



## Effective Health Care Breast Cancer Screening in High-Risk Women

### Results of Topic Selection Process & Next Steps

The nominator, Kaiser Permanente Care Management Institute, is interested in using a new systematic review to develop new guidelines pertaining to breast cancer screening in high-risk women.

We identified an ongoing systematic review commissioned by a cancer organization that covers the scope of the key questions; therefore, a new review would be duplicative of an existing in-progress product. No further activity on this topic will be undertaken by the Effective Health Care (EHC) Program.

### Topic Brief

**Topic Name:** 0752 Breast Cancer Screening in High-Risk Women

**Nomination Date:** 11/10/2017

**Topic Brief Date:** 05/15/2018

**Authors:**

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**Conflict of Interest:** None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

**Summary of Key Findings:**

- Appropriateness and importance: The topic is both appropriate and important.
- Duplication: A new review on this topic would be duplicative of an existing product. A systematic review, which encompasses the scope of the topic nomination, is currently being conducted by a cancer organization to update their guidelines.

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## Introduction

In 2018, the American Cancer Society projects breast cancer to be the most frequently diagnosed non-dermatologic malignancy (266,120 new cases) and the second leading cause of cancer death (40,920 deaths) among women in the United States.<sup>1</sup> The annual national expenditure in the United States for treatment of breast cancer was estimated to be \$39 billion in 2017.<sup>2</sup> Although the impact of population screening for breast cancer in low- and average-risk women are well reviewed,<sup>3</sup> evidence on the effectiveness and harms of breast cancer screening in high-risk women have not been adequately synthesized and subsequent practice guidelines have not been well developed. In addition, controversy remains regarding the criteria to properly categorize breast cancer risk among women with greater than average risk.<sup>4</sup>

The Kaiser Permanente Care Management Institute nominated this topic on 11/10/2017. The questions are:

Key Question 1. What is the effectiveness of breast cancer screening in reducing breast cancer mortality in asymptomatic high-risk women?

Key Question 2. What is the effectiveness of breast cancer screening in reducing breast cancer incidence in asymptomatic high-risk women?

Key Question 3. What are the harms of breast cancer screening in asymptomatic high-risk women?

Contextual Question: What is the most optimal definition of high-risk for breast cancer?

In Table 1, we define the population, interventions, comparators, outcomes, and timing (PICOT) for each Key Question.

**Table 1.** Key Questions and PICOTS

Key Questions	KQ1: What is the effectiveness of breast cancer screening in reducing breast cancer mortality in asymptomatic high-risk women?	KQ2: What is the effectiveness of breast cancer screening in reducing breast cancer incidence in asymptomatic high-risk women?	KQ3: What are the harms of breast cancer screening in asymptomatic high-risk women?
Population	<p>Adult women not diagnosed with breast cancer but are at high-risk due to any of the following:</p> <ul style="list-style-type: none"> <li>• A <i>BRCA1</i> or <i>BRCA2</i> mutation (and 1° relatives, but personally have not been tested for <i>BRCA1/2</i> mutations)</li> <li>• A personal history of ductal carcinoma in situ (DCIS), ductal carcinoma in situ (LCIS), or atypical hyperplasia</li> <li>• Radiation treatment to the chest area between ages 10-30</li> <li>• Li-Fraumeni, Cowden/<i>PTEN</i> or Bannayan-Riley-Ruvalcaba syndrome (and first-degree relatives)</li> <li>• An <i>ATM</i>, <i>CDH1</i>, <i>CHEK2</i>, <i>NBN</i>, <i>NF1</i>, <i>PALB2</i>, <i>PTEN</i>, <i>STK11</i> or <i>TP53</i> gene mutation</li> <li>• A greater than 20% lifetime risk of invasive breast cancer based mainly on family history</li> </ul>	<p>Adult women not diagnosed with breast cancer but are at high-risk due to any of the following:</p> <ul style="list-style-type: none"> <li>• A <i>BRCA1</i> or <i>BRCA2</i> mutation (and 1° relatives, but personally have not been tested for <i>BRCA1/2</i> mutations)</li> <li>• A personal history of ductal carcinoma in situ (DCIS), lobular carcinoma in situ (LCIS), or atypical hyperplasia</li> <li>• Radiation treatment to the chest area between ages 10-30</li> <li>• Li-Fraumeni, Cowden/<i>PTEN</i> or Bannayan-Riley-Ruvalcaba syndrome (and first-degree relatives)</li> <li>• An <i>ATM</i>, <i>CDH1</i>, <i>CHEK2</i>, <i>NBN</i>, <i>NF1</i>, <i>PALB2</i>, <i>PTEN</i>, <i>STK11</i> or <i>TP53</i> gene mutation</li> <li>• A greater than 20% lifetime risk of invasive breast cancer based mainly on family history</li> </ul>	<p>Adult women not diagnosed with breast cancer but are at high-risk due to any of the following:</p> <ul style="list-style-type: none"> <li>• A <i>BRCA1</i> or <i>BRCA2</i> mutation (and 1° relatives, but personally have not been tested for <i>BRCA1/2</i> mutations)</li> <li>• A personal history of ductal carcinoma in situ (DCIS), lobular carcinoma in situ (LCIS), or atypical hyperplasia</li> <li>• Radiation treatment to the chest area between ages 10-30</li> <li>• Li-Fraumeni, Cowden/<i>PTEN</i> or Bannayan-Riley-Ruvalcaba syndrome (and first-degree relatives)</li> <li>• An <i>ATM</i>, <i>CDH1</i>, <i>CHEK2</i>, <i>NBN</i>, <i>NF1</i>, <i>PALB2</i>, <i>PTEN</i>, <i>STK11</i> or <i>TP53</i> gene mutation</li> <li>• A greater than 20% lifetime risk of invasive breast cancer based mainly on family history</li> </ul>
Interventions	<ul style="list-style-type: none"> <li>• Mammography</li> <li>• MRI as an adjunct to mammography screening</li> <li>• Ultrasonography as an adjunct to mammography or as an alternative to MRI when it is not tolerated</li> <li>• Digital breast tomosynthesis</li> <li>• Clinical breast examination</li> </ul>	<ul style="list-style-type: none"> <li>• Mammography</li> <li>• MRI as an adjunct to mammography screening</li> <li>• Ultrasonography as an adjunct to mammography or as an alternative to MRI when it is not tolerated</li> <li>• Digital breast tomosynthesis</li> <li>• Clinical breast examination</li> </ul>	<ul style="list-style-type: none"> <li>• Mammography</li> <li>• MRI as an adjunct to mammography screening</li> <li>• Ultrasonography as an adjunct to mammography or as an alternative to MRI when it is not tolerated</li> <li>• Digital breast tomosynthesis</li> <li>• Clinical breast examination</li> </ul>
Comparators	No screening; screening modalities compared to each other	No screening; screening modalities compared to each other	No screening; screening modalities compared to each other

<b>Key Questions</b>	KQ1: What is the effectiveness of breast cancer screening in reducing breast cancer mortality in asymptomatic high-risk women?	KQ2: What is the effectiveness of breast cancer screening in reducing breast cancer incidence in asymptomatic high-risk women?	KQ3: What are the harms of breast cancer screening in asymptomatic high-risk women?
<b>Outcomes</b>	Breast cancer mortality; all-cause mortality	Breast cancer incidence (cancer detection rates); diagnostic accuracy	Harms (false positives, unnecessary biopsy, psychological harms)
<b>Timing</b>	All	All	All
<b>Setting</b>	Outpatient	Outpatient	Outpatient

*Abbreviations:* DCIS=Ductal Carcinoma In Situ; LCIS= Lobular Carcinoma In Situ; KQ=Key Question; MRI=Magnetic Resonance Imaging

## Methods

To assess topic nomination Breast Cancer Screening in High-Risk Women #739, for priority for a systematic review or other AHRQ EHC report, we used a modified process based on established criteria. Our assessment is hierarchical in nature, with the findings of our assessment determining the need for further evaluation. Details related to our assessment are provided in Appendix A.

1. Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. Establish the overall *importance* of a potential topic as representing a health or healthcare issue in the United States.
3. Determine the *desirability of new evidence review* by examining whether a new systematic review or other AHRQ product would be duplicative.
4. Assess the *potential impact* a new systematic review or other AHRQ product.
5. Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. Determine the *potential value* of a new systematic review or other AHRQ product.

### Appropriateness and Importance

We qualitatively assessed the nomination for appropriateness and importance.

### Desirability of New Review/Duplication

We searched for relevant high quality, completed or in-process evidence reviews from the last three years. Databases searched included AHRQ Effective Health Care Program website, VA Evidence Synthesis Program website, PubMed, Cochrane Collaboration, and PROSPERO register of systematic reviews.

### Compilation of Findings

We constructed a table outlining the selection criteria (Appendix A).

## Results

### Appropriateness and Importance

This is an appropriate and important topic. Breast cancer represents both high mortality burden for women as well as high cost burden in the United States.

### Desirability of New Review/Duplication

A new evidence review examining breast cancer screening in high-risk women would be duplicative of an existing product. A systematic review, which encompasses the scope of the topic nomination, was commissioned by a cancer organization in the United States to update their guidelines. We have withheld the organization name because they have not publicly disclosed these efforts.

In addition, we found three reviews that are relevant to KQ2.<sup>5-7</sup> One review focused on the contribution of mammography to magnetic resonance imaging (MRI) screening in *BRCA* mutation carriers.<sup>5</sup> One review examined screening MRI in women with a personal history of breast cancer<sup>6</sup> and another review assesses ultrasound as an adjunct to mammography.<sup>7</sup> See Table 2, Duplication column for the systematic review citations that were determined to address the key questions.

**Table 2.** Key questions with identified corresponding evidence reviews

Key Question	Duplication (Completed or In-Process Evidence Reviews)
KQ 1: What is the effectiveness of breast cancer screening in reducing breast cancer mortality in asymptomatic high-risk women?	Total number of completed or in-progress evidence reviews – None identified
KQ 2: What is the effectiveness of breast cancer screening in reducing breast cancer incidence in asymptomatic high-risk women?	Total number of completed or in-progress systematic reviews - 3 <ul style="list-style-type: none"> <li>• Other – 3<sup>5-7</sup></li> </ul>
KQ 3: What are the harms of breast cancer screening in asymptomatic high-risk women?	Total number of completed or in-progress evidence reviews – None identified

Abbreviations: KQ=Key Question

## Summary of Findings

- Appropriateness and Importance: The topic is both appropriate and important.
- Duplication: A new review on this topic would be duplicative of an existing product. A systematic review, which encompasses the scope of the topic nomination, is currently underway.

## References

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## Appendix A. Selection Criteria Summary

Selection Criteria	Supporting Data
<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, this topic represents a health care drug and intervention available in the U.S.
1b. Is the nomination a request for a systematic review?	Yes, this topic is a request for a systematic review.
1c. Is the focus on effectiveness or comparative effectiveness?	The focus of this review is on both effectiveness and comparative effectiveness.
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, it is biologically plausible. Yes, it is consistent with what is known about the topic.
<b>2. Importance</b>	
2a. Represents a significant disease burden; large proportion of the population	Yes, this topic represents a significant burden. Breast cancer is the second leading cause of cancer death in women in the U.S.
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, this topic affects health care decisions for a large proportion of the U.S. population. National healthcare expenditure for treating breast cancer was estimated to be \$39 billion in 2017.
2c. Represents important uncertainty for decision makers	Yes, this topic represents important uncertainty for decision makers.
2d. Incorporates issues around both clinical benefits and potential clinical	Yes, this nomination addresses both benefits and potential harms of screening interventions for breast cancer.
2e. 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, breast cancer is the second most common non-dermatologic malignancy in women in the U.S. Treatments are costly for the individual patient and to payers.
<b>3. Desirability of a New Evidence Review/Duplication</b>	
3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)	A systematic review, which encompasses the scope of the topic nomination, is being conducted by a cancer organization to update their guidelines. In addition, we found three reviews that are relevant to KQ2. <sup>5-7</sup>

*Abbreviations:* U.S.=United States; AHRQ= Agency for Healthcare Research and Quality; KQ=Key Question



## Appendix B. Search for Systematic Reviews (Duplication)

Listed below are the sources searched and results of our search for existing guidance.

Breast Cancer Screening in High-Risk Women
Source
<b>Search for Duplication: January 1, 2018</b>
AHRQ: Evidence reports and technology assessments, USPSTF recommendations
VA Products: PBM, and HSR&D (ESP) publications, and VA/DoD EBCPG Program
Cochrane Systematic Reviews and Protocols <a href="http://www.cochranelibrary.com/">http://www.cochranelibrary.com/</a>
PubMed <a href="https://www.ncbi.nlm.nih.gov/pubmed/">https://www.ncbi.nlm.nih.gov/pubmed/</a>
PROSPERO Database (international prospective register of systematic reviews and protocols) <a href="http://www.crd.york.ac.uk/prospERO/">http://www.crd.york.ac.uk/prospERO/</a>