American College of Radiology
ACR Appropriateness Criteria®
Female Breast Cancer Screening

Variant: 1 Adult female. Breast cancer screening. Average risk.

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	Usually Appropriate	☢☢
Mammography screening	Usually Appropriate	☢☢
US breast	May Be Appropriate	O
MRI breast without and with IV contrast	May Be Appropriate	O
MRI breast without and with IV contrast abbreviated	May Be Appropriate	O
Mammography with IV contrast	Usually Not Appropriate	☢☢
MRI breast without IV contrast	Usually Not Appropriate	O
MRI breast without IV contrast abbreviated	Usually Not Appropriate	O
Sestamibi MBI	Usually Not Appropriate	☢☢☢

Variant: 2 Adult female. Breast cancer screening. Intermediate risk.

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	Usually Appropriate	☢☢
Mammography screening	Usually Appropriate	☢☢
US breast	May Be Appropriate	O
Mammography with IV contrast	May Be Appropriate	☢☢
MRI breast without and with IV contrast	May Be Appropriate	O
MRI breast without and with IV contrast abbreviated	May Be Appropriate	O
MRI breast without IV contrast	Usually Not Appropriate	O
MRI breast without IV contrast abbreviated	Usually Not Appropriate	O
Sestamibi MBI	Usually Not Appropriate	☢☢☢

Variant: 3 Adult female 30 years of age or older. Breast cancer screening. High risk.

Procedure	Appropriateness Category	Relative Radiation Level
Digital breast tomosynthesis screening	Usually Appropriate	☢☢
Mammography screening	Usually Appropriate	☢☢
MRI breast without and with IV contrast	Usually Appropriate	O
MRI breast without and with IV contrast abbreviated	Usually Appropriate	O
US breast	May Be Appropriate	O
Mammography with IV contrast	May Be Appropriate	☢☢
MRI breast without IV contrast	Usually Not Appropriate	O
MRI breast without IV contrast abbreviated	Usually Not Appropriate	O
Sestamibi MBI	Usually Not Appropriate	☢☢☢

Variant: 4 Adult female younger than 30 years of age. Breast cancer screening. High risk.

Procedure	Appropriateness Category	Relative Radiation Level
MRI breast without and with IV contrast	Usually Appropriate	O

MRI breast without and with IV contrast abbreviated	Usually Appropriate	O
US breast	May Be Appropriate	O
Digital breast tomosynthesis screening	May Be Appropriate	☢☢
Mammography screening	May Be Appropriate	☢☢
Mammography with IV contrast	Usually Not Appropriate	☢☢
MRI breast without IV contrast	Usually Not Appropriate	O
MRI breast without IV contrast abbreviated	Usually Not Appropriate	O
Sestamibi MBI	Usually Not Appropriate	☢☢☢

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Summary of Literature Review

Introduction/Background

Breast cancer is the most common nonskin cancer diagnosis in females and is second only to lung cancer with respect to cancer deaths. Early detection of breast cancer from regular screening substantially reduces breast cancer mortality [1]. Because regular screening identifies tumors when they are smaller and with fewer nodal metastases, patients with screen-detected breast cancers are less likely to require mastectomy or chemotherapy, thereby also decreasing morbidity [2].

Breast cancer risk is frequently divided into 3 major categories: average, intermediate, and high risk. Numerous factors contribute to breast cancer risk, so no single method or definition is used to classify each woman into a specific risk category [3,4]. The use of validated statistical models based largely upon family history, which also incorporate additional risk factors, represents one mechanism to estimate risk. Currently, risk categories are most frequently defined by estimated lifetime risk; however, different time horizons, such as 5 or 10 year risk, may also be valuable for guideline development and informed decision-making [3]. Females at average risk are typically defined as those with <15% estimated lifetime risk for developing breast cancer, whereas intermediate-risk females are generally defined as those with a 15% to 20% estimated lifetime risk. The high-risk category typically includes females who have a >20% estimated lifetime risk: females who carry a deleterious genetic mutation that increases breast cancer risk, as well as untested first-degree relatives of patients with these mutations and females who have received radiation therapy to the thorax or upper abdomen at an early age (<30 years). Some females with a personal history of high-risk breast lesions, a personal history of breast cancer, dense breast tissue, or a family history of breast cancer may fit into the intermediate- or high-risk categories, depending upon their specific risk factors or combination of factors [3]. Elevated risk is sometimes used to refer to females in both the intermediate- and high-risk categories [3].

Breast cancer screening guidelines vary across medical professional organizations, although published guidelines agree that regular breast cancer screening decreases morbidity and breast

cancer mortality [5-8]. Medical professional organizations may also define breast cancer risk categories using different methodologies. Although screening guidelines for high-risk patients have typically been similar, discrepant recommendations for average- and intermediate-risk females have sparked controversy and confusion. In part due to differences in screening guidelines, use of breast cancer screening modalities remains suboptimal in females of all risk categories. In June 2024, the United States Preventive Services Task Force (USPSTF) updated recommendations to include biennial screening mammography for females at average risk aged 40 to 74 years based upon a commissioned systematic review, including Cancer Intervention and Surveillance Modeling Network (CISNET) modeling [9,10]. The ACR encourages patients to undergo breast cancer risk assessment by 25 years of age, so elevated-risk patients have the opportunity to benefit from earlier and more aggressive breast cancer screening regimens, when appropriate [3]. The ACR recommends that both the benefits and risks of breast cancer screening and supplemental screening be considered to assist patients in making informed decisions regarding their health care [11].

Although all patients are at risk for developing breast cancer, this document addresses breast cancer screening in cisgender females (birth assigned female with a female gender identity). For breast cancer screening in transgender and gender diverse patients, please reference the ACR Appropriateness Criteria® topic on "Transgender Breast Cancer Screening" [12]. Additional ACR Appropriateness Criteria® topics on "Supplemental Breast Cancer Screening Based on Breast Density" [13], "Imaging after Mastectomy and Breast Reconstruction" [14], "Imaging after Breast Surgery" [15], and "Breast Imaging of Pregnant and Lactating Females" [16] can be referenced in the appropriate clinical context.

Discussion of Procedures by Variant

Variant 1: Adult female. Breast cancer screening. Average risk.

The goal of imaging is to detect and diagnose breast cancer early. This imaging information improves outcome by decreasing morbidity and mortality from breast cancer.

Variant 1: Adult female. Breast cancer screening. Average risk.
A. Digital breast tomosynthesis screening

Digital breast tomosynthesis (DBT) displays reconstructed stacked images of the breast in combination with digital mammographic views, which may be synthetic mammograms reconstructed from the acquired tomosynthesis data set or full-field digital mammograms (FFDM). Compared to FFDM or synthetic mammograms alone, most studies demonstrate that DBT increases cancer detection rate (CDR) and decreases recall rates [17-25]; although some studies have not reached statistical significance [26] or have found less compelling results in subsets of females, such as those with extremely dense breasts [27,28]. Dense breast tissue decreases the sensitivity of mammography [29] and is an independent risk factor for developing breast cancer [30]. Compared to average breast density (near the threshold between heterogeneously dense and scattered areas of fibroglandular density), the relative risks for developing breast cancer are 1.2 for heterogeneously dense and 2.1 for extremely dense breasts [31]. Some health care providers may therefore consider females with extremely dense breasts to no longer be average risk. Irrespective of risk category, meta-analyses have demonstrated an incremental increase in CDR of 1.6 to 3.2 per 1,000 screening DBT examinations and a 2.2% pooled decrease in recall rate compared to digital mammography [21,32,33].

The degree of breast cancer mortality reduction from screening mammography varies with different screening regimens. Mortality reduction is greater when screening begins at 40 years of age rather than 45 or 50 years of age and when screening is done more frequently (annually rather than biennially) [9-11,34]. Annual screening with DBT led to greater reductions in mortality compared with biennial screening, with 37% median reduction with screening annually from 40 to 75 years of age [10]. Beginning screening at an earlier age and more frequent screening result in a greater number of imaging studies performed, so these screening regimens may also increase the number of false-positive examinations and biopsies [9-11,35]. To maximize the benefits, the ACR recommends screening DBT in average-risk females each year beginning at 40 years of age. Although randomized controlled trials of screening mammography did not enroll females >74 years of age, observational studies demonstrate that some females ≥75 years of age may continue to benefit from screening mammography [11,35]. There is no upper age limit agreed upon for screening mammography [5,6,11,35]. Because mortality reduction from screening mammography requires years before being fully attained, screening recommendations should be based upon life expectancy and competing comorbidities, rather than age alone [11,35-37]. Females should continue screening mammography as long as they remain in overall good health and are willing to undergo the examination and subsequent testing or biopsy, if an abnormality is identified [5,11].

Because screening mammography decreases breast cancer mortality, screening mammography or screening DBT is still performed in females undergoing supplemental screening studies [3,11,38].

Variant 1: Adult female. Breast cancer screening. Average risk.
B. Mammography screening

To date, mammography is the only screening modality shown to decrease breast cancer mortality. Multiple randomized controlled trials demonstrate that invitation to screening mammography results in at least a 22% reduction in breast cancer mortality [38]. For example, after 29 years of follow-up, the Swedish Two-County trial demonstrated a 27% to 31% reduction in breast cancer mortality in 133,065 females 40 to 74 years of age invited to screening despite use of single view mammography and the 24 to 33 month interval between subsequent screenings [1]. Randomized controlled trials of screening mammography in which advanced stage breast cancers decreased by 20% or more demonstrate even greater reductions in breast cancer mortality [11]. Observational studies, including those from population-based service screening programs, also demonstrate larger reductions in breast cancer mortality (≥40%) in females who were actually screened [11,38].

In addition to mortality reduction, screening mammography decreases treatment morbidity, because screen-detected tumors are typically lower stage (eg, smaller and more likely to be node-negative), compared to breast cancers detected by palpation [2,11]. Despite these benefits, screening mammograms also have risks. The most common perceived risks include false-positive recalls and biopsies, overdiagnosis, and patient anxiety [5,7,35]. Approximately 10% of screening mammograms result in a recall for additional imaging, although <2% result in a recommendation for percutaneous biopsy following additional imaging [11]. Overdiagnosis refers to breast cancers that are detected by screening that would not have otherwise become apparent during the patient's lifetime. The reported frequency of overdiagnosis varies widely in the published literature due to important underlying differences in study methodology. Overdiagnosis estimates that do not account for breast cancer risk, trends in breast cancer incidence, or lead time bias range from 0% to 54%, whereas adjusted estimates range from 1% to 10% [39,40]. Overdiagnosis estimates increase with age at screening [39,40]. Although the risks of screening may impact uptake and adherence to screening mammography, prior research has shown that females value early

detection of breast cancer over false-positives and screening-related anxiety [11].

Despite the established mortality benefit, published guidelines differ in their recommendations for screening mammography due to variations in the perceptions of the relative risks and benefits [5,41]. The degree of breast cancer mortality reduction from screening mammography varies with different screening regimens. Mortality reduction is greater when screening begins at 40 years of age rather than 45 or 50 years of age and when screening is done more frequently (annually rather than biennially) [9-11,34]. Annual screening mammography for females 40 to 84 years of age decreases mortality by 40% (12 lives per 1,000 females screened), whereas biennial screening mammography for females 50 to 74 years of age only decreases mortality by 23% (7 lives per 1,000 females screened) [35]. Earlier initiation of screening and more frequent screening result in a greater number of imaging studies performed, so these screening regimens also increase the number of false-positive examinations and biopsies [9-11,35]. Although randomized controlled trials of screening mammography did not enroll females >74 years of age, observational studies demonstrate that females ≥75 years of age may continue to benefit from screening mammography [11,35]. There is no upper age limit agreed upon for screening mammography [5,6,11,35]. Because mortality reduction from screening mammography requires years before being fully attained, screening recommendations should be based upon life expectancy and competing comorbidities, rather than age alone [11,35-37]. Females should continue screening mammography as long as they remain in overall good health and are willing to undergo the examination and subsequent testing or biopsy, if an abnormality is identified [5,11].

For females 40 to 49 years of age, randomized controlled trials and observational studies demonstrate that screening mammography decreases breast cancer mortality by 15% to 50% [1,11,35,36,42]. Results from CISNET suggest that annual screening mammography in females 40 to 49 years of age saves 42% more lives and life-years than biennial screening due to faster growing tumors in younger females [34]. Females screened between 40 and 49 years of age are also less likely to require mastectomy or chemotherapy than females diagnosed with palpable tumors [2].

Non-Hispanic Black, Hispanic Black, and Hispanic White females have higher breast cancer mortality than non-Hispanic White females, and minority females often present at younger ages with more aggressive tumor subtypes [3,11]. Therefore, decreasing access to screening mammography, especially in females 40 to 49 years of age, may disproportionately impact minority females. In June 2024, the USPSTF updated recommendations to start screening mammography for all average-risk females at 40 years of age, acknowledging it would mitigate disparities in breast cancer mortality and would significantly benefit Black females, who have disproportionately high mortality rates, 40% higher than White females in the United States [9].

Annual screening mammography results in a greater reduction in mortality compared to biennial screening [10,11]. In females 40 to 84 years of age, annual screening reduces mortality by 40%, compared to a 32% reduction for biennial screening [35]. With regular screening, interval breast cancers do occur with a higher frequency in females undergoing biennial or triennial screening compared to annual screening. The sensitivity of mammography is decreased in some groups of females, including those with dense breasts [43]. Dense breast tissue decreases the sensitivity of mammography [29] and is an independent risk factor for developing breast cancer [30]. Compared to average breast density (near the threshold between heterogeneously dense and scattered areas of fibroglandular density), the relative risks for developing breast cancer are 1.2 for

heterogeneously dense and 2.1 for extremely dense breasts [31]. Some health care providers may therefore consider females with extremely dense breasts to no longer be average risk. Given the limitations of mammography and to minimize interval cancers, supplemental screening modalities have been investigated in females at average risk.

Because screening mammography decreases breast cancer mortality, screening mammography or screening DBT is still performed in females undergoing supplemental screening studies [3,11,38]. Rather than supplementing screening mammography with additional imaging modalities, some have suggested limiting females offered screening mammography based upon individual patient risk assessed by various risk models, breast density, or genetic information such as single-nucleotide polymorphism. However, the randomized controlled trials demonstrating mortality reduction and most large-scale observational studies enrolled females based upon geographic location and age, not other individual patient risk factors. In an observational study in females <50 years of age, restricting screening to females with a first-degree family history, extremely dense breast tissue, or both, would cause 66% of potentially screen-detected cancers to be missed [44].

To maximize the benefits, the ACR recommends screening mammography in average-risk females each year beginning at 40 years of age. Females should continue screening mammography as long as they remain in overall good health and are willing to undergo the examination and subsequent testing or biopsy, if an abnormality is identified [5,11].

Variant 1: Adult female. Breast cancer screening. Average risk.
C. Mammography with IV contrast

Data are limited regarding the use of mammography with intravenous (IV) contrast for screening females at average risk. Most published studies evaluated mammography with IV contrast in females with dense breasts and elevated risk, so results specific to females at average risk, especially those without dense breasts, are not currently available. For supplemental screening recommendations based upon breast density, please refer to the ACR Appropriateness Criteria® topic on "Supplemental Breast Cancer Screening Based on Breast Density" [13].

Variant 1: Adult female. Breast cancer screening. Average risk.
D. MRI breast without and with IV contrast

Although data are limited regarding the use of breast MRI without and with IV contrast for screening females at average risk, a study has demonstrated that breast MRI demonstrates incremental cancer detection (15-16 cancers per 1,000 breast MRI examinations) over screening mammography with or without screening ultrasound (US) in average-risk females irrespective of breast density [45]. Breast MRI also decreases interval cancers [45,46]. In the DENSE trial, breast MRI significantly reduced interval cancers within females with extremely dense breast tissue and normal mammography, so the European Society of Breast Imaging now recommends screening breast MRI every 2 to 4 years in females 50 to 70 years of age with extremely dense breasts [46,47]. Compared to average breast density (near the threshold between heterogeneously dense and scattered areas of fibroglandular density), the relative risks for developing breast cancer are 1.2 for heterogeneously dense and 2.1 for extremely dense breasts [31]. Some health care providers may therefore consider females with extremely dense breasts to no longer be average risk.

For supplemental screening recommendations based upon breast density, please refer to the ACR Appropriateness Criteria® topic on "Supplemental Breast Cancer Screening Based on Breast Density" [13].

Variant 1: Adult female. Breast cancer screening. Average risk.
E. MRI breast without and with IV contrast abbreviated

Data are limited regarding the use of abbreviated breast MRI without and with IV contrast for screening females at average risk. The ECOG-ACRIN abbreviated MRI trial demonstrated a significantly higher CDR for abbreviated breast MRI without and with IV contrast (15 cancers per 1,000) compared with DBT (6 cancers per 1,000), although the study recruited females with dense breasts [48]. In addition to dense breasts, females enrolled in the trial had variable 5 and 10 year risk profiles based upon the Breast Cancer Surveillance Consortium risk calculator and 19% reported 1 or more first degree relatives with breast cancer [48]. Compared to average breast density (near the threshold between heterogeneously dense and scattered areas of fibroglandular density), the relative risks for developing breast cancer are 1.2 for heterogeneously dense and 2.1 for extremely dense breasts [31]. Some health care providers may therefore consider females with extremely dense breasts to no longer be average risk.

For supplemental screening recommendations based upon breast density, please refer to the ACR Appropriateness Criteria® topic on "Supplemental Breast Cancer Screening Based on Breast Density" [13].

Variant 1: Adult female. Breast cancer screening. Average risk.
F. MRI breast without IV contrast

There is no relevant literature to support the use of MRI without IV contrast for screening females at average risk.

Variant 1: Adult female. Breast cancer screening. Average risk.
G. MRI breast without IV contrast abbreviated

There is no relevant literature to support the use of abbreviated MRI without IV contrast for screening females at average risk.

Variant 1: Adult female. Breast cancer screening. Average risk.
H. Sestamibi MBI

Data are limited regarding the use of sestamibi molecular breast imaging (MBI) for screening females at average risk. Most studies have focused upon females with dense breasts and variable risk profiles. One of the larger studies published to date of 1,696 females with recent negative or benign mammographic examinations showed that sestamibi MBI yielded an incremental CDR of 7.7 cancers per 1,000 examinations; however, all 13 cancers were detected in females with dense breasts [49]. Although 92% of the females within the study had <20% estimated lifetime risk, the estimates ranged from 6.1% to 17.2% [49]. Additional retrospective and prospective studies have demonstrated similar incremental CDR for sestamibi MBI of 6.5 to 9 per 1,000 over mammography [43,50]. Sestamibi MBI demonstrates similar sensitivity, better specificity, and lower recall rate compared to supplemental screening US in females with dense breasts [50,51].

Variant 1: Adult female. Breast cancer screening. Average risk.
I. US Breast

Most studies evaluating the utility of screening with breast US have focused on females with dense breast tissue with or without other risk factors. Dense breast tissue decreases the sensitivity of mammography [29] and is an independent risk factor for developing breast cancer [30]. Screening breast US in females with mammographically dense breasts, including those with risk factors placing them at increased breast cancer risk, identifies mammographically occult, small, node-

negative invasive tumors with an increased CDR of 1.8 to 4.6 cancers per 1,000 females screened [43,52]. Although supplemental screening US in females with dense breasts results in an increased CDR, US also increases recall rate, false-positive examinations, and false-positive biopsies [29,52-58].

For supplemental screening recommendations based upon breast density, please refer to the ACR Appropriateness Criteria® topic on "Supplemental Breast Cancer Screening Based on Breast Density" [13].

Data regarding supplemental screening US in average-risk females with nondense breasts is less compelling. In a study of 1,526 average-risk females without mammographic abnormalities, screening with US demonstrated an overall incremental CDR of 3.3 per 1,000, with 5.1 per 1,000 examinations in dense breasts and 0 per 1,000 in nondense breasts compared to digital mammography [59]. In another study of 1,003 average-risk females, US yielded an overall incremental CDR of 3.2 per 1,000 examinations, with 0 per 1,000 in nondense breasts, compared to DBT with or without digital mammography [56].

Variant 2: Adult female. Breast cancer screening. Intermediate risk.

The goal of imaging is to detect and diagnose breast cancer early. This imaging information improves outcome by decreasing morbidity and mortality from breast cancer.

Evidence-based screening recommendations for intermediate-risk females are complicated by different methodologies for risk assessment using variable time spans (eg, lifetime, 5 year, 10 year), as well as the interplay between breast density and additional risk factors [43]. Compared to average breast density (near the threshold between heterogeneously dense and scattered areas of fibroglandular density), the relative risks for developing breast cancer are 1.2 for heterogeneously dense and 2.1 for extremely dense breasts [31]. Some health care providers may therefore consider females with extremely dense breasts to be at increased risk. Published data are primarily from observational studies, which have been largely retrospective with variable risk assessment methods resulting in heterogeneous patient groups. In a subset of the literature, intermediate-risk females have been grouped with high-risk females or average-risk females without stratified analyses. Image-based deep learning models have been found to accurately identify increased-risk patients in retrospective studies [60,61], and are likely to become increasingly available for personalized risk assessment. The absence of high-quality prospective studies of various supplemental imaging modalities specific to intermediate-risk patients creates challenges when developing guidelines [43]. Depending upon family and personal history of breast cancer, prior biopsies yielding high-risk lesions, and other risk factors, certain intermediate-risk females may benefit from screening starting at <40 years of age, as well as more intensive screening regimens with supplemental imaging modalities [3].

Please reference the ACR Appropriateness Criteria® topics on "Transgender Breast Cancer Screening" [12], "Supplemental Breast Cancer Screening Based on Breast Density" [13], "Imaging after Mastectomy and Breast Reconstruction" [14], "Imaging after Breast Surgery" [15], and "Breast Imaging of Pregnant and Lactating Females" [16] in the appropriate clinical context.

Variant 2: Adult female. Breast cancer screening. Intermediate risk.
A. Digital breast tomosynthesis screening

DBT displays reconstructed stacked images of the breast in combination with digital

mammographic views, which may be synthetic mammograms reconstructed from the acquired tomosynthesis dataset or FFDM. Compared to FFDM or synthetic mammograms alone, most studies demonstrate that DBT increases CDR and decreases recall rate [17-25]; although, some studies have not reached statistical significance [26] or have found less compelling results in subsets of females, such as those with extremely dense breasts [27,28]. Dense breast tissue decreases the sensitivity of mammography [29] and is an independent risk factor for developing breast cancer [30]. Compared to average breast density (near the threshold between heterogeneously dense and scattered areas of fibroglandular density), the relative risks for developing breast cancer are 1.2 for heterogeneously dense and 2.1 for extremely dense breasts [31]. Some health care providers may therefore consider females with extremely dense breasts to no longer be average risk. Irrespective of risk category, meta-analyses have demonstrated an incremental increase in CDR of 1.6 to 3.2 per 1,000 screening DBT examinations and a 2.2% pooled decrease in recall rate compared to digital mammography [21,32,33].

The degree of breast cancer mortality reduction from screening mammography varies with different screening regimens. Mortality reduction is greater when screening begins at 40 years of age rather than 45 or 50 years of age and when screening is done more frequently (annually rather than biennially) [9-11,34]. Beginning screening at an earlier age and more frequent screening, result in a greater number of imaging studies performed, so these screening regimens also increase the number of false-positive examinations and biopsies [9-11,35]. Although randomized controlled trials of screening mammography did not enroll females >74 years of age, observational studies demonstrate that some females ≥75 years of age may continue to benefit from screening mammography [11,35]. There is no upper age limit agreed upon for screening mammography [5,6,11,35]. Because mortality reduction from screening mammography requires years before being fully attained, screening recommendations should be based upon life expectancy and competing comorbidities, rather than age alone [11,35-37]. Females should continue screening mammography as long as they remain in overall good health and are willing to undergo the examination and subsequent testing or biopsy, if an abnormality is identified [5,11].

Within the limited studies of females at elevated risk due to personal and/or family history of breast cancer, DBT decreased recall rate without a significant increase in CDR compared to FFDM; however, small sample sizes restrict analyses [3,43].

Because screening mammography decreases breast cancer mortality, screening mammography or screening DBT is still performed in females undergoing supplemental screening studies [3,11,38]. The ACR recommends annual screening mammography beginning no later than 40 years of age for females at intermediate risk [3]. For those with a family history of breast cancer, mammography should begin earlier if familial breast cancer occurred at a young age, typically 10 years prior to the youngest age at presentation but generally not before age 30 [6]. For females who have lobular neoplasia or atypical hyperplasia diagnosed prior to 40 years of age, annual screening mammography should be performed from time of diagnosis but generally not prior to 30 years of age [41]. Early detection of second breast cancers improves survival, so patients with a personal history of breast cancer should undergo annual mammography or DBT for surveillance following breast conservation therapy [3].

Variant 2: Adult female. Breast cancer screening. Intermediate risk.
B. Mammography screening

To date, mammography is the only screening modality shown to decrease breast cancer mortality.

Multiple randomized controlled trials demonstrate that invitation to screening mammography results in at least a 22% reduction in breast cancer mortality [38]. For example, after 29 years of follow-up, the Swedish Two-County trial demonstrated a 27% to 31% reduction in breast cancer mortality in 133,065 females 40 to 74 years of age invited to screening despite use of single view mammography and the 24 to 33 month interval between subsequent screenings [1]. Randomized controlled trials of screening mammography in which advanced stage breast cancers decreased by 20% or more demonstrate even greater reductions in breast cancer mortality [11]. Observational studies, including those from population-based service screening programs, also demonstrate larger reductions in breast cancer mortality (≥40%) in females who were actually screened [11,38].

In addition to mortality reduction, screening mammography decreases treatment morbidity, because screen-detected tumors are typically lower stage (eg, smaller and more likely to be node-negative) compared to breast cancers detected by palpation [2,11]. Despite these benefits, screening mammograms also have risks. The most common perceived risks include false-positive recalls and biopsies, overdiagnosis [5,7,35], and patient anxiety. Approximately 10% of screening mammograms result in a recall for additional imaging, although <2% result in a recommendation for percutaneous biopsy following additional imaging [11]. Overdiagnosis refers to breast cancers that are detected by screening that would not have otherwise become apparent during the patient's lifetime. The reported frequency of overdiagnosis varies widely in the published literature, due to important underlying differences in study methodology. Overdiagnosis estimates that do not account for breast cancer risk, trends in breast cancer incidence, or lead time bias range from 0% to 54%, whereas adjusted estimates range from 1% to 10% [39,40]. Overdiagnosis estimates increase with age at screening [39,40]. Although the risks of screening may impact uptake and adherence to screening mammography, prior research has shown that females value early detection of breast cancer over false-positives and screening-related anxiety [11].

Despite the established mortality benefit, published guidelines differ in their recommendations for screening mammography due to variations in the perceptions of the relative risks and benefits [5,41]. The degree of breast cancer mortality reduction from screening mammography varies with different screening regimens. Mortality reduction is greater when screening begins 40 years of age rather than 45 or 50 years of age and when screening is done more frequently (annually rather than biennially) [9-11,34]. Annual screening mammography for females 40 to 84 years of age decreases mortality by 40% (12 lives per 1,000 females screened), whereas biennial screening mammography for females 50 to 74 years of age only decreases mortality by 23% (7 lives per 1,000 females screened) [35]. Earlier initiation of screening and more frequent screening result in a greater number of imaging studies performed, so these screening regimens also increase the number of false-positive examinations and biopsies [9-11,35]. Although randomized controlled trials of screening mammography did not enroll females >74 years of age, observational studies demonstrate that females ≥75 years of age may continue to benefit from screening mammography [11,35]. There is no upper age limit agreed upon for screening mammography [5,6,11,35]. Because mortality reduction from screening mammography requires years before being fully attained, screening recommendations should be based upon life expectancy and competing comorbidities, rather than age alone [11,35-37]. Females should continue screening mammography as long as they remain in overall good health and are willing to undergo the examination and subsequent testing or biopsy, if an abnormality is identified [5,11].

For females 40 to 49 years of age, randomized controlled trials and observational studies

demonstrate that screening mammography decreases breast cancer mortality by 15% to 50% [1,11,35,36,42]. Results from the CISNET suggest that annual screening mammography in females 40 to 49 years of age saves 42% more lives and life-years than biennial screening due to faster growing tumors in younger females [34]. Females screened between 40 and 49 years of age are also less likely to require mastectomy or chemotherapy than females diagnosed with palpable tumors [2].

Non-Hispanic black females, Hispanic black, and Hispanic white females have higher breast cancer mortality than non-Hispanic white females, and minority females often present at younger ages with more aggressive tumor subtypes [3,11]. Therefore, decreasing access to screening mammography, especially in females 40 to 49 years of age, may disproportionately impact minority females. In June 2024, the USPSTF updated recommendations to start screening mammography for all average-risk females at 40 years of age, acknowledging it would mitigate disparities in breast cancer mortality and would significantly benefit Black females, who have disproportionately high mortality rates, 40% higher than White females in the United States [9].

Annual screening mammography results in a greater reduction in mortality compared to biennial screening [10,11]. In females 40 to 84 years of age, annual screening reduces mortality by 40%, compared to a 32% reduction for biennial screening [35]. With regular screening, interval breast cancers do occur with a higher frequency in females undergoing biennial or triennial screening compared to annual screening. The sensitivity of mammography is decreased in some groups of females, including those with dense breasts [43]. Dense breast tissue decreases the sensitivity of mammography [29] and is an independent risk factor for developing breast cancer [30]. Compared to average breast density (near the threshold between heterogeneously dense and scattered areas of fibroglandular density), the relative risks for developing breast cancer are 1.2 for heterogeneously dense and 2.1 for extremely dense breasts [31]. Some health care providers may therefore consider females with extremely dense breasts to no longer be average risk. Given the limitations of mammography and to minimize interval cancers, supplemental screening modalities have been investigated in females at intermediate risk.

Because screening mammography decreases breast cancer mortality, screening mammography or screening DBT is still performed in females undergoing supplemental screening studies [3,11,38]. Rather than supplementing screening mammography with additional imaging modalities, some have suggested limiting females offered screening mammography based upon individual patient risk assessed by various risk models, breast density, or genetic information such as single-nucleotide polymorphisms. However, the randomized controlled trials demonstrating mortality reduction and most large-scale observational studies enrolled females based upon age and geographic location, not individual patient risk factors. An observational study in females <50 years of age, restricting screening to females with a first-degree family history, extremely dense breast tissue, or both, would cause 66% of potentially screen-detected cancers to be missed [44].

To maximize the benefits, the ACR recommends annual screening mammography beginning no later than 40 years of age for females at intermediate risk [3]. Females should continue screening mammography as long as they remain in overall good health and are willing to undergo the examination and subsequent testing or biopsy, if an abnormality is identified [5,11]. For those with a family history of breast cancer, mammography should begin earlier if familial breast cancer occurred at a young age, typically 10 years prior to the youngest age at presentation but generally

not before 30 years of age [6]. For females who have lobular neoplasia or atypical hyperplasia diagnosed prior to 40 years of age, annual screening mammography should be performed from time of diagnosis but generally not prior to 30 years of age [41]. Early detection of second breast cancers improves survival, so patients with a personal history of breast cancer should undergo annual mammography or DBT for surveillance following breast conservation therapy [3].

Variant 2: Adult female. Breast cancer screening. Intermediate risk.
C. Mammography with IV contrast

Data are limited regarding the use of mammography with IV contrast for breast cancer screening in intermediate-risk females. To date, published studies have predominantly included females with dense breasts and other risk factors resulting in intermediate- or high-risk profiles. Compared to mammography alone, mammography with IV contrast increases cancer detection (incremental CDR = 6.6-13 per 1,000) in females at elevated risk [62-66].

Variant 2: Adult female. Breast cancer screening. Intermediate risk.
D. MRI breast without and with IV contrast

MRI has a higher CDR than mammography alone, DBT, or mammography/DBT combined with US [67-70]. The incremental CDR of MRI in elevated-risk females ranges from 8 to 29 per 1,000 females, with lower CDR estimates in intermediate-risk females compared to high-risk BRCA mutation carriers [67-69,71,72]. In an study, breast MRI CDR was 15 per 1,000 in females with a prior biopsy demonstrating a high-risk lesion compared to 8 per 1,000 in females reporting a family history [71]. In females with a personal history of breast cancer, a meta-analysis estimated a CDR of 9 to 15 per 1,000 breast MRI [73]. Breast MRI detects small, node-negative invasive cancers at earlier tumor stages compared to mammography, as well as ductal carcinoma in situ [74,75]. Screening MRI also reduces interval cancers [75]. However, breast MRI has a higher recall rate than mammography (15.1% versus 6.4%) [76], higher frequency of BI-RADS category 3 assessment than mammography (14.8% versus 11.8%), and greater frequency of image-guided biopsies than mammography (11.8% versus 2.4%) [69].

Variant 2: Adult female. Breast cancer screening. Intermediate risk.
E. MRI breast without and with IV contrast abbreviated

Data are limited regarding the use of abbreviated breast MRI without and with IV contrast in intermediate-risk females. In an cohort of females deemed at "mildly to moderately increased risk" abbreviated breast MRI demonstrated an incremental cancer detection yield of 18 cancers per 1,000 and a high negative predictive value [77,78]. In intermediate-risk females, abbreviated breast MRI yields a lower CDR (7 per 1,000) compared to high-risk females (29 per 1,000) [56]. Multiple studies have demonstrated similar diagnostic accuracy for abbreviated protocol MRI compared to conventional full protocol breast MRI [79-81]. The ECOG-ACRIN abbreviated MRI trial demonstrated a significantly higher CDR for abbreviated breast MRI without and with IV contrast (15 cancers per 1,000) compared with DBT (6 cancers per 1,000) in females with dense breasts [48]. In addition to dense breasts, females enrolled in the trial had variable 5 and 10 year risk profiles based upon the Breast Cancer Surveillance Consortium risk calculator, and 19% reported 1 or more first degree relatives with breast cancer [48].

Variant 2: Adult female. Breast cancer screening. Intermediate risk.
F. MRI breast without IV contrast

There is no relevant literature to support the use of breast MRI without IV contrast for screening females at intermediate risk.

Variant 2: Adult female. Breast cancer screening. Intermediate risk.
G. MRI breast without IV contrast abbreviated

There is no relevant literature to support the use of abbreviated breast MRI without IV contrast for screening females at intermediate risk.

Variant 2: Adult female. Breast cancer screening. Intermediate risk.
H. Sestamibi MBI

Data are limited regarding the use of sestamibi MBI for screening females at intermediate risk. Most studies have focused upon females with dense breasts and variable risk profiles. Retrospective and prospective studies have demonstrated similar incremental CDR for sestamibi MBI of 6.5 to 9 over mammography, with a study demonstrating an incremental CDR of 16.5 per 1,000 in females at increased risk primarily due to family or personal history of breast cancer [43,50]. Sestamibi MBI demonstrates similar sensitivity, better specificity, and lower recall rate compared to supplemental screening US in females with dense breasts [50,51].

Variant 2: Adult female. Breast cancer screening. Intermediate risk.
I. US breast

Most studies evaluating the utility of screening with breast US have focused on females with dense breast tissue with or without other risk factors. Dense breast tissue decreases the sensitivity of mammography [29] and is an independent risk factor for developing breast cancer [30]. Screening breast US in females with mammographically dense breasts, including those with risk factors placing them at increased breast cancer risk, identifies predominantly mammographically occult, small, node-negative invasive tumors with an increased CDR of 1.8 to 4.6 cancers per 1,000 females screened [43,52]. Although supplemental screening US in females with dense breasts results in an increased CDR, US also increases recall rate, false-positive examinations, and false-positive biopsies [29,52-58]. In females undergoing annual mammography plus annual supplemental screening MRI, the addition of supplemental screening with US does not identify additional cancers and is therefore not routinely performed.

For supplemental screening recommendations based upon breast density, please refer to the ACR Appropriateness Criteria® topic on "Supplemental Breast Cancer Screening Based on Breast Density" [13].

The ACRIN 6666 trial enrolled females with dense breast tissue and at least 1 other breast cancer risk factor [67]. Compared to mammography alone, screening US detected 5.3 cancers per 1,000 in year 1, 3.7 cancers per 1,000 in years 2 and 3, and resulted in a larger number of false-positive examinations and false-positive biopsies each year [67]. In a prospective study limited to intermediate-risk females, sensitivity of mammography was 57%, US was 24.5%, and mammography combined with biannual US demonstrated 80.4% sensitivity [82]. In females with a personal history of breast cancer, supplemental US screening results in an incremental CDR of 2.4 to 2.9 cancers per 1,000 examinations over mammography alone; however, US screening has lower specificity [13,72].

Variant 3: Adult female 30 years of age or older. Breast cancer screening. High risk.

The goal of imaging is to detect and diagnose breast cancer early. This imaging information improves outcome by decreasing morbidity and mortality from breast cancer.

Females considered high risk for breast cancer include those with a >20% estimated lifetime risk

for developing breast cancer using a validated statistical model. Other groups of high-risk females include those carrying a pathogenic mutation within certain genes [83-85], first-degree relatives of these mutation carriers who remain untested themselves, and females with a history of thoracic or upper abdominal radiation therapy at an early age (<30 years) [86]. Image-based deep learning models have been found to accurately identify increased-risk patients in retrospective studies [60,61], and are likely to become increasingly available for personalized risk assessment. BRCA1 and BRCA2 are the most common genetic mutations, have high penetrance, and carry a lifetime breast cancer risk of 55% to 85% and 45% to 69%, respectively [87]. Other less common high penetrance genes include TP53, PTEN, and CDH1 with a 56% to 90%, 60%, and 60% lifetime risk of breast cancer, respectively, and moderate penetrance genes CHEK2, ATM, and PALB2 confer a 40%, 25%, and 25% to 40% lifetime risk of breast cancer, respectively [87]. Some females with a personal history of breast cancer may also fit into the high-risk category, particularly those diagnosed before 50 year of age or with personal history of breast cancer and dense breast tissue [3]. Females with Ashkenazi Jewish descent and African American females have increased risk for BRCA and other mutations [3]. Black females and other minorities have disproportionately higher mortality rates from breast cancer [3,9]. Females at higher risk tend to have tumors at younger ages and larger and more biologically aggressive tumors [3].

Since 2007, published guidelines have recommended that high-risk females undergo more intensive breast cancer screening regimens, typically beginning at younger ages [4]. However, recommendations vary regarding the earliest age to start screening with different modalities.

Please reference the ACR Appropriateness Criteria® topics on "Transgender Breast Cancer Screening" [12], "Supplemental Breast Cancer Screening Based on Breast Density" [13], "Imaging after Mastectomy and Breast Reconstruction" [14], "Imaging after Breast Surgery" [15], and "Breast Imaging of Pregnant and Lactating Females" [16] in the appropriate clinical context.

Variant 3: Adult female 30 years of age or older. Breast cancer screening. High risk.
A. Digital breast tomosynthesis screening

DBT displays reconstructed stacked images of the breast in combination with digital mammographic views, which may be synthetic mammograms reconstructed from the acquired tomosynthesis data set or FFDM. Compared to FFDM or synthetic mammograms alone, most studies demonstrate that DBT increases CDR and decreases recall rate [17-25]; although, some studies have not reached statistical significance [26] or have found less compelling results in subsets of females, such as those with extremely dense breasts [27,28]. Dense breast tissue decreases the sensitivity of mammography [29] and is an independent risk factor for developing breast cancer [30]. Irrespective of risk category, meta-analyses have demonstrated an incremental increase in CDR of 1.6 to 3.2 per 1,000 screening DBT examinations and a 2.2% pooled decrease in recall rate compared to digital mammography [21,32,33].

The degree of breast cancer mortality reduction from screening mammography varies with different screening regimens. Mortality reduction is greater when screening begins at 40 years of age rather than 45 or 50 years of age and when screening is done more frequently (annually rather than biennially) [9-11,34]. Annual screening with DBT led to greater reductions in mortality compared with biennial screening, with 37% median reduction with screening annually from ages 40 to 75 years [10]. Beginning screening at an earlier age and more frequent screening result in a greater number of imaging studies performed, so these screening regimens also increase the number of false-positive examinations and biopsies [9-11,35]. Although randomized controlled

trials of screening mammography did not enroll females >74 years of age, observational studies demonstrate that some females ≥75 years of age may continue to benefit from screening mammography [11,35]. There is no upper age limit agreed upon for screening mammography [5,6,11,35]. Because mortality reduction from screening mammography requires years before being fully attained, screening recommendations should be based upon life expectancy and competing comorbidities, rather than age alone [11,35-37]. Females should continue screening mammography as long as they remain in overall good health and are willing to undergo the examination and subsequent testing or biopsy, if an abnormality is identified [5,11].

Within the limited studies of females at elevated risk due to personal and/or family history of breast cancer, DBT decreased recall rate without a significant increase in CDR compared to FFDM; however, small sample sizes restrict analyses [3,43].

High-risk females due to familial or genetic factors should begin annual screening mammography at age 30 or 10 years prior to the youngest family member who had breast cancer, but generally not before age 30 [3]. Approximately one-third of breast cancers may only be detected on mammography in BRCA2 mutation carriers who are <40 years of age [88]. An early modeling study showed that mammography had more risk than benefit in younger females with BRCA mutations thought to be due to dense breast tissues and weakened DNA repair [89]. In a prospective cohort study including 8,782 high-risk females, the benefit of adding mammography to MRI in mutation carriers 30 to 39 years of age was small, as the sensitivity of mammography plus MRI was comparable to MRI alone (100% versus 96.8%) in mutation carriers [90]. In females 50 to 69 years of age, combining MRI and mammography statistically significantly increased sensitivity compared with MRI alone (96.3% versus 90.9%) [90]. In a study of 2,157 females 25 to 75 years of age, >15% lifetime risk, including 599 mutation carriers, MRI sensitivity was much higher than mammography in 24 BRCA1 patients (67% versus 25%) and slightly higher in 13 BRCA2 patients (69% versus 62%) [91]. Therefore, in some mutation carriers, some referring providers use mammography or DBT beginning at 40 years of age if patients undergo annual MRI [92].

High-risk females due to thoracic or upper abdominal radiation therapy at an early age (<30 years) should begin screening mammography 8 years after radiation therapy but not before 25 years of age [3,93,94]. Childhood leukemia or sarcoma survivors treated without chest radiation are also at elevated breast cancer risk; early initiation of annual mammography and breast MRI at <40 years of age would avert 52.6% to 64.3% of breast cancer deaths [93,95]. Increased risk of breast cancer from other childhood cancers such as non–Hodgkin lymphoma, Wilms tumors, and neuroblastomas has been observed, likely a combination of treatment effects and patient's underlying genetic factors [93].

Because screening mammography decreases breast cancer mortality, screening mammography or screening DBT is still performed in females undergoing supplemental screening studies [3,11,38].

Variant 3: Adult female 30 years of age or older. Breast cancer screening. High risk.
B. Mammography screening

To date, mammography is the only screening modality shown to decrease breast cancer mortality. Multiple randomized controlled trials demonstrate that invitation to screening mammography results in at least a 22% reduction in breast cancer mortality [38]. For example, after 29 years of follow-up, the Swedish Two-County trial demonstrated a 27% to 31% reduction in breast cancer mortality in 133,065 females 40 to 74 years of age invited to screening despite use of single view

mammography and the 24 to 33 month interval between subsequent screenings [1]. Randomized controlled trials of screening mammography in which advanced stage breast cancers decreased by 20% or more demonstrate even greater reductions in breast cancer mortality [11]. Observational studies, including those from population-based service screening programs, also demonstrate larger reductions in breast cancer mortality (≥40%) in females who were actually screened [11,38].

In addition to mortality reduction, screening mammography decreases treatment morbidity, because screen-detected tumors are typically lower stage (eg, smaller and more likely to be node-negative), compared to breast cancers detected by palpation [2,11]. Despite these benefits, screening mammograms also have risks. The most common perceived risks include false-positive recalls and biopsies, overdiagnosis [5,7,35], and patient anxiety. Approximately 10% of screening mammograms result in a recall for additional imaging, although <2% result in a recommendation for percutaneous biopsy following additional imaging [11]. Overdiagnosis refers to breast cancers that are detected by screening that would not have otherwise become apparent during the patient's lifetime. The reported frequency of overdiagnosis varies widely in the published literature due to important underlying differences in study methodology. Overdiagnosis estimates that do not account for breast cancer risk, trends in breast cancer incidence, or lead time bias range from 0% to 54%, whereas adjusted estimates range from 1% to 10% [39,40]. Overdiagnosis estimates increase with age at screening [39,40]. Although the risks of screening may impact uptake and adherence to screening mammography, prior research has shown that females value early detection of breast cancer over false-positives and screening-related anxiety [11].

Despite the established mortality benefit, published guidelines differ in their recommendations for screening mammography due to variations in the perceptions of the relative risks and benefits [5,41]. The degree of breast cancer mortality reduction from screening mammography varies with different screening regimens. Mortality reduction is greater when screening begins 40 years of age rather than 45 or 50 years of age and when screening is done more frequently (annually rather than biennially) [9-11,34]. Annual screening mammography for females 40 to 84 years of age decreases mortality by 40% (12 lives per 1,000 females screened), whereas biennial screening mammography for females 50 to 74 years of age only decreases mortality by 23% (7 lives per 1,000 females screened) [35]. Earlier initiation of screening and more frequent screening, result in a greater number of imaging studies performed, so these screening regimens also increase the number of false-positive examinations and biopsies [9-11,35]. Although randomized controlled trials of screening mammography did not enroll females >74 years of age, observational studies demonstrate that females ≥75 years of age may continue to benefit from screening mammography [11,35]. There is no upper age limit agreed upon for screening mammography [5,6,11,35]. Because mortality reduction from screening mammography requires years before being fully attained, screening recommendations should be based upon life expectancy and competing comorbidities, rather than age alone [11,35-37]. Females should continue screening mammography as long as they remain in overall good health and are willing to undergo the examination and subsequent testing or biopsy, if an abnormality is identified [5,11].

For females 40 to 49 years of age, randomized controlled trials and observational studies demonstrate that screening mammography decreases breast cancer mortality by 15% to 50% [1,11,35,36,42]. Results from the CISNET suggest that annual screening mammography in females 40 to 49 years of age saves 42% more lives and life-years than biennial screening due to faster growing tumors in younger females [34]. Females screened between 40 and 49 years of age are

also less likely to require mastectomy or chemotherapy than females diagnosed with palpable tumors [2].

Non-Hispanic Black, Hispanic Black, and Hispanic White females have higher breast cancer mortality than non-Hispanic White females, and minority females often present at younger ages with more aggressive tumor subtypes [3,11]. Therefore, decreasing access to screening mammography, especially in females 40 to 49 years of age, may disproportionately impact minority females. In June 2024, the USPSTF updated recommendations to start screening mammography for all average-risk females at 40 years of age, acknowledging it would mitigate disparities in breast cancer mortality and would significantly benefit Black females, who have disproportionately high mortality rates, 40% higher than White females in the United States [9].

Annual screening mammography results in a greater reduction in mortality compared to biennial screening [10,11]. In females 40 to 84 years of age, annual screening reduces mortality by 40%, compared to a 32% reduction for biennial screening [35]. With regular screening, interval breast cancers do occur with a higher frequency in females undergoing biennial or triennial screening compared to annual screening. The sensitivity of mammography is decreased in some groups of females, including those with dense breasts [43]. Dense breast tissue decreases the sensitivity of mammography [29] and is an independent risk factor for developing breast cancer [30]. Given the limitations of mammography and to minimize interval cancers, supplemental screening modalities have been investigated in females at high risk. Because screening mammography decreases breast cancer mortality, screening mammography or screening DBT is still performed in females undergoing supplemental screening studies [3,11,38]. Rather than supplementing screening mammography with additional imaging modalities, some have suggested limiting females offered screening mammography based upon individual patient risk assessed by various risk models, breast density, or genetic information such as single-nucleotide polymorphism. However, the randomized controlled trials demonstrating mortality reduction and most large-scale observational studies enrolled females based upon age and geographic location, not individual patient risk factors. In observational study in females <50 years of age, restricting screening to females with a first-degree family history, extremely dense breast tissue, or both, would cause 66% of potentially screen-detected cancers to be missed [44].

Numerous studies in high-risk females have evaluated the performance of mammography and supplemental screening modalities, such as US and MRI. Mammography consistently demonstrates lower sensitivity (25%-69%) than US or MRI, and high-risk females experience higher interval cancer rates than the general population [3,43]. The combination of mammography with MRI yields the highest sensitivity across high-risk groups of females (91%-98%) [3,43,96]. Because screening mammography decreases breast cancer mortality, screening mammography or screening DBT is still performed in females undergoing supplemental screening studies [3,11,38].

High-risk females due to familial or genetic factors should begin annual screening mammography at age 30 or 10 years prior to the youngest family member who had breast cancer, but generally not before age 30 [3]. Approximately one-third of breast cancers may only be detected on mammography in BRCA2 mutation carriers who are <40 years of age [88]. An early modeling study showed that mammography had more risk than benefit in younger females with BRCA mutations thought to be due to dense breast tissues and weakened DNA repair and vulnerability to radiation-induced breast cancers over their lifetime [89]. In a prospective cohort study including 8,782 high-

risk females, the benefit of adding mammography to MRI in mutation carriers 30 to 39 years of age was small, as the sensitivity of mammography plus MRI was comparable to MRI alone (100% versus 96.8%) in mutation carriers [90]. In females 50 to 69 years of age, combining MRI and mammography statistically significantly increased sensitivity compared with MRI alone (96.3% versus 90.9%) [90]. In a study of 2,157 females 25 to 75 years of age, >15% lifetime risk, including 599 mutation carriers, MRI sensitivity was much higher than mammography in 24 BRCA1 patients (67% versus 25%) and slightly higher in 13 BRCA2 patients (69% versus 62%) [91]. Therefore, in some mutation carriers, some referring providers use mammography or DBT beginning at 40 years of age if patients undergo annual MRI [92].

High-risk females due to thoracic or upper abdominal radiation therapy at an early age (<30 years) should begin screening mammography 8 years after radiation therapy but not before 25 years of age [3,93,94]. Childhood leukemia or sarcoma survivors treated without chest radiation are also at elevated breast cancer risk; early initiation of annual mammography and breast MRI at <40 years of age would avert 52.6% to 64.3% of breast cancer deaths [93,95]. Increased risk of breast cancer from other childhood cancers such as non–Hodgkin lymphoma, Wilms tumors, and neuroblastomas has been observed, likely a combination of treatment effects and patient's underlying genetic factors [93].

Variant 3: Adult female 30 years of age or older. Breast cancer screening. High risk. C. Mammography with IV contrast

Data are limited regarding the use of mammography with IV contrast for breast cancer screening in high-risk females. To date, published studies have predominantly included females with dense breasts and other risk factors resulting in intermediate- or high-risk profiles. Compared to mammography alone, mammography with IV contrast increases sensitivity and cancer detection (incremental CDR = 6.6-13 per 1,000) in females at elevated risk [62-66]. A recent prospective single institution study of 466 females at elevated risk age 35 years and older who underwent mammography with IV contrast had an incremental cancer detection rate of 23.9 per 1,000 at the prevalence round [97]. Mammography with IV contrast may be useful in high-risk females as an alternative to MRI.

Variant 3: Adult female 30 years of age or older. Breast cancer screening. High risk. D. MRI breast without and with IV contrast

MRI has a higher CDR than mammography alone, DBT, or mammography/DBT combined with US [67-70]. In high-risk females, supplemental screening MRI combined with mammography yields a 91% to 98% sensitivity, although the reported specificity of MRI is typically lower than mammography [43,96]. The incremental CDR of MRI in elevated-risk females ranges from 8 to 29 per 1,000 females, with higher CDR (26 per 1,000) in BRCA mutation carriers [67-69,71,72]. Breast MRI detects small, node-negative invasive cancers at earlier tumor stages compared to mammography, as well as ductal carcinoma in situ [74,75]. Screening MRI also reduces interval cancers [75]. However, breast MRI has a higher recall rate than mammography (15.1% versus 6.4%) [76], higher frequency of BI-RADS category 3 assessment than mammography (14.8% versus 11.8%), and a greater frequency of image-guided biopsies than mammography (11.8 versus 2.4%) [69].

In females with a personal history of breast cancer, early detection of second breast cancers improves survival; however, mammographic sensitivity is lower, and interval cancer rates are higher, prompting investigations into supplemental screening regimens in breast cancer survivors

[3,43,72]. In females previously diagnosed with breast cancer [3], a recent meta-analysis estimated a CDR of 9 to 15 per 1,000 breast MRI [73]. Due to heterogeneity in the risk of second breast cancer diagnoses, recommendations for supplemental screening MRI vary. Based upon limited modeling data, females with a personal history of breast cancer who were diagnosed before <50 years of age or females with a personal history of breast cancer and dense breast tissue may have a >20% estimated lifetime risk of a subsequent breast cancer diagnosis and may therefore be considered high risk, warranting supplemental screening breast MRI on an annual basis [3]. In a prospective observational study of females ≤50 years of age who had undergone breast conservation therapy, supplemental screening MRI increased CDR (8.2 versus 4.4 per 1,000) but had decreased specificity, compared to mammography [72]. Childhood leukemia or sarcoma survivors treated without chest radiation are also at elevated breast cancer risk; early initiation of annual mammography and breast MRI <40 years of age would avert 52.6% to 64.3% of breast cancer deaths [93,95]. Increased risk of breast cancer from other childhood cancers such as non–Hodgkin lymphoma, Wilms tumors, and neuroblastomas has been observed, likely a combination of treatment effects and patient's underlying genetic factors [93].

Since 2007, the American Cancer Society has recommended annual breast MRI for breast cancer screening in high-risk females [4]. The ACR recommends annual breast MRI in high-risk females beginning as early as 25 years of age [3].

Variant 3: Adult female 30 years of age or older. Breast cancer screening. High risk.
E. MRI breast without and with IV contrast abbreviated

Data are limited regarding the use of abbreviated breast MRI without and with IV contrast for screening in high-risk females. Following the publication of the American Cancer Society guidelines for supplemental screening breast MRI in 2007, high-risk females have traditionally undergone conventional full protocol breast MRI without and with IV contrast [3,4]. However, multiple studies have demonstrated similar diagnostic accuracy for abbreviated protocol MRI compared to conventional full protocol breast MRI [79-81]. In a study evaluating 3,037 abbreviated breast MRI in 1,975 high-risk females, the CDR was 29 per 1,000, the interval cancer rate was 0.66 per 1,000, and all cancers missed by abbreviated breast MRI were node negative early-stage invasive malignancies [78].

Variant 3: Adult female 30 years of age or older. Breast cancer screening. High risk.
F. MRI breast without IV contrast

There is no relevant literature to support the use of MRI without IV contrast for screening females at high risk.

Variant 3: Adult female 30 years of age or older. Breast cancer screening. High risk.
G. MRI breast without IV contrast abbreviated

There is no relevant literature to support the use of abbreviated breast MRI without IV contrast for screening females at high risk.

Variant 3: Adult female 30 years of age or older. Breast cancer screening. High risk.
H. Sestamibi MBI

Data are limited regarding the use of sestamibi MBI for screening females at high risk. Most studies have focused upon females with dense breasts and variable risk profiles. Retrospective and prospective studies have demonstrated similar incremental CDR for sestamibi MBI of 6.5 to 9 over mammography, with a study demonstrating an incremental CDR of 16.5 per 1,000 in females at

increased risk primarily due to family or personal history of breast cancer [43,50]. Sestamibi MBI demonstrates similar sensitivity, better specificity, and lower recall rate compared to supplemental screening US in females with dense breasts [50,51].

Variant 3: Adult female 30 years of age or older. Breast cancer screening. High risk.

I. US breast

In high-risk females undergoing annual mammography plus annual supplemental screening MRI, the addition of supplemental screening with US does not identify additional cancers and is therefore not routinely performed. Screening US may be useful in high-risk patients as an alternative to MRI. However, high-risk females who do not undergo supplemental screening MRI should be counseled that the CDR of US is inferior to MRI. MRI has a higher CDR than mammography, DBT, or mammography/DBT combined with US [67-70]. The ACRIN 6666 trial enrolled females with elevated breast cancer risk [67]. Compared to mammography alone, screening US detected 5.3 cancers per 1,000 in year 1 and 3.7 cancers per 1,000 in years 2 and 3 and resulted in a larger number of false-positive examinations and false-positive biopsies each year [67]. After 3 consecutive rounds of mammography plus US, the incremental CDR of MRI was 14.7 per 1,000, although false-positive examinations also increased [67]. In a prospective multicenter study of 687 high-risk females who underwent clinical breast examination, mammography, US, and MRI for screening, the combination of MRI plus mammography maximized the breast cancers detected [68]. Mammography identified 5 cancers per 1,000 compared to 6 per 1,000 for US, 7.7 per 1,000 for mammography plus US, 14.9 per 1,000 for MRI, 14.9 per 1,000 for MRI plus US, 16 per 1,000 for mammography plus MRI, and 16 per 1,000 for mammography plus US plus MRI [68].

In a prospective study of BRCA mutation carriers and high-risk females, sensitivity of mammography was 25% and 66% whereas US was 23% and 34%, respectively [82]. In the high-risk group, mammography combined with biannual US demonstrated 100% sensitivity [82]; however, MRI was not performed. In a subset analysis of BRCA mutation carriers, MRI sensitivity was 94% [82]. In another study of 529 high-risk females suspected or proven to carry a deleterious BRCA mutation, the performance of US was also inferior to MRI [98]. The sensitivity of mammography was 33%, US was 40%, mammography plus US was 49%, and MRI was 91% [98].

In females with a personal history of breast cancer, supplemental US screening results in an incremental CDR of 2.4 to 2.9 cancers per 1,000 examinations over mammography alone; however, US screening has lower specificity [13,72].

Variant 4: Adult female younger than 30 years of age. Breast cancer screening. High risk.

The goal of imaging is to detect and diagnose breast cancer early. This imaging information improves outcome by decreasing morbidity and mortality from breast cancer.

Females considered high risk for breast cancer include those with a >20% estimated lifetime risk for developing breast cancer using a validated statistical model. Other groups of high-risk females include those carrying a pathogenic mutation within certain genes [83-85], first-degree relatives of these mutation carriers who remain untested themselves, and females with a history of thoracic or upper abdominal radiation therapy at an early age [86]. BRCA1 and BRCA2 are the most common genetic mutations, have high penetrance, and carry a lifetime breast cancer risk of 55% to 85% and 45% to 69%, respectively [87]. Other less common high penetrance genes include TP53, PTEN, and CDH1 with a 56% to 90%, 60%, and 60% lifetime risk of breast cancer, respectively, and moderate

penetrance genes CHEK2, ATM, and PALB2 confer a 40%, 25%, and 25% to 40% lifetime risk of breast cancer, respectively [87]. Young females with a personal history of breast cancer also fit into the high-risk category, particularly those who have dense breast tissue [3]. Females with Ashkenazi Jewish descent and African American females have increased risk for BRCA and other mutations [3]. Black females and other minorities have disproportionately higher mortality rates from breast cancer [3,9]. Females at higher risk tend to have tumors at younger ages and larger and more biologically aggressive tumors [3].

Since 2007, published guidelines have recommended that high-risk females undergo more intensive breast cancer screening regimens, typically beginning at younger ages [4]. However, recommendations for the earliest age to commence screening vary by modality. In addition, for high-risk females <30 years of age, data are limited regarding the use of different modalities for breast cancer screening. Most published studies evaluate high-risk females 30 to 39 years of age and >40 years of age; therefore, recommendations for high-risk females <30 years of age are extrapolated from the available data.

Please reference the ACR Appropriateness Criteria® topics on "Transgender Breast Cancer Screening" [12], "Supplemental Breast Cancer Screening Based on Breast Density" [13], "Imaging after Mastectomy and Breast Reconstruction" [14], "Imaging after Breast Surgery" [15], and "Breast Imaging of Pregnant and Lactating Women" [16] in the appropriate clinical context.

Variant 4: Adult female younger than 30 years of age. Breast cancer screening. High risk.
A. Digital breast tomosynthesis screening

DBT displays reconstructed stacked images of the breast in combination with digital mammographic views, which may be synthetic mammograms reconstructed from the acquired tomosynthesis data set or FFDM. Compared to FFDM or synthetic mammograms alone, most studies demonstrate that DBT increases CDR and decreases recall rate [17-25]; although, some studies have not reached statistical significance [26] or have found less compelling results in subsets of females, such as those with extremely dense breasts [27,28]. Dense breast tissue decreases the sensitivity of mammography [29] and is an independent risk factor for developing breast cancer [30]. Irrespective of risk category, meta-analyses have demonstrated an incremental increase in CDR of 1.6 to 3.2 per 1,000 screening DBT examinations and a 2.2% pooled decrease in recall rate compared to digital mammography [21,32,33].

Data regarding mortality reduction from screening mammography in females <30 years of age is limited and extrapolated from available data for older age groups.

Within the limited studies of females at elevated risk due to personal and/or family history of breast cancer, DBT decreased recall rate without a significant increase in CDR compared to FFDM; however, small sample sizes restrict analyses [3,43].

High-risk females due to familial or genetic factors should begin annual screening mammography at age 30 or 10 years prior to the youngest family member who had breast cancer, but generally not before age 30 [3]. Approximately one-third of breast cancers may only be detected on mammography in BRCA2 mutation carriers who are <40 years of age [88]. An early modeling study showed that mammography had more risk than benefit in younger females with BRCA mutations thought to be due to dense breast tissues and weakened DNA repair [89]. In a prospective cohort study including 8,782 high-risk females, the benefit of adding mammography to MRI in mutation

carriers 30 to 39 years of age was small, as the sensitivity of mammography plus MRI was comparable to MRI alone (100% versus 96.8%) in mutation carriers [90]. In females 50 to 69 years of age, combining MRI and mammography statistically significantly increased sensitivity compared with MRI alone (96.3% versus 90.9%) [90]. In a study of 2,157 females 25 to 75 years of age, >15% lifetime risk, including 599 mutation carriers, MRI sensitivity was much higher than mammography in 24 BRCA1 patients (67% versus 25%) and slightly higher in 13 BRCA2 patients (69% versus 62%) [91]. Therefore, in some mutation carriers, some referring providers use mammography or DBT beginning at 40 years of age if patients undergo annual MRI [92].

High-risk females due to thoracic or upper abdominal radiation therapy at an early age should begin screening mammography 8 years after radiation therapy but not before 25 years of age [3,93,94]. Childhood leukemia or sarcoma survivors treated without chest radiation are also at elevated breast cancer risk; early initiation of annual mammography and breast MRI <40 years of age would avert 52.6% to 64.3% of breast cancer deaths [93,95]. Increased risk of breast cancer from other childhood cancers such as non–Hodgkin lymphoma, Wilms tumors, and neuroblastomas has been observed, likely a combination of treatment effects and patient's underlying genetic factors [93].

The ACR recommends annual MRI surveillance starting at ages 25 to 30 and annual mammography with a variable starting age between 25 and 40, depending on type of risk, for females with genetics-based increased risk, those with a calculated lifetime risk of 20% or more, and those exposed to chest radiation at a young age [3].

Variant 4: Adult female younger than 30 years of age. Breast cancer screening. High risk.
B. Mammography screening

To date, mammography is the only screening modality shown to decrease breast cancer mortality. Multiple randomized controlled trials demonstrate that invitation to screening mammography results in at least a 22% reduction in breast cancer mortality [38]. For example, after 29 years of follow-up, the Swedish Two-County trial demonstrated a 27% to 31% reduction in breast cancer mortality in 133,065 females 40 to 74 years of age invited to screening despite use of single view mammography and the 24 to 33 month interval between subsequent screenings [1]. Randomized controlled trials of screening mammography in which advanced stage breast cancers decreased by 20% or more demonstrate even greater reductions in breast cancer mortality [11]. Observational studies, including those from population-based service screening programs, also demonstrate larger reductions in breast cancer mortality (≥40%) in females who were actually screened [11,38].

In addition to mortality reduction, screening mammography decreases treatment morbidity, because screen-detected tumors are typically lower stage (eg, smaller and more likely to be node-negative), compared to breast cancers detected by palpation [2,11]. Despite these benefits, screening mammograms also have risks. The most common perceived risks include false-positive recalls and biopsies, overdiagnosis [5,7,35], and patient anxiety. Approximately 10% of screening mammograms result in a recall for additional imaging, although <2% result in a recommendation for percutaneous biopsy following additional imaging [11]. Overdiagnosis refers to breast cancers that are detected by screening that would not have otherwise become apparent during the patient's lifetime. The reported frequency of overdiagnosis varies widely in the published literature due to important underlying differences in study methodology. Overdiagnosis estimates that do not account for breast cancer risk, trends in breast cancer incidence, or lead time bias range from 0% to 54%, whereas adjusted estimates range from 1% to 10% [39,40]. Overdiagnosis estimates

increase with age at screening [39,40]. Although the risks of screening may impact uptake and adherence to screening mammography, prior research has shown that females value early detection of breast cancer over false-positives and screening-related anxiety [11].

Despite the established mortality benefit, published guidelines differ in their recommendations for screening mammography due to variations in the perceptions of the relative risks and benefits [5,41].

Annual screening mammography results in a greater reduction in mortality compared to biennial screening [10,11]. In females 40 to 84 years of age, annual screening reduces mortality by 40%, compared to a 32% reduction for biennial screening [35]. With regular screening, interval breast cancers do occur with a higher frequency in females undergoing biennial or triennial screening compared to annual screening. The sensitivity of mammography is decreased in some groups of females, including those with dense breasts [43]. Dense breast tissue decreases the sensitivity of mammography [29] and is an independent risk factor for developing breast cancer [30]. Given the limitations of mammography and to minimize interval cancers, supplemental screening modalities have been investigated in females at high risk. Because screening mammography decreases breast cancer mortality, screening mammography or screening DBT is still performed in females undergoing supplemental screening studies [3,11,38]. Rather than supplementing screening mammography with additional imaging modalities, some have suggested limiting females offered screening mammography based upon individual patient risk assessed by various risk models, breast density, or genetic information such as single-nucleotide polymorphism. However, the randomized controlled trials demonstrating mortality reduction and most large-scale observational studies enrolled females based upon age and geographic location, not individual patient risk factors. An observational study in females <50 years of age, restricting screening to females with a first-degree family history, extremely dense breast tissue, or both, would cause 66% of potentially screen-detected cancers to be missed [44].

Data regarding mortality reduction from screening mammography in females <30 years of age is limited and extrapolated from available data for older age groups.

Numerous studies in high-risk females have evaluated the performance of mammography and supplemental screening modalities, such as US and MRI. Mammography consistently demonstrates lower sensitivity (25%-69%) than US or MRI, and high-risk females experience higher interval cancer rates than the general population [3,43]. The combination of mammography with MRI yields the highest sensitivity across high-risk groups of females (91%-98%) [3,43,96]. Because screening mammography decreases breast cancer mortality, screening mammography or screening DBT is still performed in females undergoing supplemental screening studies [3,11,38].

High-risk females due to familial or genetic factors should begin annual screening mammography at age 30 or 10 years prior to the youngest family member who had breast cancer, but generally not before age 30 [3]. Approximately one-third of breast cancers may only be detected on mammography in BRCA2 mutation carriers who are <40 years of age [88]. An early modeling study showed that mammography had more risk than benefit in younger females with BRCA mutations thought to be due to dense breast tissues and weakened DNA repair and vulnerability to radiation-induced breast cancers over their lifetime [89]. In a prospective cohort study including 8,782 high-risk females, the benefit of adding mammography to MRI in mutation carriers 30 to 39 years of age

was small, as the sensitivity of mammography plus MRI was comparable to MRI alone (100% versus 96.8%) in mutation carriers [90]. In females 50 to 69 years of age, combining MRI and mammography statistically significantly increased sensitivity compared with MRI alone (96.3% versus 90.9%) [90]. In a study of 2,157 females 25 to 75 years of age, >15% lifetime risk, including 599 mutation carriers, MRI sensitivity was much higher than mammography in 24 BRCA1 patients (67% versus 25%) and slightly higher in 13 BRCA2 patients (69% versus 62%) [91]. Therefore, in some mutation carriers, some referring providers use mammography or DBT beginning at 40 years of age if patients undergo annual MRI [92].

High-risk females due to thoracic or upper abdominal radiation therapy at an early age should begin screening mammography 8 years after radiation therapy but not before 25 years of age [3,93,94]. Childhood leukemia or sarcoma survivors treated without chest radiation are also at elevated breast cancer risk; early initiation of annual mammography and breast MRI <40 years of age would avert 52.6% to 64.3% of breast cancer deaths [93,95]. Increased risk of breast cancer from other childhood cancers such as non–Hodgkin lymphoma, Wilms tumors, and neuroblastomas has been observed, likely a combination of treatment effects and patient's underlying genetic factors [93].

The ACR recommends annual MRI surveillance starting at ages 25 to 30 and annual mammography with a variable starting age between 25 and 40, depending on type of risk, for females with genetics-based increased risk, those with a calculated lifetime risk of 20% or more, and those exposed to chest radiation at a young age [3].

Variant 4: Adult female younger than 30 years of age. Breast cancer screening. High risk. C. Mammography with IV contrast

There is no relevant literature to support the use of mammography with IV contrast for screening females at high risk <30 year of age.

Variant 4: Adult female younger than 30 years of age. Breast cancer screening. High risk. D. MRI breast without and with IV contrast

MRI has a higher CDR than mammography alone, DBT, or mammography/DBT combined with US [67-70]. In high-risk females, supplemental screening MRI combined with mammography yields a 91% to 98% sensitivity, although the reported specificity of MRI is typically lower than mammography [43,96]. The incremental CDR of MRI in elevated-risk females ranges from 8 to 29 per 1,000 females, with higher CDR (26 per 1,000) in BRCA mutation carriers [67-69,71,72]. Breast MRI detects small, node-negative invasive cancers at earlier tumor stages compared to mammography, as well as ductal carcinoma in situ [74,75]. Screening MRI also reduces interval cancers [75]. However, breast MRI has a higher recall rate than mammography (15.1% versus 6.4%) [76], higher frequency of BI-RADS category 3 assessment than mammography (14.8% versus 11.8%), and a greater frequency of image-guided biopsies than mammography (11.8 versus 2.4%) [69].

In females with a personal history of breast cancer, early detection of second breast cancers improves survival; however, mammographic sensitivity is lower, and interval cancer rates are higher, prompting investigations into supplemental screening regimens in breast cancer survivors [3,43,72]. In females previously diagnosed with breast cancer [3], a recent meta-analysis estimated a CDR of 9 to 15 per 1,000 breast MRI [73]. Due to heterogeneity in the risk of second breast cancer diagnoses, recommendations for supplemental screening MRI vary. Based upon limited

modeling data, females with a personal history of breast cancer who were diagnosed before <50 years of age or females with a personal history of breast cancer and dense breast tissue may have a >20% estimated lifetime risk of a subsequent breast cancer diagnosis and may therefore be considered high risk, warranting supplemental screening breast MRI on an annual basis [3]. In a prospective observational study of females ≤50 years of age who had undergone breast conservation therapy, supplemental screening MRI increased CDR (8.2 versus 4.4 per 1,000) but had decreased specificity, compared to mammography [72]. Childhood leukemia or sarcoma survivors treated without chest radiation are also at elevated breast cancer risk; early initiation of annual mammography and breast MRI <40 years of age would avert 52.6% to 64.3% of breast cancer deaths [93,95]. Increased risk of breast cancer from other childhood cancers such as non–Hodgkin lymphoma, Wilms tumors, and neuroblastomas has been observed, likely a combination of treatment effects and patient's underlying genetic factors [93].

Since 2007, the American Cancer Society has recommended annual breast MRI for breast cancer screening in high-risk females [4]. The ACR recommends annual breast MRI in high-risk females beginning as early as 25 years of age [3].

Variant 4: Adult female younger than 30 years of age. Breast cancer screening. High risk. E. MRI breast without and with IV contrast abbreviated

Data are limited regarding the use of abbreviated breast MRI without and with IV contrast for screening in high-risk females. The studies that have included high-risk females <30 years of age have not stratified results on this subset of young patients. Following the publication of the American Cancer Society guidelines for supplemental screening breast MRI in 2007, high-risk females have traditionally undergone conventional full protocol breast MRI without and with IV contrast [3,4]. However, multiple studies have demonstrated similar diagnostic accuracy for abbreviated protocol MRI compared to conventional full protocol breast MRI [79-81]. In a study evaluating 3,037 abbreviated breast MRI in 1,975 high-risk females, the CDR was 29 per 1,000, the interval cancer rate was 0.66 per 1,000, and all cancers missed by abbreviated breast MRI were node negative early-stage invasive malignancies [78].

Variant 4: Adult female younger than 30 years of age. Breast cancer screening. High risk. F. MRI breast without IV contrast

There is no relevant literature to support the use of MRI without IV contrast for screening females at high risk less than age 30.

Variant 4: Adult female younger than 30 years of age. Breast cancer screening. High risk. G. MRI breast without IV contrast abbreviated

There is no relevant literature to support the use of abbreviated breast MRI without IV contrast for screening females at high risk less than age 30.

Variant 4: Adult female younger than 30 years of age. Breast cancer screening. High risk. H. Sestamibi MBI

There is no relevant literature to support the use of sestamibi MBI for screening females at high risk less than age 30.

Variant 4: Adult female younger than 30 years of age. Breast cancer screening. High risk. I. US breast

In high-risk females undergoing annual mammography plus annual supplemental screening MRI, the addition of supplemental screening with US does not identify additional cancers and is

therefore not routinely performed. The studies that have included high risk females less than age 30 have had small numbers of patients less than age 30 and have not stratified data by this subset.

Screening US may be useful in high-risk patients as an alternative to MRI. However, high-risk females who do not undergo supplemental screening MRI should be counseled that the CDR of US is inferior to MRI. MRI has a higher CDR than mammography, DBT, or mammography/DBT combined with US [67-70]. The ACRIN 6666 trial enrolled females with elevated breast cancer risk [67]. Compared to mammography alone, screening US detected 5.3 cancers per 1,000 in year 1 and 3.7 cancers per 1,000 in years 2 and 3 and resulted in a larger number of false-positive examinations and false-positive biopsies each year [67]. After 3 consecutive rounds of mammography plus US, the incremental CDR of MRI was 14.7 per 1,000, although false-positive examinations also increased [67]. In a prospective multicenter study of 687 high-risk females who underwent clinical breast examination, mammography, US, and MRI for screening, the combination of MRI plus mammography maximized the breast cancers detected [68]. Mammography identified 5 cancers per 1,000 compared to 6 per 1,000 for US, 7.7 per 1,000 for mammography plus US, 14.9 per 1,000 for MRI, 14.9 per 1,000 for MRI plus US, 16 per 1,000 for mammography plus MRI, and 16 per 1,000 for mammography plus US plus MRI [68].

In a prospective study of BRCA mutation carriers and high-risk females, sensitivity of mammography was 25% and 66% whereas US was 23% and 34%, respectively [82]. In the high-risk group, mammography combined with biannual US demonstrated 100% sensitivity [82]; however, MRI was not performed. In a subset analysis of BRCA mutation carriers, MRI sensitivity was 94% [82]. In another study of 529 high-risk females suspected or proven to carry a deleterious BRCA mutation, the performance of US was also inferior to MRI [98]. The sensitivity of mammography was 33%, US was 40%, mammography plus US was 49%, and MRI was 91% [98].

In females with a personal history of breast cancer, supplemental US screening results in an incremental CDR of 2.4 to 2.9 cancers per 1,000 examinations over mammography alone; however, US screening has lower specificity [13,72].

Summary of Highlights

This is a summary of the key recommendations from the variant tables. Refer to the complete narrative document for more information.

- **Variant 1**: DBT screening and mammography screening are usually appropriate for breast cancer screening in an adult female at average risk. These procedures are alternatives.
- **Variant 2**: DBT screening and mammography screening are usually appropriate for breast cancer screening in an adult female at intermediate risk. These procedures are alternatives.
- **Variant 3**: DBT screening, mammography screening, MRI breast without and with IV contrast, and abbreviated MRI breast without and with IV contrast are usually appropriate for breast cancer screening in an adult female at high risk ≥30 years of age. DBT screening and mammography screening are alternatives. MRI breast without and with IV contrast and abbreviated MRI breast without and with IV contrast are alternatives. DBT screening and mammography screening are complementary to MRI breast without and with IV contrast and abbreviated MRI breast without and with IV contrast. In adult women at high risk, breast cancer detection on imaging is maximized with the use of these 2 complementary screening

examinations.

- **Variant 4**: MRI breast without and with IV contrast or abbreviated MRI breast without and with IV contrast are usually appropriate for breast cancer screening in an adult female at high risk <30 years of age.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation

dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document.

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

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Disclaimer

The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

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