruction[Title/Abstract]) OR Breast Reconstructions[Title/Abstract]) OR Mammaplasty[Title/Abstract])
implant-based	((("Breast Implants"[Mesh]) OR "Breast Implantation"[Mesh])) OR (((implant[Title/Abstract] OR implants[Title/Abstract] OR implantation[Title/Abstract] OR prosthesis[Title/Abstract] OR prostheses[Title/Abstract]))) AND breast[Title/Abstract])
autologous	((("Transplantation, Autologous"[Mesh]) OR "Autografts"[Mesh])) OR (((Autotransplantation[Title/Abstract] OR Autotransplantations[Title/Abstract] OR Autografting[Title/Abstract] OR Autograftings[Title/Abstract] OR Autologous OR)) OR (Autograft[Title/Abstract] OR Autotransplants[Title/Abstract] OR Autotransplant[Title/Abstract]))
<b>N=138 SR=2 RCT=40 Other=96</b>	Filters activated: published in the last 5 years, English, Female, Adult: 19+ years.

<p>Question 2 For adult women undergoing a mastectomy and requiring one or more of the following oncologic treatment(s) for breast cancer, what is the optimal time for implant-based breast reconstruction?</p>	
mastectomy	("Mastectomy"[Mesh]) OR (((Mastectomy[Title/Abstract] OR Mammectomies[Title/Abstract])) OR (Mastectomies[Title/Abstract] OR Mammectomy[Title/Abstract]))
breast reconstruction	("Mammaplasty"[Mesh]) OR ((((((Mammaplasties[Title/Abstract]) OR Mammoplasty[Title/Abstract]) OR Mammoplasties[Title/Abstract]) OR Breast Reconstruction[Title/Abstract]) OR Breast Reconstructions[Title/Abstract]) OR Mammaplasty[Title/Abstract])
implant-based	((("Breast Implants"[Mesh]) OR "Breast Implantation"[Mesh])) OR (((implant[Title/Abstract] OR implants[Title/Abstract] OR implantation[Title/Abstract] OR prosthesis[Title/Abstract] OR prostheses[Title/Abstract]))) AND breast[Title/Abstract])
optimal time	("Time Factors"[Mesh]) OR ((time[Title/Abstract] OR timing[Title/Abstract] OR early[Title/Abstract] OR late[Title/Abstract] OR Immediate[Title/Abstract] OR delayed[Title/Abstract]))
<b>N=356 SR=3 RCT=116 Other=237</b>	Filters activated: published in the last 5 years, English, Female, Adult: 19+ years.

<p>Question 3</p> <p>For adult women undergoing an implant-based breast reconstruction following a mastectomy, what is the comparative effectiveness of different types of implants (e.g., silicone, saline)?</p>	
mastectomy	("Mastectomy"[Mesh]) OR (((Mastectomy[Title/Abstract] OR Mammectomies[Title/Abstract])) OR (Mastectomies[Title/Abstract] OR Mammectomy[Title/Abstract]))
breast reconstruction	("Mammoplasty"[Mesh]) OR ((((((Mammoplasties[Title/Abstract] OR Mammoplasty[Title/Abstract] OR Mammoplasties[Title/Abstract] OR Breast Reconstruction[Title/Abstract] OR Breast Reconstructions[Title/Abstract] OR Mammoplasty[Title/Abstract]))
implant-based	((("Breast Implants"[Mesh]) OR "Breast Implantation"[Mesh])) OR (((implant[Title/Abstract] OR implants[Title/Abstract] OR implantation[Title/Abstract] OR prosthesis[Title/Abstract] OR prostheses[Title/Abstract]))) AND breast[Title/Abstract])
types of implants (e.g., silicone, saline)	(((((("Silicones"[Mesh]) OR "Saline Solution"[Mesh]) OR "Prosthesis Design"[Mesh]))) OR ((Silicone[Title/Abstract] OR silicones[Title/Abstract] OR saline[Title/Abstract] OR "gummy bear"[Title/Abstract] OR nanomaterials[Title/Abstract]))
<p><b>N=48</b>  <b>SR=1</b>  <b>RCT=13</b>  <b>Other=34</b></p>	Filters activated: published in the last 5 years, English, Female, Adult: 19+ years.

<p>Question 4</p> <p>For adult women undergoing an implant-based breast reconstruction following a mastectomy, what is the comparative effectiveness of prepectoral vs subpectoral implant placement technique?</p>	
mastectomy	("Mastectomy"[Mesh]) OR (((Mastectomy[Title/Abstract] OR Mammectomies[Title/Abstract])) OR (Mastectomies[Title/Abstract] OR Mammectomy[Title/Abstract]))
breast reconstruction	("Mammoplasty"[Mesh]) OR ((((((Mammoplasties[Title/Abstract] OR Mammoplasty[Title/Abstract] OR Mammoplasties[Title/Abstract] OR Breast Reconstruction[Title/Abstract] OR Breast Reconstructions[Title/Abstract] OR Mammoplasty[Title/Abstract]))
implant-based	((("Breast Implants"[Mesh]) OR "Breast Implantation"[Mesh])) OR (((implant[Title/Abstract] OR implants[Title/Abstract] OR implantation[Title/Abstract] OR prosthesis[Title/Abstract] OR prostheses[Title/Abstract]))) AND breast[Title/Abstract])
prepectoral vs subpectoral implant placement technique	("Breast Implantation/methods"[Mesh]) OR ((submuscular[Title/Abstract] OR prepectoral[Title/Abstract] OR Muscle-sparing[Title/Abstract] OR Subpectoral[Title/Abstract] OR dual-plane[Title/Abstract]))
<p><b>N=130</b>  <b>SR=0</b>  <b>RCT=36</b>  <b>Other=94</b></p>	Filters activated: published in the last 5 years, English, Female, Adult: 19+ years.

<p>Question 5</p> <p>For adult women undergoing an implant-based breast reconstruction following a mastectomy, what is the comparative effectiveness of implant- based breast reconstruction with vs without the use of an acellular dermal matrix (ADM) in the reconstruction procedure?</p>	
mastectomy	("Mastectomy"[Mesh]) OR (((Mastectomy[Title/Abstract] OR Mammectomies[Title/Abstract])) OR (Mastectomies[Title/Abstract] OR Mammectomy[Title/Abstract]))
breast reconstruction	("Mammoplasty"[Mesh]) OR ((((((Mammoplasties[Title/Abstract] OR Mammoplasty[Title/Abstract] OR Mammoplasties[Title/Abstract] OR Breast Reconstruction[Title/Abstract] OR Breast Reconstructions[Title/Abstract] OR Mammoplasty[Title/Abstract]))
implant-based	((("Breast Implants"[Mesh]) OR "Breast Implantation"[Mesh])) OR (((implant[Title/Abstract] OR implants[Title/Abstract] OR implantation[Title/Abstract] OR prosthesis[Title/Abstract] OR prostheses[Title/Abstract]))) AND breast[Title/Abstract])
acellular dermal matrix (ADM)	((("Acellular Dermis"[Mesh]) OR "Tissue Expansion Devices"[Mesh])) OR (((acellular[Title/Abstract] OR dermal[Title/Abstract] OR peritoneal[Title/Abstract])) AND (matrices[Title/Abstract] OR matrix[Title/Abstract]))
<p><b>N=173</b></p> <p><b>SR=0</b></p> <p><b>RCT=58</b></p> <p><b>Other=115</b></p>	Filters activated: published in the last 5 years, English, Female, Adult: 19+ years.

<p>Question 6</p> <p>For adult women undergoing an autologous breast reconstruction following a mastectomy, what is the comparative effectiveness of different surgical techniques/flap types of autologous breast reconstruction?</p>	
mastectomy	("Mastectomy"[Mesh]) OR (((Mastectomy[Title/Abstract] OR Mammectomies[Title/Abstract])) OR (Mastectomies[Title/Abstract] OR Mammectomy[Title/Abstract]))
breast reconstruction	("Mammoplasty"[Mesh]) OR ((((((Mammoplasties[Title/Abstract] OR Mammoplasty[Title/Abstract] OR Mammoplasties[Title/Abstract] OR Breast Reconstruction[Title/Abstract] OR Breast Reconstructions[Title/Abstract] OR Mammoplasty[Title/Abstract]))
autologous	((("Transplantation, Autologous"[Mesh]) OR "Autografts"[Mesh])) OR (((Autotransplantation[Title/Abstract] OR Autotransplantations[Title/Abstract] OR Autografting[Title/Abstract] OR Autograftings[Title/Abstract] OR Autologous OR)) OR (Autograft[Title/Abstract] OR Autotransplants[Title/Abstract] OR Autotransplant[Title/Abstract]))
surgical techniques/flap	(((((("Surgical Flaps"[Mesh]) OR "Transplantation, Autologous/methods"[Mesh] OR "Adipose Tissue/transplantation"[Mesh] OR "Tissue Transplantation/methods"[Mesh])) OR (((flap[Title/Abstract] OR flaps[Title/Abstract])) AND (surgical[Title/Abstract] OR surgery[Title/Abstract]))

<b>N=204</b> <b>SR=1</b> <b>RCT=51</b> <b>Other=152</b>	Filters activated: published in the last 5 years, English, Female, Adult: 19+ years.
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### **Value**

We assessed the nomination for value. We considered whether or not the clinical, consumer, or policymaking context had the potential to respond with evidence-based change; and if a partner organization would use this evidence review to influence practice.

## Appendix B. Selection Criteria Assessment

Selection Criteria	Assessment
<b>1. Appropriateness</b>	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes
1b. Is the nomination a request for an evidence report?	Yes
1c. Is the focus on effectiveness or comparative effectiveness?	Yes
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes
<b>2. Importance</b>	
2a. Represents a significant disease burden; large proportion of the population	Yes, approximately 106,000 women underwent breast reconstruction following a mastectomy in 2017, and implant-based and autologous forms of breast reconstruction are the two most widely used modalities of breast reconstruction.
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes, breast cancer is the leading cancer cause among women with 266,000 hundred and 20 cases of invasive breast cancer diagnosed in 2018. To put it another way, 1 in 8 American women (approximately 12%) will develop invasive breast cancer during their lifetime. Breast reconstruction following a mastectomy is an important physical and emotional aspect of cancer treatment.
2c. Incorporates issues around both clinical benefits and potential clinical harms	Yes
2d. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes, after the passage of the Women's Health and Cancer Rights Act of 1998, health insurance plans that provide coverage for mastectomy must also provide coverage for breast reconstruction procedures.
<b>3. Desirability of a New Evidence Review/Absence of Duplication</b>	
3. A recent high-quality systematic review or other evidence review is not available on this topic	Yes, a new evidence review would not be redundant. We did not identify any relevant high-quality systematic reviews.
<b>4. Impact of a New Evidence Review</b>	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	Yes, the current ASPS guidelines are based on limited evidence regarding the comparative effectiveness of implant-based versus autologous breast reconstruction as well as the comparative effectiveness of different subcategories of these types of breast reconstruction. There is a need for more robust evidence to support clinical recommendations for the updated ASPS clinical practice guidelines.
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	No, there is no evidence that current practice is inconsistent with the available guidelines. Rather, there is a need for more up-to-date evidence-based guidelines to inform clinical practice.

Selection Criteria	Assessment
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: <ul style="list-style-type: none"> <li>- Adequacy (type and volume) of research for conducting a systematic review</li> <li>- Newly available evidence (particularly for updates or new technologies)</li> </ul>	Below are our literature findings for each of the six questions: Question 1: 1 RCT and 25 observational studies. Question 2: 2 RCTs and 22 observational study. Question 3: 1 observational study. Question 4: 6 observational studies. Question 5: 4 RCTs and 16 observational studies. Question 6: 29 observational studies.
6. Value	
6a. The proposed topic exists within a clinical, consumer, or policy-making context that is amenable to evidence-based change	Yes, breast reconstruction procedures are amenable to evidence-based change.
6b. Identified partner who will use the systematic review to influence practice (such as a guideline or recommendation)	Yes, this topic was nominated by the American Society of Plastic Surgeons (ASPS) who will use a systematic review to update practice guidelines from the 2013 on breast reconstruction with expanders and implants and 2017 on autologous breast reconstruction.

*Abbreviations: AHRQ = Agency for Healthcare Research and Quality; ASPS = American Society of Plastic Surgeons.*