Progress in breast cancer screening over the past 50 years: A remarkable story, but still work to do

Expert perspective on the myriad factors that play a role in breast cancer screening recommendations and the guidelines to consider when engaging patients in shared decision making

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Meaningful progress has been made in reducing deaths due to breast cancer over the last half century, with a 43% decrease in mortality *rate* (breast cancer deaths per 100,000 population).[1] Screening mammography (SM) has contributed greatly to that success, accounting for 30% to 70% of the reduced mortality rate, with the remainder due to advancements in breast cancer treatment.[2] Despite these improvements, invasive breast cancer remains the highest incident cancer in the United States and in the world, is the second leading cause of cancer death in the United States, and results in more years of life lost than any other cancer (**TABLE 1**).[1,3]

While the benefits and harms of SM are reasonably well understood, different guidelines groups have approached the relative value of the risks and benefits differently, which has led to challenges in implementation of shared decision making, particularly around the age to initiate routine screening.[4-6] In this article, we will focus on the data behind the controversy, current gaps in knowledge, challenges related to breast density and screening in diverse groups, and emerging technologies to address these gaps and provide a construct for appropriate counseling of the patient across the risk spectrum.

Disclaimer: Gender-neutral terms ("persons," "people," "patients," "individuals," "they," etc) are used throughout this article, but the use of screening mammography and other breast cancer screening tools generally references persons who were assigned female sex at birth.

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New series on cancer screening

In recognition of 35 years of publication of OBG MANAGEMENT, this article on breast cancer screening by Mark D. Pearlman, MD, kicks off a series that focuses on various cancer screening modalities and expert recommendations.

Stay tuned for articles on the future of cervical cancer screening and genetic testing for cancer risk beyond *BRCA* testing.

We look forward to continuing OBG MANAGEMENT's mission of enhancing the quality of reproductive health care and the professional development of ObGyns and all women's health care clinicians.

Breast cancer risk

Variables that affect risk

While female sex and older age are the 2 greatest risks for the development of breast cancer,

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TABLE 1 Invasive breast cancer statistics

	United States (2022)[1]	Global (2020)[a]	Rank among cancers (US)[1]
Incidence	287,750	2.3 million	1 (not including non-melanoma skin cancer)
Survivors (prevalence)	4.1 million	7.8 million diagnosed within the previous 5 years	1 (22% of all cancer survivors)
Deaths due to breast cancer	43,250	685,000	2 (lung cancer, 1) Breast cancer is the leading cause of cancer mortality in Black and Hispanic women
Median age (years) at diagnosis	62 (overall) • 60 (Black) • 57 (Hispanic) • 58 (Asian/Pacific Islander) • 64 (White) • 61 (American Indian/Alaskan Native)		

[a]World Health Organization. Breast cancer. March 26, 2021. https://www.who.int/news-room/fact-sheets/detail/breast-cancer.

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Validated risk assessment tools combine known risk factors and, depending on the specific tool, can provide estimates of 5-year, 10-year, or lifetime risk of breast cancer

many other factors can either increase or decrease breast cancer risk in a person's lifetime. The importance of identifying risk factors is 3-fold:

1. to perform risk assessment to determine if individuals would benefit from average-risk versus high-risk breast cancer surveillance
2. to identify persons who might benefit from *BRCA* genetic counseling and screening, risk reduction medications or procedures, and
3. to allow patients to determine whether any modification in their lifestyle or reproductive choices would make sense to them to reduce their future breast cancer risk.

Most of these risk variables are largely inalterable (for example, family history of breast cancer, carriage of genetic pathogenic variants such as *BRCA1* and *BRCA2*, age of menarche and menopause), but some are potentially modifiable, such as parity, age at first birth, lactation and duration, and dietary factors, among others. **TABLE 2** lists common breast cancer risk factors.

Breast cancer risk assessment

Several validated tools have been developed to estimate a person's breast cancer risk (**TABLE 3**). These tools combine known risk factors and, depending on the specific tool, can provide estimates of 5-year, 10-year, or lifetime risk of breast cancer. Patients at highest risk can benefit from earlier screening, supplemental screening with breast magnetic resonance imaging (MRI), or risk reduction (see the section, "High-risk screening"). Ideally, a risk assessment should be done by age 30 so that patients at high risk can be identified for earlier or more intensive screening and for possible genetic testing in those at risk for carriage of the *BRCA* or other breast cancer gene pathogenic variants.[5,7]

Breast cancer screening: Efficacy and harms

The earliest studies of breast cancer screening with mammography were randomized controlled trials (RCTs) that compared screened and unscreened patients aged 40 to 74. Nearly all the RCTs and numerous well-designed incidence-based and case-control studies have demonstrated that SM results in a clinically and statistically significant reduction in breast cancer mortality (**TABLE 4**).[4,6,8] Since the mid-1980s and continuing to the current day, SM programs are routinely recommended in the United States. In addition to the mortality benefit outlined in TABLE 4, SM also is associated with a need for less invasive treatments if breast cancer is diagnosed.[9,10]

With several decades of experience, SM programs have demonstrated that multiple harms are associated with SM, including callbacks, false-positive mammograms that result in a benign biopsy, and overdiagnosis of breast cancer (TABLE 4). Overdiagnosis is a

mammographic detection of a breast cancer that would not have harmed that woman in her lifetime. Overdiagnosis leads to overtreatment of breast cancers with its attendant side effects, the emotional harms of a breast cancer diagnosis, and the substantial financial cost of cancer treatment. Estimates of overdiagnosis range from 0% to 50%, with the most likely estimate of invasive breast cancer overdiagnosis from SM between 5% and 15%.[11-13] Some of these overdiagnosed cancers are due to very slow growing cancers or breast cancers that may even regress. However, the higher rates of overdiagnosis occur in older persons who are screened and in whom competing causes of mortality become more prevalent. It is estimated that overdiagnosis of invasive breast cancer in patients younger than age 60 is less than 1%, but it exceeds 14% in those older than age 80 (TABLE 4).[14]

A structured approach is needed to counsel patients about SM so that they understand both the substantial benefit (earlier-stage diagnosis, reduced need for treatment, reduced breast cancer and all-cause mortality) and the potential harms (callback, false-positive results, and overdiagnosis). Moreover, the relative balance of the benefits and harms are influenced throughout their lifetime by both aging and changes in their personal and family medical history.

Counseling should consider factors beyond just the performance of mammography (sensitivity and specificity), such as the patient's current health and age (competing causes of mortality), likelihood of developing breast cancer based on risk assessment (more benefit in higher-risk persons), and the individual patient's values on the importance of the benefits and harms. The differing emphases on mammography performance and the relative value of the benefits and harms have led experts to produce disparate national guideline recommendations (**TABLE 5**).

Should SM start at age 40, 45, or 50 in average-risk persons?

There is not clear consensus about the age at which to begin to recommend routine SM in patients at average risk. The National Comprehensive Cancer Network (NCCN),[7] American Cancer Society (ACS),[4] and the US Preventive Services Task Force (USPSTF)[5] recommend that those at average risk start SM at age 40, 45, and 50, respectively (TABLE 5). While the guideline groups listed in TABLE 5 agree that there is level 1 evidence that SM reduces breast cancer mortality in the general population for persons starting at age 40, because the incidence of breast cancer is lower in younger persons (**TABLE 6**),[4] the net population-based screening benefit is lower in this group, and the number needed to invite to screening to save a single life due to breast cancer varies.

For patients in their 40s, it is estimated that 1,904 individuals need to be invited to SM to save 1 life, whereas for patients in their 50s, it is 1,339.[15] However, for patients in their 40s, the number needed to screen to save 1 life due to breast cancer decreases from 1 in 1,904 if invited to be screened to 1 in 588 if they are actually screened.[16] Furthermore, if a patient is diagnosed with breast cancer at age 40–50, the likelihood of dying is reduced at least 22% and perhaps as high as 48% if her cancer was diagnosed on SM compared with an unscreened individual with a symptomatic presentation (for example, palpable mass).[4,15,17,18] Another benefit of SM in the fifth decade of life (40s) is the decreased need for more extensive treatment, including a higher risk of need for chemotherapy (odds ratio [OR], 2.81; 95% confidence interval [CI], 1.16–6.84); need for mastectomy (OR, 3.41; 95% CI, 1.36–8.52); and need for axillary lymph node dissection (OR, 5.76; 95% CI, 2.40–13.82) in unscreened (compared with screened) patients diagnosed with breast cancer.[10]

The harms associated with SM are not inconsequential and include callbacks (approximately 1 in 10), false-positive biopsy (approximately 1 in 100), and overdiagnosis (likely <1% of all breast cancers in persons younger than age 50). Because most patients in their 40s will not develop breast cancer (TABLE 6), the benefit of reduced breast cancer mortality will not be experienced by most in this decade of life, but they are still just as

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likely to experience a callback, false-positive biopsy, or the possibility of overdiagnosis. Interpretation of this balance on a population level is the crux of the various guideline groups' development of differing recommendations as to *when* screening should start. Despite this seeming disagreement, all the guideline groups listed in TABLE 5 concur that persons at average risk for breast cancer should be offered SM if they desire starting at age 40 after a shared decision-making conversation that incorporates the patient's view on the relative value of the benefits and risks.

High-risk screening

Unlike in screening average-risk patients, there is less disagreement about screening in high-risk groups. **TABLE 7** outlines the various

TABLE 2 Breast cancer risk factors frequently used to determine "high risk" status

Category	Description
Commonly used factors	
Genetic pathogenic variants (mutations)	*BRCA1, BRCA2, CDH1, CHEK2, NF1, PALB2, PTEN, STK11, TP53*
Lifetime risk ≥20%	Based on models that are largely dependent on family history. Examples include Tyrer-Cuzick, CanRisk, Claus, BRCAPRO[a] (see also Table 3)
Thoracic radiation therapy between ages 10 and 30 years	Typical doses vary from 10–45 Gy
High-risk breast lesions: LCIS, ADH, ALH	High-risk breast biopsies that increase future risk of breast cancer all result in a lifetime risk >20%. Actual LTR depends on histologic characteristics and age of diagnosis
Reproductive risk factors	• Age of menarche (earlier → increased risk) • Age of menopause (later → increased risk) • Parity and age at first birth. Risk is increased in nulliparous or later age at first birth • Lactation and duration of breastfeeding (decreased risk) • Use of exogenous hormones (increased risk menopausal hormone therapy with estrogen and progestin). Minimal increased risk in current users of combined hormonal contraception and LNG IUD (1 in 50,000 for individuals under age 35)[30]
Race/ethnicity	• White women have greater lifetime risk of breast cancer incidence compared with Black, Hispanic, Asian women[31]
BMI/diet	• A higher BMI is associated with a greater incidence of breast cancer in menopausal persons • Greater perimenopausal weight gain is associated with greater breast cancer risk • Low-fat diet in postmenopause may reduce breast cancer risk (not consistent in studies)
Emerging/controversial areas	
Dense breasts	• BI-RADS category C (heterogeneously dense breasts) • BI-RADS category D (extremely dense breasts)
Polygenic risk score (PRS)	Single nucleotide variants (SNV) that individually confer little risk of cancer, but when combined may estimate larger breast cancer risk
5-year risk, 10-year risk (as opposed to lifetime risk) of breast cancer	

[a]Breast Cancer Risk Assessment Tool (frequently referred to as the Gail model) was validated for breast cancer risk reduction, but it does not provide comprehensive family history and is not recommended for use in determining eligibility for high-risk screening.

Abbreviations: ADH, atypical ductal hyperplasia; ALH, atypical lobular hyperplasia; BI-RADS, Breast Imaging Reporting And Data System; BMI, body mass index; LCIS, lobular carcinoma in situ; LNG IUD, levonorgestrel-releasing intrauterine device; LTR, lifetime risk; MRI, magnetic resonance imaging; PRS, polygenic risk score; SNV, single nucleotide variant.

categories and recommended strategies that qualify for screening at younger ages or more intensive screening. Adding breast MRI to SM in high-risk individuals results in both higher cancer detection rates and less interval breast cancers (cancers diagnosed between screening rounds) diagnosed compared with SM alone.[19,20] Interval breast cancer tends to be more aggressive and is used as a surrogate marker for more recognized factors, such as breast cancer mortality. In addition to less interval breast cancers, high-risk patients are more likely to be diagnosed with node-negative disease if screening breast MRI is added to SM.

Long-term mortality benefit studies using MRI have not been conducted due to the prolonged follow-up times needed. Expense, lower specificity compared with

	Comment
	Age at which to start screening varies based on specific gene mutation (Table 7) For purposes of breast cancer screening, untested blood relatives of known breast cancer gene pathogenic variants are considered high risk until their testing has been performed and negative
	Models vary but typically include current age, family history of breast (and other) cancers, reproductive risk factors, breast density, BMI, absence (or unknown) cancer gene pathogenic variants
	• Most commonly, these are patients who were treated for Hodgkin lymphoma • Dose depends largely on the decade it was administered
	Use of MRI for surveillance can be offered, but some have questioned value[32]
	• These reproductive factors are incorporated into risk assessment tools • Reproductive risk factors alone are usually insufficient to characterize an individual patient as "high risk"
	Despite the higher incidence in White women, Black women are at greater risk for regional or advanced disease (46% vs 36%) and breast cancer–specific mortality (30 vs 21 deaths per 100,000 women)
	Higher BMI is associated with a lower breast cancer risk in premenopausal patients, particularly in early adulthood
	While breast density is typically incorporated into lifetime risk models, controversy exists on whether any supplemental screening should be recommended based on breast density alone (especially for those with extremely dense breasts)
	Use of PRS alone has not been validated for conferring high-risk status outside of research settings. PRS may be combined with more traditional risk tools (eg, Tyrer-Cusick) to develop "customized" risk scores. The ideal goal of PRS is to better advise patients to individualize breast cancer screening compared to a one-size-fits-all approach. National guideline groups have not yet recommended the use of PRS until more confirmatory data are available.
	Many experts argue that 5-year and 10-year risk are better measures than lifetime risk to guide when to start with intensive surveillance

TABLE 3 Commonly used breast cancer risk evaluation tools

Breast cancer risk estimation tool	Web link	Output	Comment
Breast Cancer Risk Assessment Tool	https://bcrisktool.cancer.gov/	5-year breast cancer risk Lifetime risk of breast cancer (compares to average risk similarly aged person assigned female at birth)	**Advantages:** Incorporates race/ethnicity, prior breast biopsies, and reproductive history. No cost to use **Disadvantages:** Does not incorporate BMI or breast density. Does not utilize any second-degree relatives or paternal family history. Should not be used to designate "high risk" for purposes of supplemental MRI
Breast Cancer Surveillance Consortium Risk Calculator	https://tools.bcsc-scc.org/BC5yearRisk/intro.htm	5-year breast cancer risk 10-year breast cancer risk (compares to average risk similarly aged persons)	**Advantages:** Incorporates race/ethnicity, breast density, prior breast biopsies. No cost to use **Disadvantages:** Does not incorporate reproductive risk factors or BMI. Does not utilize any second-degree relatives or paternal family history. Should not be used to designate "high risk" for purposes of supplemental MRI. Does not ask questions about *BRCA* status, exposure to radiation
CanRisk (formerly BOADECIA)	www.canrisk.org	5-year breast cancer risk 10-year breast cancer risk Lifetime breast cancer risk (compares to similarly aged person assigned female at birth) Includes age-based graph and pictogram of breast cancer risk 5-year, 10-year and lifetime risk of ovarian cancer	**Advantages:** More comprehensive family history including details on breast cancer history. Tool is appropriate for calculating LTR to offer MRI. Also estimates LTR of ovarian cancer. Incorporates risk of various cancer gene mutations (*BRCA1, BRCA2* among others). Incorporates reproductive risk factors, alcohol use, breast density, targeted medical history, polygenic risk score (if available) and BMI. **Disadvantages:** Takes longer to fill out than other tools. Validation has largely been performed in European, White populations so may not provide accurate estimates in the United States, particularly in Black populations.
Claus	No official online model available. Some derivative models available (eg, https://www.princetonradiology.com/service/mammography/breast-cancer-risk-assessment/)	Lifetime risk of breast cancer (based on current age)	**Advantages:** Very simple. Can be used to estimate lifetime risk for recommendations of supplemental MRI. Incorporates more comprehensive family history (breast cancer only). **Disadvantages:** Does not include any other risk factors
Tyrer-Cuzick (IBIS)	https://ibis.ikonopedia.com/ (rapid online)	10-year breast cancer risk Lifetime breast cancer risk (compares to similarly aged person assigned female at birth)	**Advantages:** More comprehensive family history. Tool is appropriate for calculating lifetime breast cancer risk to offer supplemental MRI screening. Incorporates personal and family history of *BRCA* mutations, reproductive risk factors, breast density, Ashkenazi Jewish ancestry, prior breast biopsies, and BMI. **Disadvantages:** Takes longer to fill out than other tools. Validation has largely been performed in European, White populations so may not provide accurate estimates in the United States, particularly in Black populations.

Abbreviations: BMI, body mass index; LTR, lifetime risk; MRI, magnetic resonance imaging.

TABLE 4 Efficacy and harms of screening mammography[4,14,15]

Benefits				
Mortality reduction				
RCTs	RR, 0.81 (0.74–0.87)			
Incidence-based studies	RR, 0.62 (0.56–0.69) actually screened RR, 0.75 (0.69–0.81) invited to screening			
Case-control studies	OR, 0.46 (0.4–0.54) actually screened OR, 0.69 (0.57–0.83) invited to screening			
Reduction in treatment				
Increased need for chemotherapy in unscreened	See text page 35			

Harms of screening	**Callbacks**	**Benign breast biopsies**	**Overdiagnosis**	
	~10%	~1%	**Risk by age (in next decade)**	**Invasive, %**
			40	0.3
			50	0.8
			60	2.1
			70	6.5
			80	14.8

Abbreviations: OR, odds ratio; RCTs, randomized controlled trials; RR, risk ratio.

mammography (that is, more false-positive results), and need for the use of gadolinium limit more widespread use of breast MRI screening in average-risk persons.

Screening in patients with dense breasts

Half of patients undergoing SM in the United States have dense breasts (heterogeneously dense breasts, 40%; extremely dense breasts, 10%). Importantly, increasing breast density is associated with a lower cancer detection rate with SM and is an independent risk factor for developing breast cancer. While most states already require patients to be notified if they have dense breasts identified on SM, the US Food and Drug Administration will soon make breast density patient notification a national standard (see: https://delauro.house.gov/media-center/press-releases/delauro-secures-timeline-fda-rollout-breast-density-notification-rule).

Most of the risk assessment tools listed in TABLE 3 incorporate breast density into their calculation of breast cancer risk. If that calculation places a patient into one of the highest-risk groups (based on additional factors like strong family history of breast cancer, reproductive risk factors, *BRCA* carriage, and so on), more intensive surveillance should be recommended (TABLE 7).[7] However, once these risk calculations are done, most persons with dense breasts will remain in an average-risk category.

Because of the frequency and risks associated with dense breasts, different and alternative strategies have been recommended for screening persons who are at average risk with dense breasts. Supplemental screening with MRI, ultrasonography, contrast-enhanced mammography, and

TABLE 5 Recommendations for breast cancer screening mammography in average-risk women[4,5,7,33]

Guideline group	Age to initiate	Interval	Age to stop	Use of DM vs DBT
USPSTF (2016)	40—offer based on SDM 50—recommend	Biennial	Continue to age 74, insufficient data afterward	Insufficient evidence
NCCN (2022)	40—recommend	Annual	Continue to age 74, consider continuing afterward unless <10 years of life expectancy	Recommend DBT if available, DM is acceptable
ACS (2015)	40—offer based on SDM 45—recommend	Annual ages 40–55; consider biennial after age 55	Continue to age 74, consider continuing afterward unless <10 years of life expectancy	Insufficient data
ACOG (2017)	40—offer based on SDM 50—recommend	Every 1–2 years	Continue to age 74, consider continuing afterward unless <10 years of life expectancy	Insufficient data to recommend (2013)

Abbreviations: ACOG, American College of Obstetricians and Gynecologists; ACS, American Cancer Society; DBT, digital breast tomosynthesis; DM, digital mammography; NCCN, National Comprehensive Cancer Network; SDM, shared decision making based on a discussion of potential risks, benefits, and patient's values; USPSTF, US Preventive Services Task Force.

molecular breast imaging are all being considered but have not been studied sufficiently to demonstrate mortality benefit or cost-effectiveness.

Of all the supplemental modalities used to screen patients with dense breasts, MRI has been the best studied. A large RCT in the Netherlands evaluated supplemental MRI screening in persons with extremely dense breasts after a negative mammogram.[21] Compared with no supplemental screening, the MRI group had 17 additional cancers detected per 1,000 screened and a 50% reduction in interval breast cancers; in addition, MRI was associated with a positive predictive value of 26% for biopsies. At present, high cost and limited access to standard breast MRI has not allowed its routine use for persons with dense breasts in the United States, but this may change with more experience and more widespread introduction and experience with abbreviated (or rapid) breast MRI in the future (**TABLE 8**).

Equitable screening

Black persons who are diagnosed with breast cancer have a 40% higher risk of dying than White patients due to multiple factors, including systemic racial factors (implicit and unconscious bias), reduced access to care, and a lower likelihood of receiving standard of care once diagnosed.[22-24] In addition, Black patients have twice the likelihood of being

TABLE 6 Age-specific 10-year risk of breast cancer incidence and breast cancer mortality in the United States[4]

Current age	Risk of diagnosis with invasive breast cancer in next 10 years	Risk of breast cancer mortality in next 10 years
20	0.1% (1 in 1,439)	< 0.1% (1 in 18,209)
30	0.55% (1 in 204)	<0.1% (1 in 2,945)
40	1.6% (1 in 63)	0.1% (1 in 674)
50	2.4% (1 in 41)	0.3% (1 in 324)
60	3.5% (1 in 28)	0.5% (1 in 203)
70	4.1% (1 in 24)	0.7% (1 in 137)
80	3.0% (1 in 33)	1.0% (1 in 100)
Lifetime risk	12.9% (1 in 8)	2.5% (1 in 39)

TABLE 7 Recommendations for breast cancer screening in high-risk women[7]

Risk factor	Modality					
	Digital breast tomosynthesis (DBT)/ digital mammography (DM)[a]			Breast MRI		
	Age to initiate	Interval frequency	Comment	Age to initiate	Interval frequency	Comment
Pathogenic breast cancer genes: *BRCA1, BRCA2, TP53, PTEN*	30	Annual	Later initiation time for mammography than MRI based on both limiting radiation and reduced sensitivity in younger breasts	25	Annual	
Breast cancer genes: *CHEK2*	Variable	Annual		Variable	Annual	
ADH/ALH/LCIS	After diagnosis	Annual		After diagnosis	Annual	Use of MRI is recommended to be offered. Recent data suggest no improvement compared with mammography alone
Therapeutic radiation exposure at ages 10–30	7–10 years after exposure but not before age 30	Annual		7–10 years after exposure but not before age 25	Annual	
Strong family history of breast cancer with LTR ≥20%	7–10 years prior to youngest relative with breast cancer, but not before age 30	Annual		7–10 years prior to youngest relative with breast cancer, but not before age 25	Annual	

[a]Based on screening characteristics (slightly improved cancer detection rate and specificity with DBT), both SM and DBT are appropriate, but tomosynthesis is preferred if available.

Abbreviations: ADH, atypical ductal hyperplasia; ALH, atypical lobular hyperplasia; DBT, digital breast tomosynthesis; DM, digital mammography; LCIS, lobular carcinoma in situ; LTR, lifetime risk; MRI, magnetic resonance imaging.

diagnosed with triple-negative breast cancers, a biologically more aggressive tumor.[22-24] Among Black, Asian, and Hispanic persons diagnosed with breast cancer, one-third are diagnosed younger than age 50, which is higher than for non-Hispanic White persons. Prior to the age of 50, Black, Asian, and Hispanic patients also have a 72% more likelihood of being diagnosed with invasive breast cancer, have a 58% greater risk of advanced-stage disease, and have a 127% higher risk of dying from breast cancer compared with White patients.[25,26] Based on all of these factors, delaying SM until age 50 may adversely affect the Black, Asian, and Hispanic populations.

Persons in the LGBTQ+ community do not present for SM as frequently as the general population, often because they feel threatened or unwelcome.[27] Clinicians and breast imaging units should review their inclusivity policies and training to provide a welcoming and respectful environment to all persons in an effort to reduce these barriers. While data are limited and largely depend on expert opinion, current recommendations for screening in the transgender patient depend on sex assigned at birth, the type and duration of hormone use, and surgical history. In patients assigned female sex at birth, average-risk and high-risk screening recommendations are similar to those for the general population unless bilateral mastectomy has been

TABLE 8 Breast cancer screening imaging modalities used for average- and high-risk breast cancer screening[14,34-36]

Modality	Advantages	Disadvantages
Mammography • Digital mammography (DM)	• Multiple large RCTs demonstrating breast cancer (and all-cause) mortality benefit in persons ages 40–74 • Covered as preventive care by most insurance providers	• Small breast radiation exposure (~1 mSv/image) • False positives (callbacks, breast biopsy, overdiagnosis) • Lower sensitivity in patients with dense breasts • Disagreements on value (risk/benefit) for patients ages 40–49 and screening interval (annual vs biennial)
• Digital breast tomosynthesis (DBT; "3D mammography")	• Most studies demonstrating slightly improved cancer detection rates with DBT compared with DM • Most studies suggest improvement in specificity (less callbacks)	• Small increase in radiation exposure compared with DM • Machines more expensive than DM. Some facilities increase charges to patients, not always covered by insurance • Like DM, lower sensitivity in those with dense breasts
Breast MRI	• Improved sensitivity compared with DM/DBT (75%–100%) • Significantly fewer interval cancers (symptomatic breast cancers that are detected between rounds of screening) and more node-negative disease compared with mammography alone • No radiation exposure	• Reduced specificity compared with DM/DBT • No proven mortality benefit in high risk (insufficiently studied) • Expensive compared with DM/DBT • Requires IV injection of gadolinium
Abbreviated breast MRI	• Image acquisition time substantially reduced compared with standard breast MRI (time in machine reduced at least 50%) • Appears to have comparable performance to standard breast MRI in early studies • Should reduce cost compared with standard breast MRI	• Not as well studied as standard MRI
Contrast-enhanced mammography	• Significantly improved sensitivity (cancer detection rate) with comparable specificity compared with DM/DBT	• Requires IV injection of iodine-based dye • Many facilities do not currently offer
Molecular breast imaging	• Very high sensitivity irrespective of breast density	• Higher radiation exposure to breast (and entire body)
Ultrasonography	• Incremental cancer detection rate, particularly if dense breasts • No radiation or dye/gadolinium injection needed	• Lower incremental cancer detection rate compared with supplemental breast MRI, contrast-enhanced mammography, or molecular breast imaging • Low positive predictive value compared with DM/DBT or breast MRI

Abbreviations: DBT, digital breast tomosynthesis; DM, digital mammography; IV, intravenous; MRI, magnetic resonance imaging; RCTs, randomized controlled trials.

performed.[28] In transfeminine patients who have used hormones for longer than 5 years, some groups recommend annual screening starting at age 40, although well-designed studies are lacking.[29]

We have done well, can we do better?

Screening mammography clearly has been an important and effective tool in the effort to reduce breast cancer mortality, but there are clear limitations. These include moderate sensitivity of mammography, particularly in patients with dense breasts, and a specificity that results in either callbacks (10%), breast biopsies for benign disease (1%), or the reality of overdiagnosis, which becomes increasingly important in older patients.

With the introduction of mammography in the mid-1980s, a one-size-fits-all approach has proved challenging more recently due

	Current recommendations for screening
	• Recommend for screening in both average and high risk
	• Recommended for screening in both average and high risk
	• Recommended for high-risk screening in cancer gene carriers and other high-risk groups (Table 7) along with mammography
	• Not routinely used, may require more published research before it replaces standard MRI
	• May be considered as alternative for high-risk persons who cannot undergo MRI (eg, gadolinium allergy, claustrophobia) • Lower radiation doses with newer image processing algorithms are emerging
	• Not routinely recommended for screening

to an increased recognition of the harms of screening. As a result of this evolving understanding, different recommendations for average-risk screening have emerged. With the advent of breast MRI, risk-based screening is an important but underutilized tool to identify highest-risk individuals, which is associated with improved cancer detection rates, reduced node-positive disease, and fewer diagnosed interval breast cancers. Assuring that nearly all of this highest-risk group is identified through routine breast cancer risk assessment remains a challenge for clinicians.

But what SM recommendations should be offered to persons who fall into an intermediate-risk group (15%–20%), very low-risk groups (<5%), or patients with dense breasts? These are challenges that could be met through novel and individualized approaches (for example, polygenic risk scoring, further research on newer modalities of screening [TABLE 8]), improved screening algorithms for persons with dense breasts, and enhanced clinician engagement to achieve universal breast cancer and *BRCA* risk assessment of patients by age 25 to 30.

In 2023, best practice and consensus guidelines for intermediate- and low-risk breast cancer groups remain unclear, and one of the many ongoing challenges is to further reduce the impact of breast cancer on the lives of persons affected and the recognized harms of SM.

In the meantime, there is consensus in average-risk patients to provide counseling about SM by age 40. My approach has been to counsel all average-risk patients on the risks and benefits of mammography using the acronym TIP-V:

- Use a *Tool* to calculate breast cancer risk (TABLE 3). If they are at high risk, provide recommendations for high-risk management (TABLE 7).[7]
- For average-risk patients, counsel that their *Incidence* of developing breast cancer in the next decade is approximately 1 in 70 (TABLE 6).[4]
- *Provide* data and guidance on the benefits of SM for patients in their 40s (mortality improvement, decreased treatment) and the likelihood of harm from breast cancer screening (10% callback, 1% benign biopsy, and <1% likelihood of overdiagnosis [TABLE 4]).[4,14,15]
- Engage the patient to better understand their relative *Values* of the benefits and harms and make a shared decision on screening starting at age 40, 45, or 50.

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There is consensus in average-risk patients to provide counseling about SM by age 40

Looking forward

In summary, SM remains an important tool

in the effort to decrease the risk of mortality due to breast cancer. Given the limitations of SM, however, newer tools and methods—abbreviated MRI, contrast-enhanced mammography, molecular breast imaging, customized screening intervals depending on individual risk/polygenic risk score, and customized counseling and screening based on risk factors (TABLES 2 and 7)—will play an increased role in recommendations for breast cancer screening in the future. ●

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