

Breast Imaging Screening 2026: Implications of Risk-Based Screening

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Screening mammography reduces breast cancer mortality and saves lives. Conventional screening protocols are based primarily (and often exclusively) on patient age. With technologic advances and discoveries at the genetic and molecular levels, there is increasing interest in risk-based breast cancer screening. Instead of a one-size-fits-all approach, an individualized screening protocol may allow earlier detection of breast cancer in higher-risk patients while reducing unnecessary procedures in others. Risk-based screening needs to consider multiple variables, and various risk assessment models have been developed. Augmented by artificial intelligence (AI), risk-based screening aims to use available imaging modalities in a cost-effective manner to optimize patient care.

Randomized controlled trials have established screening mammography as the method in saving lives. Breast cancer screening guidelines have historically prioritized age as the primary criterion. As technology improves and expands and medical knowledge grows, interest in the potential application of risk-based (instead of population-based or universal) breast cancer screening has increased. Rather than a one-size-fits-all process, a more tailored approach may detect breast cancers earlier and more effectively in higher-risk patients. Such a personalized approach may also allow the best allocation of resources, identifying cancers in higher-risk patients while decreasing unnecessary procedures. An independent review from the National Health Service Breast Screening Program estimated that for each breast cancer death prevented, about three women are overdiagnosed and treated [1].

The concept of risk-based screening marks a significant shift, enabled by data advances like machine learning and genetic insights such as polygenic risk scores. It allows more precise, patient-centered care. Risk-based screening personalizes screening guidelines by determining when to start, how often to screen, and when to stop based on the individual risk profile, aiming to detect aggressive cancers early while reducing costs such as false-positives and overdiagnosis. Ultimately, risk-based screening seeks to improve screening programs by incorporating genetic research and customizing prevention strategies for different risk groups [2].

This chapter explores risk-based screening implications, covering scientific basis, clinical guidelines, technologic advances, effectiveness, costs, ethics, logistics, and policy. It highlights the transformative potential of personalized strategies.

Breast Cancer Screening Guidelines

The landscape of breast cancer screening guidelines is dynamic, with major professional organizations increasingly integrating risk assessment into their recommendations. Although a consensus is emerging on the importance of individual risk, variations in specific age and frequency recommendations persist, reflecting ongoing scientific discourse and varying interpretations of benefit-cost profiles. Table 1 summarizes the current guidelines of various professional organizations [3–7].

A common theme in these major guidelines is the consistent recommendation for early risk assessment, usually by age 25–30, as a key step to tailor screening schedules and methods. This marks a notable shift from uniform age-based protocols. Another emerging area of clinical importance is breast density and its clinical significance in screening. This increasing recognition is reflected in the FDA's policy that mandates mammography facilities inform patients about their breast density and the possible need for additional screening tests [8].

By tailoring recommendations based on an individual's specific risk profile, personalized screening based on key principles of risk stratification, tailored interventions, and dynamic assessment endeavors to optimize resource utilization, enhance diagnostic accuracy, and ultimately improve patient outcomes while minimizing risks associated with conventional screening methods [2].

Risk Assessment

Methods and Risk Factors

The foundation of risk-based breast cancer screening lies in accurately assessing an individual's propensity for developing breast cancer. This involves identifying and quantifying various risk factors through sophisticated and validated prediction models. A woman's risk of developing breast cancer is influenced by a multitude of factors beyond chronologic age only, which forms

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TABLE 1: Summary of Breast Cancer Screening Guidelines

Organization	Target Population	Starting Age (y)	Screening Modality	Screening Frequency	Key Considerations
ACR/SBI [3]	All women (risk assessment by age 25)	40	Mammography	Annual	Emphasizes risk assessment by age 25 to tailor; supplemental screening for dense breasts/high risk (DBT, MRI, US, CEM)
ACS [4]	Women with average risk	45 (option at 40–44)	Mammography	Annual (age 45–54), then biennial (age 55 or older)	Continue as long as good health or at least 10 years life expectancy; screening can start at age 30 for women with high risk
USPSTF [5]	All women	40	Mammography	Biennial (every 2 years) until age 74	Focus on health equity, especially for Black women; this is a shift from 2016 guidelines
NCCN [6]	Women with average risk	40	Mammography with tomosynthesis	Annual	Risk assessment by age 25; increased risk ($\geq 20\%$ lifetime) starts 10 years before youngest relative's diagnosis (but not before age 30) or age 40, plus annual MRI
EUSOBI [7]	All women (risk assessment by age 25)	25 (MRI, for high risk), 40–45 (mammography)	MRI (for high risk), mammography (primary), US/CEM (supplemental)	Annual MRI (for high risk), biennial mammography (for average risk, age 50–69)	Advocates for risk-based approach; annual MRI from age 25 for high risk; supplemental MRI for extremely dense breasts every 2–3 years

Note—ACR = American College of Radiology, SBI = Society of Breast Imaging, DBT = digital breast tomosynthesis, US = ultrasound, CEM = contrast-enhanced mammography, ACS = American Cancer Society, USPSTF = U.S. Preventive Services Task Force, EUSOBI = European Society of Breast Imaging.

the scientific basis for personalized screening. These risk factors may be categorized into clinical, genetic, breast density, and lifestyle and environmental factors.

Clinical factors—Relevant clinical factors include demographic characteristics such as age, race, and ethnicity as well as reproductive history (e.g., age at menarche, age at first live birth, menopausal status, overall childbirth history). A personal history of breast biopsies, particu-

larly those revealing atypical hyperplasia or lobular carcinoma in situ, significantly elevates risk [9].

Genetic factors—A family history of breast cancer, especially among first-degree relatives and considering their age at diagnosis, is a strong indicator of inherited risk. The presence of known genetic mutations, such as *BRCA1/2*, *PALB2*, *ATM*, or *CHEK2*, also significantly increases risk [9, 10]. The various genes associated

with breast cancer are listed in Table 2. Individual breast cancer susceptibility variants, known as single nucleotide polymorphisms (SNPs), contribute a slight increase in risk on their own. Approximately 313 SNPs have been identified, and they are associated with a higher risk of developing breast cancer [11]. When combined, these variants can substantially elevate the risk of developing breast cancer. A polygenic risk score combines the effects of these

TABLE 2: Key Genetic Mutations and Associated Breast Cancer Risk

Gene	Associated Risk Level	Lifetime Risk	Key Characteristics	Management Guidelines
<i>BRCA1</i>	Significantly elevated	82%	Increased propensity for triple-negative tumors	Surveillance with breast MRI and mammography, pharmacologic risk reduction (tamoxifen/aromatase inhibitors), prophylactic mastectomies
<i>BRCA2</i>	Significantly elevated	82%	Increased risk across various breast cancer subtypes	Surveillance with breast MRI and mammography, pharmacologic risk reduction, prophylactic mastectomies
<i>PTEN</i>	Significantly elevated (Cowden syndrome)	$\leq 85\%$	Associated with benign and malignant tumors	High-risk surveillance, risk-reducing interventions
<i>TP53</i>	High (Li-Fraumeni syndrome)	25%	Associated with multiple cancer types, including breast cancer	High-risk surveillance, risk-reducing interventions
<i>STK11</i>	High (Peutz-Jeghers syndrome)	32%	Associated with polyps and various cancers	High-risk surveillance, risk-reducing interventions
<i>CDH1</i>	High (familial gastric cancer)	39%*	Primarily gastric cancer, but also lobular breast cancer	High-risk surveillance, risk-reducing interventions
<i>ATM</i>	Moderate	Two- to threefold increase	Risk modified by family history	Personalized approach, annual screening is often recommended
<i>PALB2</i>	Moderate	Two- to threefold increase	Risk modified by family history	Personalized approach, annual screening is often recommended
<i>CHEK2</i>	Moderate	Two- to threefold increase	Risk modified by family history	Personalized approach, annual screening is often recommended

Note—Some information contained in this table was previously published by Shiovitz and Korde [10].

*Risk of lobular cancer.

variants identified through genome-wide association studies. Polygenic risk scores are being incorporated into risk assessment, providing a more comprehensive genetic profile.

Breast density—Denser breast tissue is an established independent risk factor for breast cancer. Furthermore, it significantly impacts the efficacy of mammography as dense tissue can obscure cancerous lesions, making detection more challenging [12]. There are fully automated methods to assess breast density [13]. Recently, AI and machine learning methods have been created to assess breast density from mammograms, achieving accuracy similar to that of humans in predicting breast cancer [14].

Lifestyle and environmental factors—Modifiable factors such as high body weight or obesity, the use of hormone replacement therapy, smoking, and alcohol consumption are also recognized as contributing to breast cancer risk. However, the intricate interactions between modifiable lifestyle factors and inherited genetic risks (e.g., in individuals with *BRCA* mutations) require further dedicated study to elucidate their combined impact fully [9].

Multifactorial risk assessment—The imperative for multifactorial risk assessment stems from the sheer number and diversity of risk factors. Relying on a single variable, such as age, is inherently inadequate given the complex pathogenesis of breast cancer. The transition to risk-based screening is fundamentally driven by the

scientific understanding that a comprehensive integration of diverse variables—clinical, genetic, breast density, and lifestyle and environment—is necessary for a more accurate risk prediction. This moves beyond identifying a single high-risk gene to a more holistic understanding of an individual's total risk profile.

Risk Prediction Models

Risk prediction models are computational tools designed to estimate a woman's probability of developing breast cancer over defined periods, such as 5 years or across her lifetime. Table 3 presents some of the widely used risk models [15–18].

Although risk models are increasingly recognized, their integration into actual clinical protocols remains somewhat limited in scope. Additional prospective studies are necessary to assess their clinical utility comprehensively. It is crucial to recognize that these models are inherently imperfect; they do not achieve 100% accuracy and should not be used to substitute for professional medical consultation or routine mammography. They provide a probability rather than an absolute assurance of developing breast cancer. Furthermore, considerable challenges persist in accurately validating the intricate interactions among various risk factors and effectively incorporating these into existing models [19].

A key concern is the so-called data gap in developing and validating risk models. Most analyses omit models that

include molecular diagnostics and SNPs. A comparative analysis by Terry et al. [20] found that the Tyrer-Cuzick model and the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) outperformed BRCAPRO and the Breast Cancer Risk Assessment Tool (BCRAT). They also determined that models based on multigenerational family history are more accurate for predicting breast cancer, though a hybrid model could improve results further. Moreover, some non-web-based risk models showed that individualized coherent absolute risk estimation models perform as well as, or better than, BCRAT and the Tyrer-Cuzick model [21].

Imaging Modalities in Risk-Based Screening

The advent of risk-based screening necessitates a comprehensive approach to breast imaging, moving beyond a single modality to a tailored combination of technologies that optimize detection based on individual risk and breast-tissue characteristics.

Primary Imaging

Mammography—Mammography continues to serve as the primary method for breast cancer screening (Fig. 1) and is the only imaging modality conclusively proven to reduce mortality rates associated with breast cancer. Mammography typically employs minimal doses of ionizing radiation. A notable limitation is its

TABLE 3: Overview of Breast Cancer Risk Assessment Models

Model Name	Key Risk Factors Included	Calculated Risks	Target Population/ Applicability	Limitations
Gail (BCRAT) [15]	Age, race and ethnicity, reproductive history, breast biopsies, first-degree family history	5-Year, lifetime	General population	Underestimates risk in Black women with prior biopsies and Hispanic women born outside the United States; not for <i>BRCA</i> carriers or women with previous breast cancer
Tyrer-Cuzick (IBIS) [16]	Age, family history (first- and second-degree), breast density, hormonal/reproductive factors, biopsies (ALH, ADH, LCIS)	10-Year, lifetime	General population (more comprehensive than Gail)	May overestimate risk in Hispanic women; not for women with previous breast cancer
BCSC [17,18]	Age, race and ethnicity, family history, breast biopsies, breast density	5-Year, 10-year	Multiracial/multiethnic U.S. population	May underestimate risk in younger women and those with low breast density
Polygenic risk scores [17,18]	Cumulative effects of common genetic variants	Variable (often integrated into other models for absolute risk)	General population, familial cases	Complex interpretation; clinical applicability in familial cases is under investigation

Note—BCRAT = Breast Cancer Risk Assessment Tool, IBIS = International Breast Intervention Study, ALH = atypical lobular hyperplasia, ADH = atypical ductal hyperplasia, LCIS = lobular carcinoma in situ, BCSC = Breast Cancer Surveillance Consortium.

reduced sensitivity in women with dense breast tissue, wherein malignant lesions may be obscured by overlapping glandular tissue [3].

Digital breast tomosynthesis—Digital breast tomosynthesis (DBT) substantially improves screening sensitivity by offering radiologists enhanced, detailed views of breast tissue through multiple thin (usually 1 mm) slices. This technology has shown a higher detection rate of breast cancer and a reduction in recall rates in screening. DBT is notably effective in mitigating the masking effect in dense breast tissue, thereby facilitating the identification of smaller and obscured subtle cancers [22, 23]. Although highly promising, its widespread implementation as a routine screening modality continues to develop, partly owing to marginally increased radiation exposure, longer image interpretation times rela-

tive to conventional mammography, and higher equipment costs.

Supplemental Imaging

For individuals with elevated risk or dense breast tissue, supplemental imaging modalities play a crucial role in enhancing cancer detection.

Breast ultrasound—Typically utilized in conjunction with mammography, breast ultrasound (Figs. 1 and 2) is frequently the initial imaging modality employed for young patients (under 30 years old) presenting with breast symptoms. As a supplementary screening technique, it has the potential to augment cancer detection rates somewhat; however, this benefit is accompanied by an increased rate of false-positives. Ultrasound represents a valuable option for women at high risk who are unable to undergo MRI or an alternative to MRI for individuals with

extremely dense breasts when MRI is unavailable [3, 24].

Breast MRI—MRI is recognized for its high sensitivity and is frequently recommended for women at elevated risk of breast cancer, irrespective of breast density (Figs. 2 and 3). The American College of Radiology recommends annual screening breast MRI commencing between age 25 and age 30 for women with a genetic predisposition or a lifetime risk of 20% or greater [3, 24]. The European Society of Breast Imaging advocates for annual breast MRI as the primary screening modality for women at high risk, starting as early as age 25 [25].

Abbreviated breast MRI—This expedited, usually 10-minute (or faster) MRI procedure is intended as a supplementary screening modality in conjunction with mammography for women presenting with dense breast tissue who are at average or intermediate risk [26].

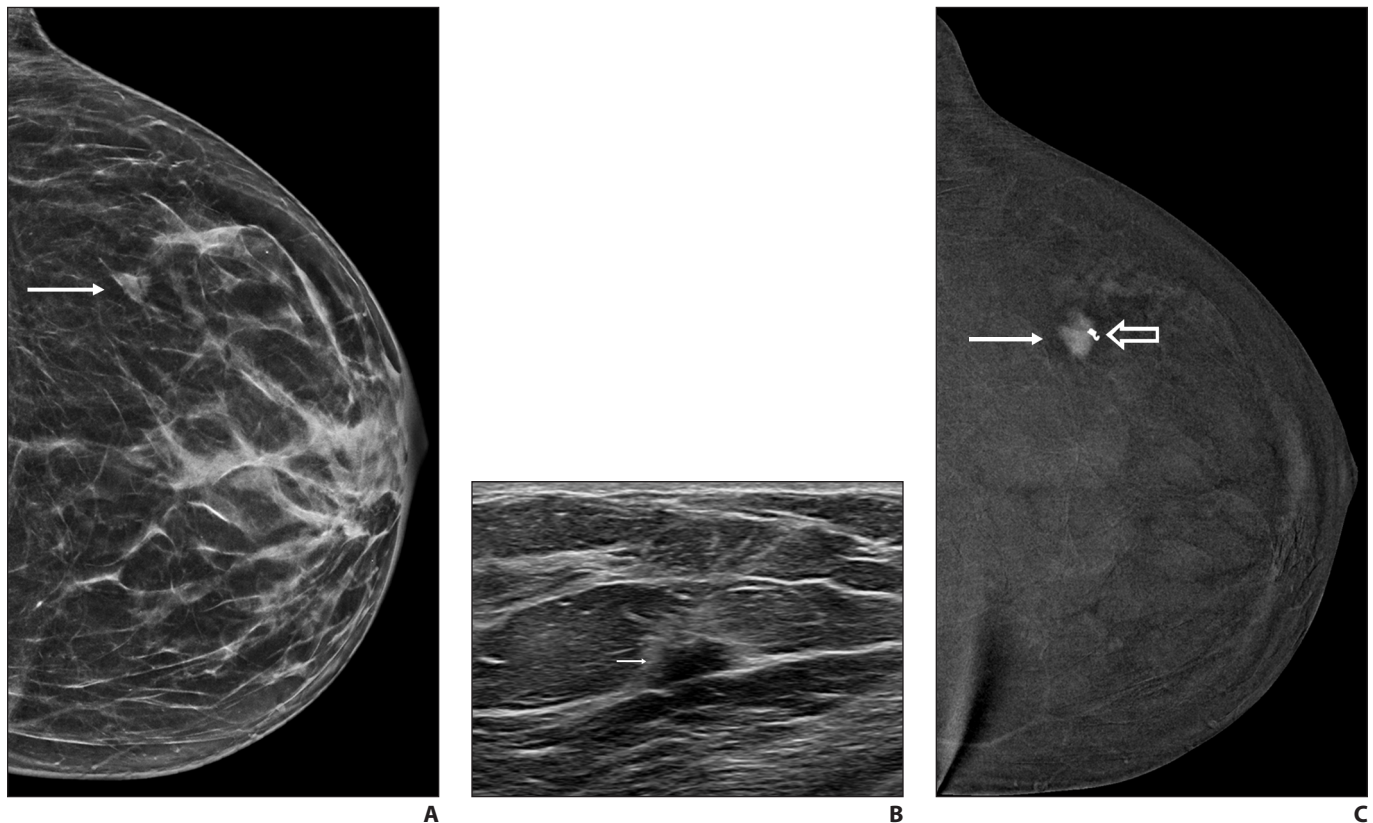


Fig. 1—52-year-old woman with family history of breast cancer who underwent screening mammography. Asymptomatic breast cancer was initially detected on mammography and was also seen on subsequent ultrasound and contrast-enhanced mammography. **A**, Left craniocaudal mammogram shows mass (arrow) in outer breast. **B**, Left breast ultrasound shows irregular, indistinct, hypoechoic mass associated with echogenic rind (arrow) corresponding to mammographic mass. Subsequent biopsy revealed invasive ductal carcinoma. **C**, Contrast-enhanced mammography performed after biopsy shows that mass (solid arrow) is homogeneously enhancing on recombined craniocaudal image. Biopsy clip (open arrow) is seen at anterior aspect of mass.



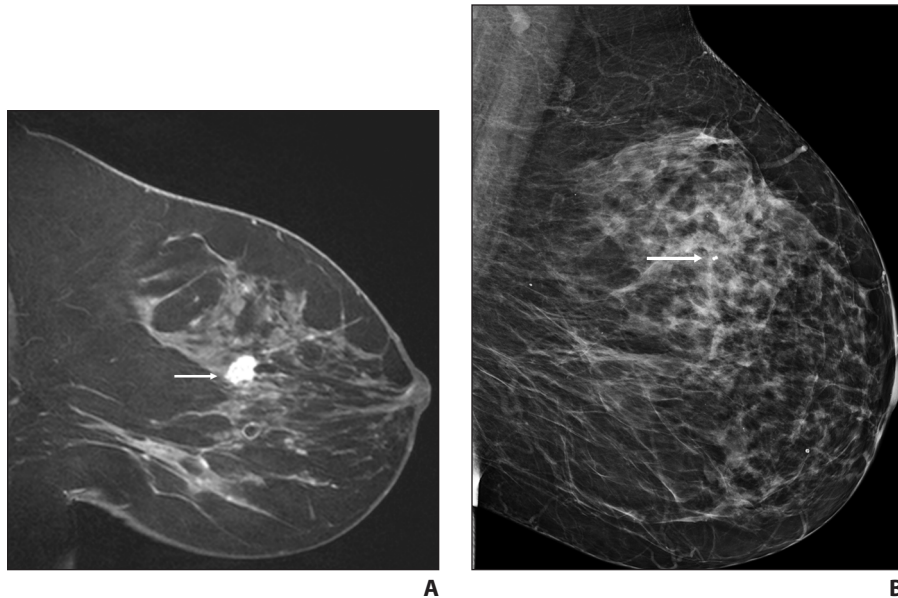


Fig. 3—46-year-old woman with family history of breast cancer who underwent screening mammography and MRI. Asymptomatic breast cancer was detected on MRI but not on mammography. **A**, Sagittal contrast-enhanced subtraction MRI shows irregular, enhancing mass (arrow) in left breast, with subsequent biopsy revealing invasive lobular carcinoma. **B**, Left mediolateral oblique mammogram performed after biopsy shows biopsy clip (arrow) denoting location of cancer. No mammographic evidence of malignancy is seen at site of biopsy clip.

Contrast-enhanced mammography—Contrast-enhanced mammography (CEM) shows significant promise as a supplemental screening method (Fig. 1). It is beneficial for intermediate-risk women with dense breasts and for women at high risk [3]. Its effectiveness has been studied in women with intermediate risk and dense breasts who have been recalled after screening [27, 28].

The randomized controlled Breast Screening–Risk Adapted Imaging for Density (BRAID) trial is comparing automated breast ultrasound, abbreviated breast MRI, and CEM as a supplemental modality in screening dense breasts and has found that supplemental imaging indeed detects additional cancers beyond standard mammography [29].

Imaging choices depend on a woman's risk and breast density, creating a modality-risk-density triad. Although mammography remains standard for average risk, dense breasts or higher risk may require MRI or ultrasound, leading to a personalized screening approach. Advanced modalities including DBT, CEM, and MRI offer increased cancer detection but are more expensive and less accessible. The vascular-based modalities of MRI and CEM also require contrast administration.

The optimal modality (or combination of modalities) depends on individual risk factors, balancing benefits and costs in a tailored strategy.

Clinical Considerations of Risk-Based Screening Efficacy

The shift to risk-based screening carries significant clinical implications, aiming to enhance the efficacy of breast cancer detection while carefully managing the associated benefits and costs. Risk-based screening aims to improve early cancer detection and outcomes in high-risk patients. Personalized screening that incorporates medical data and machine learning can detect cancer early, especially in higher-risk groups [30]. As shown in the past 3 decades, population-based screening mammography has reduced breast cancer mortality by 30–40%, with a 44% overall reduction due to early detection and improved treatments [31, 32]. Combining annual mammography with MRI for moderate-risk patients can further lower death rates. Screen-detected cancers are less likely to be advanced, require mastectomy, or result in death when compared with cancers that pres-

ent symptomatically. Although screening offers benefits, risk-based methods aim to minimize risks such as false-positives and overdiagnosis by avoiding unnecessary procedures for lower-risk groups.

Economics

The economic viability and efficiency of risk-based breast screening programs are critical considerations for their successful widespread implementation. Cost-effectiveness analyses, often employing quality-adjusted life years, provide a framework for evaluating the value of these interventions.

Economic models and quality-adjusted life years—Cost-effectiveness analyses frequently use quality-adjusted life years as a metric to compare health interventions, balancing gains in life expectancy with the quality of life experienced. Economic models, such as Markov models, are specifically developed to estimate the lifetime costs and health effects of various screening programs.

Comparative cost analysis with age-based screening—The cost-effectiveness of risk-based screening versus conventional age-based screening remains a topic of debate. Some studies suggest that reducing or skipping screening for lower-risk women while increasing frequency for higher-risk women could be more cost-effective [33, 34]. It is widely recognized that annual screening reduces mortality and increases quality-adjusted life years. Emerging evidence indicates that AI-driven, risk-stratified programs might be more cost-effective, offering health benefits with fewer resources. It has also been suggested that increasing screening intervals for some women at lower risk while increasing them for higher-risk groups may favorably impact the cost analysis [34].

Cost challenges—A significant barrier to the adoption of risk-based screening is complexity in estimating and comparing costs and benefits. Cost-effectiveness depends on factors like risk stratification methods, screening technologies, quality of life assumptions, patient participation, risk thresholds, and included costs. Many studies omit the direct costs of risk stratification and diagnostics. Although fewer procedures could improve the benefit-to-

cost ratio and reduce expenses, methodologic differences and variable inputs limit definitive conclusions.

The economics of personalized medicine show a paradox. Although risk-based screening strives for efficiency, evidence indicates mixed economic benefits. Reducing unnecessary screening for lower-risk groups saves costs, but screening higher-risk individuals with expensive tests like MRI and biopsies can increase costs. Cost-effectiveness depends on maximizing health value, often measured in quality-adjusted life years, which complicates financial analyses [33–35].

Many models overlook the initial and ongoing costs of implementing risk stratification and diagnostics. Setting up risk-based screening requires investments in risk tools, genetic testing, data systems, and staff training. Not accounting for these costs results in incomplete, misleading financial assessments. Policymakers need comprehensive evaluations covering the entire lifecycle—from initial assessment to long-term follow-up—to accurately measure financial impact and support sustainable, effective risk-based screening programs [36].

Psychologic Impact

The psychologic impact of risk communication and screening outcomes needs to be considered. Breast cancer screening

outcomes, especially false-positives, can cause patient anxiety and distress and reduce quality of life. Although risk-based screening aims to minimize unnecessary procedures, it may increase anxiety about cancer, though some studies show only minimal distress with proper communication. Health care providers must provide clear and accurate information and support for informed decisions [37, 38].

Logistic Challenges and Implementation Strategies

The transition to widespread risk-based breast screening presents considerable logistic challenges, necessitating innovative implementation strategies and a concerted effort to address existing barriers. Table 4 describes the various trials studying implementation of risk-based screening [39–42]. The European Collaborative on Personalized Early Detection and Prevention of Breast Cancer (ENVISION) network meeting included participants from 14 European countries (Austria, Belgium, Denmark, Estonia, Finland, France, Germany, Italy, The Netherlands, Slovenia, Spain, Switzerland, Sweden, and the UK) as well as Israel, the United States, Canada, Malaysia, and Australia. They released a consensus statement addressing risk assessment, preventive measures, risk-stratified early detection, and program implementation [43].

Several significant hurdles impede the broad adoption of risk-based screening, including complex risk communication involving polygenic scores and model outputs. This complex material may be challenging for a patient to understand and remain engaged. Validating complex risk factors and models remains difficult, especially when integrating the interactions of various factors. Advanced genetic tests for rare variants are expensive and resource-intensive, limiting widespread adoption. Technologies for interpreting moderate- and high-risk data are not yet scalable due to their inherent complexities. Many small health care practices lack the staff, equipment, and networks necessary for sophisticated screening. Proper training for health care professionals is crucial but not always present. Patient acceptance is a significant barrier, particularly when reducing screening frequency for lower-risk individuals. A clear business model for expanding risk programs remains to be established [43].

Integrating big data into clinical practice is challenging, requiring unification of diverse datasets—clinical, genetic, and imaging—into a clear, accessible, easy-to-use risk tool for health care providers. Current infrastructure and training often fall short, highlighting the need for robust decision support systems and information technology investment. Patient engagement and

TABLE 4: Studies of Implementation of Risk-Based Breast Cancer Screening

Study	Method	Key Risk Factors and/or Technology Assessed	Country or Region
WISDOM [39]	Women informed to screen depending on measures of risk	Multicenter, pragmatic, adaptive, preference-tolerant randomized controlled trial comparing risk-based screening to annual screening of women 40–74 years old. Determine if personalized breast cancer screening will lead to fewer risks, improve breast cancer prevention, and be acceptable to women in comparison with standard annual screening	United States
MyPeBS [40]	Personalized breast screening	Multicountry randomized trial of personalized breast cancer screening comparing risk-based screening to standard screening offered in each participating country among women 40–70 years old. Assess if individual risk-based screening is noninferior or superior to the current standard of care in terms of reduction of the incidence of stage II or higher breast cancer	European Union
PERSPECTIVE I & I [41]	Personalized risk assessment for prevention and early detection of breast cancer	Identification and validation of novel moderate- to high-risk breast cancer susceptibility genes. Improvement, validation, and adaptation of a web-based tool for comprehensive breast cancer risk prediction that is suitable for Canada. Development of a framework to support implementation of a personalized risk-based approach to breast cancer screening within existing mammography centers. Economic analyses for optimal personalized risk-based screening implementation	Canada
PROCAS2 [42]	Predicting risk of cancer at screening	Assess the feasibility of individualized risk assessment during screening appointments. Assess a range of effects of implementing personalized risk assessment on women, health care staff, and related organizations	United Kingdom

education are also critical for implementing risk-based screening [43].

AI

AI is poised to revolutionize breast cancer screening. AI models offer the capacity for immediate estimation of short-term cancer risk and hold promise for developing more cost-effective screening programs. Machine learning frameworks are being proposed to leverage claims data to recommend personalized, data-driven, and dynamic screening decisions, further enhancing the precision of risk-based approaches [44].

Rather than a one-size-fits-all approach, a highly focused, personalized paradigm for breast cancer screening is envisioned for the future. As risk-based screening becomes more sophisticated with the integration of AI and noninvasive tests, the definition of preventive care will likely expand to encompass these new, personalized paradigms and risk assessments.

Conclusion

Breast cancer screening is undergoing a meaningful transformation, moving from a uniform, age-based approach to a highly personalized, risk-based model. This shift is driven by an increased understanding of individual risk factors, advances in imaging technologies, and the need to maximize screening benefits while reducing costs and potential harms. Breast cancer screening will become increasingly personalized, fueled by ongoing research, rapid technologic progress in AI and noninvasive tests, and evolving policy frameworks. The primary aim is to improve the benefit-to-cost ratio, boost early detection, and enhance patient outcomes by thoughtfully customizing screening strategies based on individual risk, thereby progressing toward a more precise, equitable, and patient-centered approach to breast cancer prevention and early detection.

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