Clinical Policy Title: Breast cancer screening in women

Clinical Policy Number: 17.01.03

Effective Date: February 1, 2016
Initial Review Date: November 18, 2015
Most Recent Review Date: January 11, 2018
Next Review Date: January 2019

Related policies:
CP# 02.01.02 Genetic testing for breast and ovarian cancer
CP# 02.01.14 Gene expression profile testing for breast cancer
CP# 05.01.04 Molecular analysis for targeted therapy for lung cancer

ABOUT THIS POLICY: Select Health of South Carolina has developed clinical policies to assist with making coverage determinations. Select Health of South Carolina’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Select Health of South Carolina when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Select Health of South Carolina’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Select Health of South Carolina’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Select Health of South Carolina will update its clinical policies as necessary. Select Health of South Carolina’s clinical policies are not guarantees of payment.

Coverage policy

Select Health of South Carolina considers the use of preventive care and breast cancer screening to be clinically proven and, therefore, medically necessary (Havrilesky, 2014; Myers, 2015; Nelson, 2016; Oeffinger, 2015; Siu, 2016).

Limitations:

Preventive care and breast cancer screening with mammography is limited to once per annum in women considered at average risk for breast cancer (as defined in this policy) beginning at the age of 40 years.

Preventive care and breast cancer screening with magnetic resonance imaging (MRI) and a mammogram is limited to once per annum in women considered at high risk for breast cancer (as defined in this policy) beginning at the age of 30 years (Myers, 2015; Oeffinger, 2015; Siu/U.S. Preventive Services Task Force [USPSTF], 2016).
Alternative covered services:

Routine preventive care by a primary care provider.

**Background**

Breast cancer is the most common cancer among women worldwide and the leading cause of premature mortality among women in the United States.

Mammography screening has resulted in a significant reduction in breast cancer mortality. A mammogram can find breast changes that could be cancer years before symptoms or physical signs develop. A mammogram can often help find aggressive breast cancer at an early stage, when treatment is most likely to be successful. Mammography has consistently been shown to significantly reduce a woman's risk of dying from breast cancer, though the amount of benefit varies depending on the design of the study.

However, mammograms are not perfect, and they miss some cancers. They may initiate a cascade of more tests, including biopsies, to find out if something found on a mammogram is or is not cancer. There is a possibility of complications from these procedures and studies, including risks related to harmful exposure to additional radiation. There is also a small possibility of a woman being diagnosed with a cancer that never would have caused any problems had it not been found during screening.

In October 2015, the American Cancer Society (ACS) updated its guidelines for when women at average risk for breast cancer should be screened for the condition (Appendix A). These new recommendations are less straightforward than past versions, resulting in a re-examination of the merits and detriments of screening for breast cancer with annual health care provider manual breast examination and mammography.

Women with a personal history of breast cancer, a family history of breast cancer, a genetic mutation known to increase risk of breast cancer (such as BRCA), and women who had radiation therapy to the chest before the age of 30 are at higher risk for breast cancer, not average-risk. Women who are at high risk for breast cancer based on certain factors should get an MRI scan and a mammogram every year.

ACS concluded that screening is associated with a reduction in breast cancer deaths across a range of study designs, and inferential evidence supports breast cancer screening for women 70 years old and older who are in good health. Estimates of the cumulative lifetime risk of false-positive examination results are greater if screening begins at younger ages because of the greater number of mammograms, as well as the higher recall rate in younger women; however, the quality of the evidence for over-diagnosis is not sufficient to estimate a lifetime risk with confidence. The ACS cited more favorable tumor characteristics when premenopausal women are screened annually as the basis for
recommending a one-year interval between screenings. And finally, ACS cited a lack of evidence to support routine clinical breast examination (CBE) as a screening method for women at average risk, and dropped this recommendation from its guidelines.

The USPSTF subsequently promulgated guidelines in this regard (Appendix B) that vary from previous recommendations of annual breast cancer screening for women over 40 years of age.

The USPSTF recommended that women age ≥ 40 years presenting with an average risk of breast cancer begin biennial mammography screening at age 50, continuing through age 74. Women younger than age 50 may choose to begin mammography screening based on individual factors, and those placing a higher value on the potential benefits than potential harms may consider biennial screening between 40 and 49 years of age.

Because current evidence remains insufficient regarding the benefits versus harms of screening in women older than 75 years of age, as well as the benefits versus harm of digital breast tomosynthesis, ultrasonography, and MRI, these and other screening technologies and methods were not recommended.

Breast cancer prevention is designated an “Essential Health Benefit” (also known as EHB) under the Patient Protection and Affordable Care Act (ACA), and there are federal mandates that apply to health insurance coverage of provider breast examination and mammography. The Center for Consumer Information and Insurance Oversight has compiled a 50-state list, including the District of Columbia (D.C.), with information on Essential Health Benefit benchmark plans with links to details for each (Appendix C). The ACA does not directly change or preempt state laws that require or mandate coverage of specific benefits and provider services.

States are making breast cancer screening more available to medically underserved women through the Centers for Disease Control and Prevention’s (CDC) National Breast and Cervical Cancer Early Detection Program (NBCCEDP). The NBCCEDP attempts to reach as many women in medically underserved communities as possible, including older women, women without health insurance, and women who are members of racial and ethnic minorities. Age and income requirements vary by state. The program provides both screening and diagnostic services to low-income, uninsured, and underserved women for free or at very low cost, including mammograms, diagnostic testing for women whose screening results are abnormal, surgical consultations, and referrals to treatment.

Searches

Select Health of South Carolina searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).
We conducted searches on December 1, 2017. Search terms were: "breast cancer" (MeSH), "screening for breast cancer" (MeSH), and "guidelines for breast cancer screening."

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews.**
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

An exhaustive synthesis of seven systematic reviews, 10 randomized controlled trials (RCTs), and several observational studies from the last 15 years (Myers, 2015) found for women of all ages at average risk, screening for breast cancer in the U.S. is associated with a reduction in mortality of approximately 20 percent, although there remains uncertainty about quantitative estimates of outcomes for different breast cancer screening strategies (e.g., annual versus biennial). The authors could not extrapolate from available data the exact figure of breast cancer mortality reduction with screening across the entire population of women in this country; nor could they offer evidence of the superiority of annual screening compared to biennial screening. Evidence for the relationship between screening and life expectancy and quality-adjusted life expectancy was low in quality as well. There was no direct evidence for any additional mortality benefit with the addition of CBE to mammography, but observational evidence suggested an increase in false-positive findings compared with mammography alone. The authors identified an estimated 55 additional false-positive findings per extra breast cancer detected with the addition of CBE. For women with a first mammography screening at age 40 years, estimated 10-year cumulative risk of a false-positive biopsy result was 7 percent; for women who commenced screening at age 50, the lifetime probability of a false positive finding was lower.

Based on the Myers et al. (2015) work, ACS revised its recommendations for screening mammography in women at average risk for breast cancer ages 40 to 69 years of age in a special communication in the same edition of the Journal of the American Medical Association (Oeffinger, 2015). The full 2015 ACS recommendations for women at average risk and for women at higher than average risk for breast cancer are found in Appendix A. Women with a personal history of breast cancer, a family history of breast cancer, a genetic mutation known to increase risk of breast cancer (such as BRCA), and women who had radiation therapy to the chest before age 30 are at higher risk for breast cancer. Women who are at high risk for breast cancer based on certain factors should get an MRI scan and a mammogram every year.
ACS concluded that screening is associated with a reduction in breast cancer deaths across a range of study designs, and inferential evidence supports breast cancer screening for women 70 years old and older who are in good health. Estimates of the cumulative lifetime risk of false-positive examination results are greater if screening begins at younger ages because of the greater number of mammograms, as well as the higher recall rate in younger women; however, the quality of the evidence for over-diagnosis is not sufficient to estimate a lifetime risk with confidence. The ACS cited more favorable tumor characteristics when premenopausal women are screened annually as the basis for recommending a one-year interval between screenings. And finally, ACS cited a lack of evidence to support routine CBE as a screening method for women at average risk, and dropped this recommendation from its guidelines.

In the wake of the ACS breast cancer screening guidelines, the USPSTF amended their recommendations as well, concluding with moderate certainty that the net benefit of screening mammography in women ages 50 to 74 years is moderate (Siu, 2016). The final 2016 USPSTF recommendations for women at average risk and for women at higher than average risk for breast cancer are found in Appendix B. The USPSTF concluded with moderate certainty that the net benefit of screening mammography in the general population of women ages 40 – 49 years, while positive, is small. Finally, the USPSTF concluded that the evidence on mammography screening in women age 75 and older is insufficient, and the balance of benefits and harms cannot be determined.

Specifically, meta-analysis and systemic review of clinical trials considered by the USPSTF showed that, during a 10-year period, screening 10,000 women ages 60 to 69 will result in 21 fewer breast cancer deaths. Screening 10,000 women ages 50 to 59 years will result in eight fewer breast cancer deaths. Screening 10,000 women ages 40 to 49 years will result in three fewer breast cancer deaths.

With regard to screening technology, the USPSTF concluded that the evidence on digital breast tomosynthesis as a primary screening method for breast cancer is insufficient, and the balance of benefits and harms cannot be determined. The body also concluded that the evidence on adjunctive screening for breast cancer using breast ultrasound, MRI, digital breast tomosynthesis, or other methods in women identified to have dense breasts on an otherwise negative screening mammogram is insufficient, and the balance of benefits and harms cannot be determined.

A cohort of women with a first-degree relative, including a parent, sibling, or child, who had a breast cancer diagnosis were considered by USPSTF to be at higher risk, and thus would benefit from screening beginning at age 40. Additional clinically significant risks included women with a BRCA1 or BRCA2 gene mutation or other hereditary genetic syndromes, as well as women with a history of high-dose radiation therapy to the chest that occurred at a young age.

A systematic review from the Duke Evidence Synthesis Group (Havrilesky, 2014) found that breast cancer mortality and incidence figures vary widely, depending on study design, when and where the study was performed, and the methods of analysis used to estimate effects. The problem is exacerbated by trends in clinical practice that may affect the absolute risk of breast cancer (e.g., a decline in the use
of hormone replacement therapy), the absolute risk of dying once diagnosed with breast cancer as it is impacted by advances in treatment, and factors that may affect the consequences of over-diagnosis (e.g., markers for prediction of progression in ductal carcinoma in situ [DCIS]); moreover, the authors noted that the relevant data may not be fully representative of the totality of clinical experience and that study design has traditionally hamstrung efforts to create a clear picture of the true and full impact of screening. The authors were persuaded to offer their conclusions couched in conditional terms of “high” and “low” certainty.

For example, evidence is consistent that breast cancer mortality is reduced when a comparison is made between screened and unscreened women and when the comparison is between women invited to screening versus women not invited. The strength of evidence that screening reduces mortality at all ages is high, but there is uncertainty about the magnitude of this effect. Estimated absolute reduction is lower in younger women than in older women, because of a lower overall incidence of breast cancer, but direct evidence for older women is very limited, and registry data strongly suggests that women 75 years old and older diagnosed with breast cancer are more likely to die from other causes than from breast cancer. There is low confidence that annual screening reduces mortality in women ages 40 – 49 years compared to biennial screening.

The most recently reported large scale observational trial in Canada, the Pan-Canadian Study, included more than 2.7 million women (Coldman, 2014). It showed that mammography screening decreased breast cancer mortality by 40 percent. This was true of all age groups. Estimates of breast cancer mortality reduction for women who are actually screened are 48 percent reduction in case control studies and 38 percent reduction in cohort studies. Use of mammography also results in a substantial reduction in incidence of late-stage breast cancer (37 percent decrease). Overall, women age 40 years old and older who choose mammography screening can expect to decrease their chances of dying from breast cancer by about 40 percent.

A Cochrane systematic review (Gøtzsche, 2011) analyzed eight clinical trials inclusive of 600,000 women screened for breast cancer with mammography and found disparate results based on study design. Three trials with adequate randomization did not show a significant reduction in breast cancer mortality at 13 years of follow-up, while four trials with suboptimal randomization showed a significant reduction in breast cancer mortality. The authors also noted that numbers of lumpectomies and mastectomies were significantly larger in women undergoing screening with mammography versus control without mammography, and that the use of radiotherapy was similarly increased.

An authoritative assessment of the future of breast cancer screening in the age of the Essential Health Benefit and ACA (Plescia, 2013) found wide disparity between organizational recommendations of who and when to screen for breast cancer and what actually is done in the patient encounter by providers. The authors noted discordant screening of women who are unlikely to benefit from it, including women who are terminally ill, as well as mammography use among women younger than 40 years of age. They also determined irregularities in process that need attention, such as a study of primary care providers’
practices that found just 40 percent reported that they had a system to remind women with appropriate indication to come in for breast cancer screenings.

Essential Health Benefit is defined in Section 1302(b) of the ACA. The permanent statute citation is 42 U. S. C. § 300gg-13(a)(4) and related regulations. It includes at least the following general categories:

- Ambulatory patient services.
- Emergency services.
- Hospitalization.
- Maternity and newborn care.
- Mental health and substance use disorder services, including behavioral health treatment.
- Prescription drugs.
- Rehabilitative and habilitative services and devices.
- Laboratory services.
- Preventive and wellness and chronic disease management services (details directly below).
- Pediatric services, including oral and vision care.
- Preventive services for adults, women, and children.

Women’s preventive health services were defined in detail via federal regulations published August 1, 2011, requiring broad coverage, without copayments or deductibles, of:

- Annual preventive care medical visits and exams.
- Contraceptives (products approved by the U.S. Food and Drug Administration [FDA]) — with exemptions for religious employers, a temporary enforcement safe harbor.
- Mammograms.
- Colonoscopies.
- Blood pressure tests.
- Childhood immunizations.
- Domestic violence screenings for interpersonal and domestic violence.
- HIV screenings.
- Breast-feeding counseling and equipment, including breast pumps, at no charge.
- Gestational diabetes in pregnant women screening.
- DNA tests for human papillomavirus (HPV) as part of cervical cancer screening.

Each state’s Department of Health has information on how to contact the nearest NBCCEDP screening and early detection program within its geographic boundaries. Potential enrollees can also contact the CDC at 1-800-CDC-INFO (1-800-232-4636) or online at www.cdc.gov/cancer/nbccedp.

**Policy updates:**

A systematic review sought to determine the fiscal prudence of using BRCA testing (D’Andrea, 2016). The authors considered four different clinical scenarios:
- Population-based genetic screening of individuals without cancer, either comprehensive or targeted based on ancestry.
- Family history-based genetic screening (i.e., testing individuals without cancer but with family ties suggestive of BRCA mutation).
- Familial mutation-based genetic screening (i.e., testing individuals without cancer but with known familial BRCA mutation.
- Cancer-based genetic screening (i.e., testing individuals with BRCA-related cancers).

They concluded that population-based screening represents good value for the money among Ashkenazi Jews only. Family history-based screening is potentially very cost-effective, although further studies that include costs of identifying high-risk women are needed. There is no evidence of cost effectiveness for BRCA screening of all newly diagnosed cases of breast or ovarian cancers followed by cascade testing of relatives, but programs that include tools for identifying affected women at higher risk for inherited forms are promising. Cost effectiveness is highly sensitive to the cost of BRCA testing.

Hayes (2016) reviewed a proprietary genetic test for breast and ovarian cancers (OncogeneDx® Breast and Ovarian Cancer panel). Neither the analytical validity (which includes the ability of the test to identify a pathogenic variant when present, the false-positive rate, and the rate of test failure) nor the clinical validity and utility could be assessed. All of these components are crucial to rate a test and are not available. Hayes concluded there is insufficient evidence to recommend the test for adoption or use at this time.

Three references were added to the Summary of Clinical Evidence in January 2018 (Phi, 2016; Phi, 2017; Yun, 2017). Findings from an individual patient data meta-analysis support the current policy (Phi, 2017). Among women with a strong familial risk for breast cancer but without a known gene mutation, combining MRI and mammography increased sensitivity but decreased specificity both before and after the age of 50. In a separate analysis, among women with BRCA2 mutation younger than 40 years, a third of breast cancers were detected by mammography alone (Phi, 2016). The number of screenings needed for mammography to detect one breast cancer not identified by MRI was much higher for BRCA1 compared with BRCA2 mutation carriers at initial and repeat screenings. Added sensitivity from mammography above that from MRI is limited in BRCA1 mutation carriers, while mammography contributes to screening sensitivity in BRCA2 mutation carriers, especially in women under age 40.

In a meta-analysis of digital breast tomosynthesis added to digital mammography, a higher cancer detection rate was found for several types of cancers (invasive cancer, stage T1, nodal-negative, all histologic grades, and histologic types of invasive cancer), but not for carcinoma in situ, stage ≥ 2, or nodal-positive cancer, resulting in the conclusion that in this combined sample, combining digital breast tomosynthesis to digital mammography allows detection of some cancers that would otherwise be missed (Yun, 2017). The authors interpret this to mean that dual screening may facilitate treatment planning and help predict outcomes.
Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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<tbody>
<tr>
<td>Phi (2017)</td>
<td><strong>Key points:</strong></td>
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| Accuracy of screening women at familial risk of breast cancer without a known gene mutation | - Data are based on six prospective screening trials of women at increased risk by virtue of strong familial risk. A total of 2,226 women of mean age 41 were included.  
- Breast cancer rate was 12 (95% CI 9.3-14) in 1,000 woman-years, based on follow-up of 7,478 person-years.  
- Mammography screening had a sensitivity of 55% (standard error of mean [SE] 7.0) and a specificity of 94% (SE 1.3). MRI screening alone had a sensitivity of 89% (SE 4.6) and a specificity of 83% (SE 2.8). Combining MRI and mammography increased sensitivity to 98% (SE 1.8, P < 0.01 compared to mammography alone) but lowered specificity to 79% (SE 2.7, P < 0.01 compared with solely mammography). |
| Yun (2017)        | **Key points:**                    |
| Benefits of adding digital breast tomosynthesis to digital mammography | - This meta-analysis included 11 studies.  
- Pooled risk ratios showed a greater cancer detection for digital breast tomosynthesis plus full field digital mammography than for mammography alone for invasive cancer (1.327; 95% CI, 1.168-1.508), stage T1 (1.388; 95% CI, 1.137-1.695), nodal-negative (1.451; 95% CI, 1.209-1.742), all histologic grades (grade I, 1.812; grade II/III, 1.403), and histologic types of invasive cancer (ductal, 1.437; lobular, 1.901).  
- The addition of digital breast tomosynthesis did not increase detection of carcinoma in situ (1.198; 95% CI, 0.942-1.524), stage ≥T2 (1.391; 95% CI, 0.895-2.163), or nodal-positive cancer (1.336; 95% CI, 0.921-1.938).  
- Heterogeneity among studies was not significant in any subset analysis.  
- The findings could allow improved treatment planning and prediction of long-term patient outcomes. |
| D'Andrea (2016)   | **Key points:**                    |
| Which BRCA genetic testing programs are ready for implementation in health care? | - There is considerable evidence regarding the efficacy and effectiveness of BRCA genetic testing programs.  
- Nine economic evaluations found BRCA population-based screening represents good value for the money among Ashkenazi Jews only.  
- Family history-based screening is potentially very cost effective, although further studies that include costs of identifying high-risk women are needed.  
- There is no evidence of cost effectiveness for BRCA screening of all newly diagnosed cases of breast or ovarian cancers followed by cascade testing of relatives, but programs that include tools for identifying affected women at higher risk for inherited forms are promising.  
- Cost effectiveness is highly sensitive to the cost of BRCA testing. |
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| Hayes (2016)                   | **Breast/ovarian cancer panel**  
| **Key points:**               |  
| - There is no published literature; therefore, neither the analytical validity (which includes the ability of the test to identify a pathogenic variant when present, the false-positive rate, and the rate of test failure) nor the clinical validity and utility of the breast and ovarian cancer panel could be assessed.  
| - There is insufficient evidence published to perform a health technology assessment of the panel; therefore, it cannot be recommended for adoption or use at this time.  
| - In addition, a systematic review of the literature on the association between pathogenic variants and breast and/or ovarian cancer and the impact of such genetic testing on patient management is necessary. |
| Phi (2016)                     | **Contribution of mammography to MRI screening in BRCA mutation carriers**  
| **Key points:**               |  
| - A individual patient data meta-analysis of six studies including 1,951 women examined mammography with MRI in BRCA1/2 mutation carriers.  
| - Among mutation carriers of all ages (BRCA1 ¼ 1219 and BRCA2 ¼ 732), adding mammography to MRI did not significantly increase screening sensitivity (increased by 3.9% in BRCA1 and 12.6% in BRCA2 mutation carriers, P<0.05).  
| - Among women with BRCA2 mutation younger than 40 years old, a third of breast cancers were detected by mammography alone.  
| - The number of screens needed for mammography to detect one breast cancer not identified by MRI was much higher for BRCA1 compared with BRCA2 mutation carriers at initial and repeat screening. Added sensitivity from mammography above that from MRI is limited in BRCA1 mutation carriers, while mammography contributes to screening sensitivity in BRCA2 mutation carriers, especially those under age 40. |
| Siu/USPSTF (2016)              | **Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement**  
| **Key points:**               |  
| - Systematic review and meta-analysis showed that, during a 10-year period, screening 10,000 women ages 60 – 69 will result in 21 fewer breast cancer deaths.  
| - Screening 10,000 women ages 50 – 59 will result in eight fewer breast cancer deaths.  
| - Screening 10,000 women ages 40 – 49 will result in three fewer breast cancer deaths, evidenced with moderate certainty that the net benefit of screening mammography in women ages 50 – 74 is moderate.  
| - The USPSTF concluded with moderate certainty that the net benefit of screening mammography in the general population of women ages 40 – 49, while positive, is small.  
| - Finally, the USPSTF concluded that the evidence on mammography screening in women age ≥ 75 is insufficient, and the balance of benefits and harms cannot be determined.  
| - With regard to screening technology, the USPSTF concluded that the evidence of digital breast tomosynthesis as a primary screening method for breast cancer is insufficient, and the balance of benefits and harms cannot be determined.  
| - The body also concluded that the evidence on adjunctive screening for breast cancer using breast ultrasound, MRI, digital breast tomosynthesis, or other methods in women identified to have dense breasts on an otherwise negative screening mammogram is insufficient, and the balance of benefits and harms cannot be determined.  
<p>| - A cohort of women with a first-degree relative, including a parent, sibling, or child, who had a breast cancer diagnosis were considered by USPSTF at higher risk and thus would benefit from screening beginning at age 40. |</p>
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<td>Myers (2015)</td>
<td>- Additional clinically significant risks included women with a BRCA1 or BRCA2 gene mutation or other hereditary genetic syndromes, as well as women with a history of high-dose radiation therapy to the chest that occurred at a young age.</td>
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<td>Key points:</td>
<td>- An exhaustive synthesis of seven systematic reviews, 10 RCTs, and several observational studies from the past 15 years. - Found that for women of all ages at average risk, screening for breast cancer in the U.S. is associated with a reduction in mortality of approximately 20 percent. - Cited uncertainty about quantitative estimates of outcomes for different breast cancer screening strategies (e.g., annual versus biennial). - There was no direct evidence for any additional mortality benefit with the addition of CBE to mammography. - The authors identified an estimated 55 additional false-positive findings per extra breast cancer detected with the addition of CBE.</td>
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<td>Oeffinger/ACS (2015)</td>
<td>- Women ages 40 – 44 at average risk for breast cancer should have the choice to start annual breast cancer screening with mammograms if they wish to do so. The risks of screening as well as the potential benefits should be considered. - Women ages 45 – 54 should get mammograms every year. - Women age 55 and older should switch to mammograms every two years, or have the choice to continue yearly screening. - Screening should continue as long as a woman is in good health and is expected to live 10 more years or longer. - The ACS concluded that screening is associated with a reduction in breast cancer deaths across a range of study designs, and inferential evidence supports breast cancer screening for women ≥ 70 who are in good health. - Women with a personal history of breast cancer, a family history of breast cancer, a genetic mutation known to increase risk of breast cancer (such as BRCA), and women who had radiation therapy to the chest before age 30 are at higher risk for breast cancer. - Women who are at high risk for breast cancer based on certain factors should get an MRI scan and a mammogram every year. - The ACS cited a lack of evidence to support routine CBE as a screening method for women at average risk and dropped this recommendation from its guidelines.</td>
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<td>Havrilesky (2014)</td>
<td>- A systematic review from the Duke Evidence Synthesis Group found that breast cancer mortality and incidence figures vary widely depending on study design, when and where the study was performed, and the methods of analysis used to estimate effects. - The problem is exacerbated by trends in clinical practice that may affect the absolute risk of breast cancer (e.g., a decline in the use of hormone replacement therapy), the absolute risk of dying once diagnosed with breast cancer as it is impacted by advances in treatment, and factors that may affect the consequences of over-diagnosis (e.g., markers for prediction of progression in DCIS). - The authors noted that the relevant data may not be fully representative of the totality of...</td>
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| Coldman (2014) Pan-Canadian study of mammography screening and mortality from breast cancer | **Key points:**
- The Pan-Canadian Observational study included more than 2.7 million women and showed that mammography screening decreased breast cancer mortality by 40 percent across all age groups.
- Estimates of breast cancer mortality reduction for women who are actually screened are 48 percent reduction in case control studies and 38 percent reduction in cohort studies.
- Use of mammography also results in a substantial reduction in the incidence of late-stage breast cancer (37 percent decrease).
- Overall, women age 40 and older who choose mammography screening can expect to decrease their chances of dying from breast cancer by about 40 percent. |
| Plescia (2013) The National Prevention Strategy and breast cancer screening | **Key points:**
- An assessment of the future of breast cancer screening found wide disparity between organizational recommendations of who and when to screen for breast cancer and what actually is done in the patient encounter by physicians.
- The authors noted discordant screening of women who are unlikely to benefit from it, including women who are terminally ill, as well as mammography use among women younger than age 40.
- They also determined irregularities in process that need attention, such as a study of primary care providers’ practices that found just 40 percent reported that they had a system to remind women with appropriate indication to come in for breast cancer screening. |
| Gøtzsche (2011) Screening for breast cancer with mammography | **Key points:**
- A Cochrane review of eight clinical trials inclusive of 600,000 women screened for breast cancer with mammography found disparate results based on study design.
- Three trials with adequate randomization did not show a significant reduction in breast cancer mortality at 13 years of follow-up while four trials with suboptimal randomization showed a significant reduction in breast cancer mortality.
- Authors noted that numbers of lumpectomies and mastectomies were significantly larger in women undergoing screening with mammography versus control without mammography, and that the use of radiotherapy was similarly increased. |

**References**
Professional society guidelines/other:


Peer-reviewed references:


**CMS National Coverage Determinations (NCDs):**


**Local Coverage Determinations (LCDs):**

No LCDs identified as of the writing of this policy.

**Commonly submitted codes**

Below are the most commonly submitted codes for the services and items subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill in accordance with those manuals.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comments</th>
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<tbody>
<tr>
<td>77057</td>
<td>Screening mammography, bilateral (two view film study, each breast)</td>
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<tr>
<td>77058</td>
<td>MRI, imaging, breast, with/without contrast; unilateral</td>
<td></td>
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<tr>
<td>77063</td>
<td>Screening digital breast tomosynthesis, bilateral (List separately in addition to code for primary procedure)</td>
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<tr>
<th>ICD-10 Code</th>
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<tbody>
<tr>
<td>Z12.31</td>
<td>Encounter for screening mammogram for malignant neoplasm breast</td>
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<td>Z12.39</td>
<td>Encounter for other screening for malignant neoplasm, breast</td>
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<tr>
<td>Z80.3</td>
<td>Family history of malignant neoplasm, breast</td>
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<tr>
<td>G0202</td>
<td>Screening mammography, bilateral (2-view study of each breast), including</td>
<td></td>
</tr>
<tr>
<td></td>
<td>computer-aided detection (CAD) when performed.</td>
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**Appendix A**

The following are the ACS 2015 recommendations for early breast cancer detection in women without breast symptoms.

These guidelines are for women at average risk for breast cancer. Women with a personal history of breast cancer, a family history of breast cancer, a genetic mutation known to increase risk of breast cancer (such as BRCA), and women who had radiation therapy to the chest before the age of 30 are at higher risk for breast cancer, not average-risk. (See below for guidelines for women at higher than average risk.)

- Women ages 40 to 44 should have the choice to start annual breast cancer screening with mammograms if they wish to do so. The risks of screening as well as the potential benefits should be considered.
- Women age 45 to 54 should get mammograms every year.
- Women age 55 and older should switch to mammograms every two years, or have the choice to continue yearly screening.
- Screening should continue as long as a woman is in good health and is expected to live 10 more years or longer.

All women should be familiar with the known benefits, limitations, and potential harms associated with breast cancer screening. They should also be familiar with how their breasts normally look and feel and report any changes to a health care provider right away.

Clinical breast exam and breast self-exam research does not show a clear benefit of physical breast exams done by either a health professional or by the woman for breast cancer screening. Due to this lack of evidence, regular clinical breast exam and breast self-exam are not recommended. Still, all women should be familiar with how their breasts normally look and feel and report any changes to a health care provider right away.

The following guidelines are for women at higher than average risk. Women who are at high risk for breast cancer based on certain factors should get an MRI and a mammogram every year. This includes women who:

- Have a lifetime risk of breast cancer of about 20 percent to 25 percent or greater, according to risk assessment tools that are based mainly on family history.
- Have a known BRCA1 or BRCA2 gene mutation.
- Have a first-degree relative (parent, brother, sister, or child) with a BRCA1 or BRCA2 gene mutation, and have not had genetic testing themselves.
• Had radiation therapy to the chest when they were between the ages of 10 and 30 years.
• Have Li-Fraumeni syndrome, Cowden syndrome, or Bannayan-Riley-Ruvalcaba syndrome, or have first-degree relatives with one of these syndromes.

The ACS recommends against MRI screening for women whose lifetime risk of breast cancer is less than 15 percent.

There’s not enough evidence to make a recommendation for or against yearly MRI screenings for women who have a moderately increased risk of breast cancer (a lifetime risk of 15 percent to 20 percent according to risk assessment tools that are based mainly on family history) or who may be at increased risk of breast cancer based on certain factors, such as:
• Having a personal history of breast cancer, ductal carcinoma in situ (DCIS), lobular carcinoma in situ (LCIS), atypical ductal hyperplasia (ADH), or atypical lobular hyperplasia (ALH).
• Having dense breasts (“extremely” or “heterogeneously” dense) as seen on a mammogram.
• If MRI is used, it should be in addition to, not instead of, a screening mammogram. This is because although an MRI is a more sensitive test (it’s more likely to detect cancer than a mammogram), it may still miss some cancers that a mammogram would detect.

For most women at high risk, screening with MRI and mammograms should begin at age 30 years and continue for as long as a woman is in good health. But because the evidence is limited about the best age at which to start screening, this decision should be based on shared decision-making between patients and their health care providers, taking into account personal circumstances and preferences.

Tools used to assess breast cancer risk:

Several risk assessment tools, with names such as the Gail model, the Claus model, and the Tyrer-Cuzick model, are available to help health professionals estimate a woman’s breast cancer risk. These tools give approximate, rather than precise, estimates of breast cancer risk based on different combinations of risk factors and different data sets.

Because the different tools use different factors to estimate risk, they may give different risk estimates for the same woman. For example, the Gail model bases its risk estimates on certain personal risk factors, like current age, age at first menstrual period and history of prior breast biopsies, along with any history of breast cancer in first-degree relatives. In contrast, the Claus model estimates risk based only on family history of breast cancer in both first and second-degree relatives. These two models could easily give different estimates for the same person.

Risk assessment tools (e.g., the Gail model) that are not based mainly on family history are not appropriate to use with the ACS guidelines to decide if a woman should have MRI screening. The use of any of the risk assessment tools and its results should be discussed by a woman with her health care provider.
It is recommended that women who get a screening MRI do so at a facility that can do an MRI-guided breast biopsy at the same time if needed. Otherwise, the woman will have to have a second MRI done at another facility when she has the biopsy.

There’s no evidence right now that MRI is an effective screening tool for women at average risk. While MRI is more sensitive than mammograms, it also has a higher false-positive rate. (This means it’s more likely to find something that turns out not to be cancer.) This would lead to unneeded biopsies and other tests in many of the women screened, which can lead to a lot of worry and anxiety.

The ACS believes the use of mammograms and MRI (in women at high risk), according to the recommendations outlined above offers women the best chance to reduce their risk of dying from breast cancer. This approach is clearly better than anyone exam or test alone.

Appendix B

The 2016 USPSTF final recommendations for screening for breast cancer are excerpted below. They, along with a summary figure, can be viewed in full at http://annals.org/aim/fullarticle/2480757/screening-breast-cancer-u-s-preventive-services-task-force-recommendation.

The USPSTF recommends biennial screening mammography for women aged 50 to 74 years. (B recommendation)

The decision to start screening mammography in women prior to age 50 years should be an individual one. Women who place a higher value on the potential benefit than the potential harms may choose to begin biennial screening between the ages of 40 and 49 years. (C recommendation)

- For women who are at average risk for breast cancer, most of the benefit of mammography results from biennial screening during ages 50 to 74 years. Of all of the age groups, women aged 60 to 69 years are most likely to avoid breast cancer death through mammography screening. While screening mammography in women aged 40 to 49 years may reduce the risk for breast cancer death, the number of deaths averted is smaller than that in older women and the number of false-positive results and unnecessary biopsies is larger. The balance of benefits and harms is likely to improve as women move from their early to late 40s.
- In addition to false-positive results and unnecessary biopsies, all women undergoing regular screening mammography are at risk for the diagnosis and treatment of noninvasive and invasive breast cancer that would otherwise not have become a threat to their health, or even apparent, during their lifetime (known as “overdiagnosis”). Beginning mammography screening at a younger age and screening more frequently may increase the risk for overdiagnosis and subsequent overtreatment.
• Women with a parent, sibling, or child with breast cancer are at higher risk for breast cancer and thus may benefit more than average-risk women from beginning screening in their 40s.

Go to the Clinical Considerations section for information on implementation of the C recommendation.

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women aged 75 years or older. (I statement)

The USPSTF concludes that the current evidence is insufficient to assess the benefits and harms of digital breast tomosynthesis (DBT) as a primary screening method for breast cancer. (I statement)

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of adjunctive screening for breast cancer using breast ultrasonography, magnetic resonance imaging (MRI), DBT, or other methods in women identified to have dense breasts on an otherwise negative screening mammogram. (I statement)

These recommendations apply to asymptomatic women aged 40 years or older who do not have preexisting breast cancer or a previously diagnosed high-risk breast lesion and who are not at high risk for breast cancer because of a known underlying genetic mutation (such as a \textit{BRCA1} or \textit{BRCA2} gene mutation or other familial breast cancer syndrome) or a history of chest radiation at a young age.

Appendix C

The following is excerpted from the webpage of the Center for Consumer Information & Insurance Oversight of the Centers for Medicare & Medicaid Services. The most current version can be viewed at \url{https://www.cms.gov/cciio/resources/data-resources/ehb.html}.

Preventive services:

The EHB benchmark plans displayed may not offer the preventive services described in 45 CFR 147.130. However, as described in 45 CFR 156.115(a)(4), EHB plans must comply with that section.

State-required benefits:

For purposes of determining EHB, state-required benefits (or mandates) are considered to include only requirements that a health plan cover specific care, treatment or services. Provider mandates, which require a health plan to reimburse specific health care professionals who render a covered service within their scope of practice, are not considered to be state-required benefits for purposes of EHB coverage. Similarly, state-required benefits are not considered to include dependent mandates, which require a health plan to define dependents in a specific manner or to cover dependents under certain circumstances (e.g., newborn coverage, adopted children, domestic partners, and disabled children).
Finally, state anti-discrimination requirements relating to service delivery method (e.g., telemedicine) are not considered to be state-required benefits.

**Essential health benefits benchmark plans:**

The Center for Consumer Information & Insurance Oversight of the Centers for Medicare & Medicaid Services maintains a webpage with links for Essential Health Benefits Benchmark Plans by state. These can be viewed at [https://www.cms.gov/ccio/resources/data-resources/ehb.html](https://www.cms.gov/ccio/resources/data-resources/ehb.html).