Breast cancer screening

Clinical Policy ID: CCP.1204

Recent review date: 2/2020

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Policy contains: Breast biopsy; breast cancer screening; clinical breast examination; magnetic resonance imaging; mammography.

AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas' 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 AmeriHealth Caritas 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. AmeriHealth Caritas' 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. AmeriHealth Caritas' clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas' clinical policies are not guarantees of payment.

Coverage policy

The use of preventive care and breast cancer screening is clinically proven and, therefore, medically necessary in the following populations:

- In cis-gender and transgender women (American Cancer Society, 2017; Havrilesky, 2014; Myers, 2015; Nelson, 2016; Oeffinger, 2015; Siu [writing for the U.S. Preventive Services Task Force], 2016).
- In transgender men (people who were designated female at birth and are currently male or on the male spectrum) (Magetto, 2019; Phillips, 2014).

In assessing risk in transgender populations, family history as well as cross-sex hormone exposure in transgender women and men should be considered (de Blok, 2019).

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 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 [writing for the U.S. Preventive Services Task Force], 2016).

Alternative covered services

Routine preventive care by a primary care provider.

Background

Mammography screening has resulted in a significant reduction in mortality from breast cancer, the leading cause of premature mortality among women in the United States. A mammogram can find breast changes that could be cancerous 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 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 updated its guidelines for screening women at average risk for breast cancer. 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 manual breast examinations from a health care provider and mammography. The American Cancer Society revised these guidelines in 2017.

Women with a personal history of breast cancer, a family history of breast cancer, or 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 than average risk for breast cancer. Women who are at high risk for breast cancer based on certain factors should get a magnetic resonance imaging scan and a mammogram every year.

The American Cancer Society 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 overdiagnosis is not sufficient to estimate a lifetime risk with confidence. The American Cancer Society cited more favorable tumor characteristics when premenopausal women are screened annually as the basis for recommending a one-year interval between screenings. And finally, the American Cancer Society cited a lack of evidence to support routine clinical breast examination as a screening method for women at average risk, and dropped this recommendation from its guidelines.

The U.S. Preventive Services Task Force (2016) promulgated guidelines in this regard that vary from previous recommendations of annual breast cancer screening for women over 40 years of age. The U.S. Preventive Services Task Force recommended that women over 40 years of age 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 harms of digital breast tomosynthesis, ultrasonography, and magnetic resonance imaging, these and other screening technologies and methods were not recommended.

Breast cancer prevention is designated an “essential health benefit” under the Patient Protection and Affordable Care Act, 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 (undated) has compiled a list with information on essential health benefit benchmark plans with links to details for each of the 50 states and the District of Columbia. The Affordable Care Act 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 National Breast and Cervical Cancer Early Detection Program, a program that 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. These services include mammograms, diagnostic testing for women whose screening results are abnormal, surgical consultations, and referrals to treatment.

Findings

An exhaustive synthesis of seven systematic reviews, 10 randomized controlled trials, 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 United States is associated with a reduction in mortality of approximately 20%, 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 clinical breast exam 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 clinical breast exam. For women with a first mammography screening at age 40, estimated 10-year cumulative risk of a false-positive biopsy result was 7%; 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, the American Cancer Society 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). Women with a personal history of breast cancer, a family history of breast cancer, or 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 a magnetic resonance imaging scan and a mammogram every year.

In the wake of the American Cancer Society breast cancer screening guidelines, the U.S. Preventive Services Task Force amended its 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 U.S. Preventive Services Task Force recommendations for women at average risk and for women at higher than average risk for breast cancer 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 U.S. Preventive Services Task Force 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 U.S. Preventive Services Task Force 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 will result in eight fewer breast cancer deaths. Screening 10,000 women ages 40 to 49 will result in three fewer breast cancer deaths.

With regard to screening technology, the U.S. Preventive Services Task Force 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, magnetic resonance imaging, 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 the U.S. Preventive Services Task Force 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 overdiagnosis (e.g., markers for prediction of progression in ductal carcinoma in situ; 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 or 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%. This was true of all age groups. Estimates of breast cancer mortality reduction for women who are screened are a 48% reduction in case control studies and a 38% reduction in cohort studies. Use of mammography also results in a substantial reduction in incidence of late-stage breast cancer (37% 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%.

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 Affordable Care Act (Plescia, 2013) found a 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% reported that they had a system to remind women with appropriate indication to come in for breast cancer screenings.

The term "essential health benefit" is defined in Section 1302(b) of the Affordable Care Act. The permanent statute citation is 42 U.S.C. § 300gg-13(a)(4) and related regulations. Essential health benefits include the following services:

- 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 services and chronic disease management, for adults, women, and children.
- Pediatric services, including oral and vision care.

The Health Resources & Service Administration supports the Women's Preventive Services Initiative (2016) clinical recommendations listed below for preventive services that address health needs specific to women and fill gaps in existing guidelines. These services were updated in 2019 from federal regulations originally published in 2011, requiring broad coverage, without copayments or deductibles, of:

- Screening for anxiety.
- Breast cancer screening for women at average risk.
- Breastfeeding counseling and education services and supplies.

- Screening for cervical cancer.
- Contraceptives (for exceptions, see Religious Exemptions and Accommodations for Coverage of Certain Preventive Services Under the Affordable Care Act, 45 CFR Part 147 [Department of Health and Human Services, 2017).
- Screening for gestational diabetes.
- Human immunodeficiency virus screenings.
- Screenings for interpersonal and domestic violence.
- Counseling for sexually transmitted infections.
- Well-woman preventive medical visits and exams, including the delivery and coordination of services as determined by age and risk factors.
- Screening for urinary incontinence.
- Screening for diabetes mellitis after pregnancy.

Each state's department of health has information on how to contact the nearest National Breast and Cervical Cancer Early Detection Program 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.

References

On January 30, 2020, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were 'breast cancer" (MeSH), "screening for breast cancer" (MeSH), and "guidelines for breast cancer screening We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

11/2015: initial review date and clinical policy effective date: 2/2016

12/2016: References updated.
12/2017: References updated.
1/2018: References updated. The policy ID changed from 17.01.03 to CCP.1204.
1/2020: We added four publications to the reference list. A small but growing body of work addresses breast cancer risk in transgender, or trans, populations. Transgender men are people with natal female sex who are currently male or on the male spectrum. Transgender women are people with natal male sex who are currently female or on the female spectrum. Transgender people may have surgery or take hormones to help their body conform to their gender identity. It has been hypothesized that cross-sex hormones may elevate risk for breast cancer, and that transgender men retain the same breast cancer risk as cisgender females in general. Cisgender is defined as having a gender identity that is consistent with one's natal gender.
To examine the risk for breast cancer and existing guidelines for breast cancer screening in transgender populations, Megetto (2019) conducted two systematic reviews of primary research (one examining the effect of cross-sex hormones on breast cancer risk, prognosis and mortality, and the second examining the benefits and harms of breast screening), and a third systematic review of current guidelines on breast cancer screening recommendations for transgender people. The conclusions were as follows:

- There is minimal research published on the topics of breast screening and the effect of cross-sex hormones on breast cancer risk and outcomes in transgender populations. The authors identified a need for large-scale prospective, comparative, trans-specific, quantitative studies with long-term

follow-up in order to produce reliable estimates of the effects of cross-sex hormones on breast cancer outcomes and the potential benefits and harms of screening.

- There was minimal agreement on screening recommendations for transgender people. The majority of the clinical practice documents identified by the authors provided recommendations for distinct subgroups of transgender people based on the presence of breast tissue and history of cross-sex hormone exposure. There was an observed preference for routine screening with mammography for transgender men without chest reconstruction, to be expected as transgender men without chest reconstruction and with no history of cross-sex hormone use likely have the same risk for breast cancer as most cisgender women (Phillips, 2014).
- The publications reviewed were in agreement that cross-sex hormone exposure should be considered when determining breast screening eligibility for transgender women.
- Regarding the effect of cross-sex hormones on breast cancer risk in transgender women and in transgender men, the authors identified limited evidence of very low certainty that did not show an effect of cross-sex hormones on breast cancer risk, prognosis, or mortality.
- Regarding evidence on the benefits of breast screening, the authors identified no certain benefits and very little evidence on harms. Further evidence of very low certainty due to study limitations showed that transgender women stated they experienced minimal pain during mammography and ultrasonography.

We identified one recent report (de Blok, 2019) on the results of a Dutch nationwide retrospective cohort study of 2,260 adult transgender women and 1,229 adult transgender men, all of whom took cross-sex hormones, that found an elevated rate of breast cancer among transgender women.

- Among the transgender women in the cohort, 15 cases of invasive breast cancer were identified. The median duration of hormone treatment was 18 years (range 7 – 37 years). This case number was 46 times higher than among cisgender men (standardized incidence ratio 46.7, 95% confidence interval 27.2 to 75.4), but it was lower than among cisgender women (incidence ratio 0.3, 95% confidence interval 0.2 to 0.4). The majority of tumors were of ductal origin and estrogen- and progesterone-receptor positive, and 8.3% were human epidermal growth factor 2-positive.
- Among the transgender men in the cohort, four cases of invasive breast cancer were identified (median duration of hormone treatment 15 years; range 2 – 17 years). This was lower than expected compared with cisgender women (standardized incidence ratio 0.2, 95% confidence interval 0.1 to 0.5).
- The authors concluded that the findings showed an elevated risk of breast cancer in transgender women compared with cisgender men, and a lower risk in transgender men compared with cisgender women. Notably, in transgender women, the risk increased during a relatively short duration of hormone treatment and the characteristics of the breast cancer resembled a more female pattern. These results suggest that breast cancer screening guidelines for cisgender people are sufficient for transgender people using hormone treatment.

Transgender people are considered a sexual and gender minority (SGM) by the National Institutes of Health. The National Institutes of Health's Sexual & Gender Minority Research Office issued a notice (2019) defining sexual and gender minorities as follows: *"SGM populations include, but are not limited to, individuals who identify as lesbian, gay, bisexual, asexual, transgender, two-spirit, queer, and/or intersex..."* [italics in original]. The statement continues regarding sexual and gender minorities as a population who experience disproportionately high health disparities: "SGM individuals face unique health challenges, and a continually growing body of evidence suggests that SGM individuals suffer disproportionately from a variety of conditions and diseases."

We are amending the policy coverage to include routine mammography for transgender men who have not had chest reconstruction, and for clinicians to consider exposure to cross-sex hormones and family history in both transgender women and men in assessing risk.