Breast cancer screening in an era of personalized regimens: A conceptual model and National Cancer Institute initiative for risk-based and preference-based approaches at a population level

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Accessibility
Breast Cancer Screening in an Era of Personalized Regimens:
A Conceptual Model and National Cancer Institute Initiative for Risk-Based and Preference-Based Approaches at a Population Level

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Abstract

Breast cancer screening holds a prominent place in public health, health care delivery, policy, and women’s health care decisions. Several factors are driving shifts in how population-based breast cancer screening is approached, including advanced imaging technologies, health system performance measures, health care reform, concern for “overdiagnosis,” and improved understanding of risk. Maximizing benefits while minimizing the harms of screening requires moving from a “1-size-fits-all” guideline paradigm to more personalized strategies. A refined conceptual model for breast cancer screening is needed to align women’s risks and preferences with screening regimens. A conceptual model of personalized breast cancer screening is presented herein that emphasizes key domains and transitions throughout the screening process, as well as multilevel perspectives. The key domains of screening awareness, detection, diagnosis, and treatment and survivorship are conceptualized to function at the level of the patient, provider, facility, health care system, and population/policy arena. Personalized breast cancer screening can be assessed across these domains with both process and outcome measures. Identifying,
evaluating, and monitoring process measures in screening is a focus of a National Cancer Institute initiative entitled PROSPR (Population-based Research Optimizing Screening through Personalized Regimens), which will provide generalizable evidence for a risk-based model of breast cancer screening. The model presented builds on prior breast cancer screening models and may serve to identify new measures to optimize benefits-to-harms tradeoffs in population-based screening, which is a timely goal in the era of health care reform.

Keywords
screening; breast cancer; process of care; mammography; guidelines

INTRODUCTION
Breast cancer screening is one of the most common forms of cancer screening in the United States, with approximately 37 million screening examinations performed annually.\(^1\) Prevalence estimates vary but range from 64% to 81% of the eligible population screened regularly.\(^2\)-\(^4\) Several conceptual models have been put forth that provide frameworks for improving cancer screening care\(^5\) and identifying gaps in screening processes\(^6\),\(^7\) while incorporating multilevel factors across the cancer care continuum.\(^8\) These conceptual models have been important in advancing the delivery of guideline-based breast cancer screening as well as identifying areas along the screening continuum in which failures may occur and determining those factors associated with such failures. However, there is now increasing demand for personalization of breast cancer screening, based largely on patient preferences and assessment of benefits and harms given individual risk, to optimize the benefit-to-harm ratio associated with screening. Although mammography remains the cornerstone of breast cancer screening, new imaging modalities such as breast magnetic resonance imaging (MRI) may be appropriate for some women at high risk.\(^9\) To provide a framework for evaluating and developing personalized breast cancer screening strategies, we propose a conceptual model in which the tradeoffs of screening for individual women are accounted for within screening processes of care. This conceptual model will be informed by the National Cancer Institute’s (NCI’s) initiative to understand how to improve the screening process across systems of care and to align processes to minimize harms and maximize benefits based on risk.\(^10\) The PROSPR (Population-based Research Optimizing Screening through Personalized Regimens) initiative, including 3 breast cancer screening research centers, is addressing gaps in what is known regarding risk-based processes of care.

Brief Background of Breast Screening
Breast cancer screening has a long history among population-based screening efforts, with decades of evidence, both experimental and observational, existing in regard to its effectiveness. Based on the what to our knowledge are the 7 largest randomized controlled trials published to date, screening mammography performed biannually among women aged 50 years to 70 years is estimated to reduce breast cancer mortality by 20% to 30%.\(^11\),\(^12\) Large observational studies have added to this evidence, demonstrating similar benefits, although the age range and screening interval have differed among studies. Population
trends in breast cancer mortality correspond closely with broad-scale mammography screening, thereby providing support for effectiveness. In the United States, Canada, Sweden, England, Australia, and the Netherlands, decreases from 20% to 30% have occurred in breast cancer mortality since 1990, the point at which most population-based screening began, even though death rates had been largely stable in the decades prior. An estimated 50% of this mortality reduction is due to screening mammography. Dissemination of screening mammography at a population level has had an unprecedented impact on public health efforts in early cancer detection. Some of the first national guidelines for breast cancer screening were issued by the American Cancer Society in 1976, followed by other national organizations. In addition to changing practice for women and providers, these guidelines are the basis for quality measures, pay-for-performance, and other health care delivery policies. Despite how tightly breast screening appears to be woven into the fabric of current clinical practice, public health, and care delivery, controversy remains regarding the actual tradeoffs of benefits and harms involved.

**Benefits and Harms of Screening**

The main goal of cancer screening is early detection to reduce breast cancer mortality. Early detection represents “two sides of the same coin” in that some early detection may lead to timely treatment, the need for less or less toxic treatment, and lower mortality whereas some early detection may lead to more treatment than necessary and no reductions in mortality. Early detection without any survival benefit can be considered a harm (ie, overdiagnosis), particularly when unnecessary treatment ensues (ie, over-treatment). In patients with breast cancer, ductal carcinoma in situ (DCIS) likely contributes to the majority of the overdiagnosis associated with breast cancer screening, representing approximately 15% of incident cancer diagnoses. Although DCIS is considered a true precursor to invasive breast cancer, multiple lines of evidence have suggested that fewer than one-half of DCIS cases would progress to invasive breast cancer if left untreated. Although a DCIS diagnosis is associated with an increased risk of developing invasive breast cancer, < 5% of women diagnosed with DCIS will die of breast cancer within 30 years after their diagnosis. However, because the minority of DCIS cases that are likely to progress cannot be reliably identified, most women with DCIS are treated similarly with surgery, radiation therapy, and hormone therapy. Overtreatment may also occur among patients with localized invasive breast cancer, the rates of which have increased notably with the introduction of screening mammography despite modest declines in advanced-stage disease.

Aside from cancer diagnoses, screening mammography may also lead to false-positive examinations, which result in further imaging and/or biopsy. In fact, several studies have shown that given 10 years of annual screening, 50% of women will have a false-positive mammogram. Additional workup from false-positive screening mammograms may be associated with psychological and financial burdens. Conversely, some women may feel reassured by having regular screening, even if a false-positive result occurs, if detecting a true-positive finding is most valuable to them.
The fact that there are both benefits and harms of breast cancer screening is less of a debate than how to weigh them in screening decisions. Breast cancer screening decisions are personal for women, and are based not only on scientific evidence and their own breast cancer risk but also on preferences and access to care. However, because breast screening guidelines are aimed at populations, they are not typically tailored to specific individuals or significant subgroups, such as young women at a high risk of developing breast cancer or healthy older women who may have a relatively longer expected lifespan.

Technology and Screening

An important dimension of breast cancer screening is the dissemination of new imaging technologies. For example, in 2003, rapid diffusion of digital mammography began in the United States. This technology increased false-positive results and cost, with benefits noted only among overlapping subsets of premenopausal women, those with dense breasts, or those aged < 50 years. Other breast cancer screening technologies that have been adopted or advocated over the past decade include computer-aided detection, breast MRI, and breast tomosynthesis. Each of these modalities holds the promise to improve screening performance for some women, but research is required at the population level and within the context of clinical practice to determine the conditions under which these modalities maximize benefit and minimize harm.

US Breast Cancer Screening Guidelines

Population-based breast cancer screening in the 19 countries that comprise the International Breast Cancer Screening Network is guided by national guidelines established by each country. The evidence base for these guidelines is the same, yet variations in screening practices are notable both between and within countries. For example, most countries have biennial screening, except for Uruguay, which has annual screening, and the United Kingdom, which is triennial. The age at which to initiate screening also varies, with the majority of countries recommending age 50 years but with women in Sweden, Iceland, and Uruguay beginning at age 40 years. Within the United States, guidelines regarding the age at which to initiate screening and the screening interval vary. The US Preventive Services Task Force, the American College of Radiology, and the American Cancer Society are perhaps the dominant organizations from which breast screening guidelines are issued in the United States, but they do not share the same recommendations (Table 1). These guidelines are for women of average risk, and therefore are not tailored by individual profiles but rather are more of a “one-size-fits-all” approach. Although such an approach can be useful for standardization to deliver high-quality equitable care, the “one-size-fits-all” approach does not account for comparative effectiveness evidence based on risk, screening modalities, and preferences.

Have We Outgrown “one-Size-Fits-All” Screening?

Considering the variability in screening recommendations based on the totality of evidence, the notable controversy that continues for breast cancer screening, and the challenges for women in their decision-making process, the “one-size-fits-all” approach of population screening guidelines should be reconsidered. Increasingly, the rationale for personalized...
Breast cancer screening tailored to a woman’s risks and preferences, with the goal of maximizing benefit and minimizing harm, holds the most promise. This approach includes the appropriate use of imaging modalities based on performance data, such as the improved accuracy of digital mammography in women with dense breasts, and increased false-positive results with no increased rate of cancer detection in women of average risk of breast cancer undergoing screening mammography. With regard to defining the harms of screening, such as false-positive mammograms, this will vary at the individual level based on differing values and preferences. However, evidence must always constrain a woman’s decisions regarding screening to provide ethical and cost-effective care. For example, an average-risk woman may be anxious about breast cancer and prefer to be screened annually with breast MRI, but evidence does not support that option as a clinical strategy. Thus, evolving away from the “one-size-fits-all” approach to personalized regimens still holds fast to the evidence base and, in fact, seeks to expand evidence to better align individual risk with specific screening strategies.

**Incorporating New Care Delivery Models and Technologies**

Breast cancer screening occurs within the context of health care delivery systems, often spanning several clinical settings: primary care, radiology, and surgery. New models of health care delivery such as medical homes, accountable care organizations, and health insurance exchanges offer opportunities to improve the delivery of breast cancer screening, particularly as the meaningful use of electronic health records increasingly enhances delivery models. As new screening technologies are disseminated into practice, their use should be limited to those women for whom evidence suggests a benefit when weighed against harms. A risk-based screening paradigm would ensure the effective use of technology and health services, particularly when paired with delivery models that reward risk assessment and shared decision-making rather than simply adherence to a chosen guideline. We present a conceptual model to help organize and drive forward the pursuit of high-value evidence to be used in personalized screening and to facilitate a paradigm shift that will translate into improvements in breast cancer screening.

**Conceptual Model for Personalized Regimens**

Recognizing that breast cancer screening is a multilevel endeavor with distinct phases across the care continuum, we first present a high-level conceptual view (Fig. 1). Breast cancer screening is delivered through multiple nested units, namely patients, providers, facilities, health care systems, and regional/national bodies that create policies. Each of these units has specific objectives of screening, many of which are synergistic across levels. For example, the patient-level objectives of risk-based and preference-based care, together with early detection, are integral to the provider-level objective of optimizing patient management, which in turn feeds into the facility-level objective of population management and the health care system-level objectives of efficient high-quality care and achieving performance benchmarks. Although not exhaustive, key screening objectives across hierarchical levels include: 1) patient: risk-based and preference-based care, accessibility, early detection, decreased mortality, and quality of life; 2) provider: safe and effective quality care,
optimizing patient management, and achieving practice benchmarks; 3) facility: population
management, quality care, and fiscal incentives; 4) health care system: integrated, efficient,
and quality care and performance benchmarking; and 5) regional/national bodies for policy:
evidence-based guidelines, equitable care, quality care, and reductions in unnecessary
variation.

These objectives are sought within 4 distinct key domains of 1) screening awareness, 2)
detection, 3) diagnosis, and 4) treatment and survivorship (Fig. 1). These key domains are
linked by the common principles of risk assessment, effective modalities, and preference-
based care. The entire screening process spans from the time before screening through breast
cancer survivorship, and occurs within multilevel systems. Within each key domain along
this care continuum, individual tradeoffs for benefits and harms must be assessed in relation
to existing evidence, measurable processes and outcomes, and preferences. Building from
the overview in Figure 1, Figure 2 presents a conceptual model of care delivery across these
domains, which represents risk-based and preference-based care within multilevel systems
(Fig. 2). The focus of this model is to identify important factors in a personalized screening
approach, some of which should be standardized measures of process and outcomes to
monitor, improve, and generate new evidence regarding the breast screening process.

Screening awareness

Before any breast cancer screening can occur, there must be awareness of breast health and
screening. Women may learn if they are eligible, decide whether they want screening, and
determine what modalities and intervals are most appropriate for them. Discussions of
screening would include provider knowledge of risk-benefit evidence, patient perception and
preferences, and use of decision-making tools. Concurrently, risk should be assessed,
recorded, and used by the patient and provider to drive screening decisions. Validated breast
cancer risk models should be used, which are based primarily on age, family history, and
personal characteristics such as age at menarche and hormone replacement use.\textsuperscript{37} Refined
risk models should be incorporated as they are developed, particularly those that include
breast density, lifestyle factors, competing risks, and genetic information, for identifying
women who are appropriate for consideration of BRCA testing and who may require
different risk management strategies if they are found to have mutations. Furthermore,
emerging opportunities for risk-based interventions, such as chemo-prevention among some
high-risk women,\textsuperscript{38} would occur in this phase of the screening continuum. The domain of
screening awareness is critical to aligning the “right woman” with the “right test” at the
“right time.” For example, a woman aged 57 years who is considered to be at high risk may
appropriately be recommended for a screening breast MRI, but a woman aged 44 years
considered to be at average risk should not be.\textsuperscript{35} Because to the best of our knowledge there
are currently no accepted quality measures based on this phase of screening, we propose that
the process measures of discussing breast cancer screening tradeoffs and performing risk
assessment be measured in health care systems. In addition, screening rates within a patient
population should incorporate patient preferences and use a denominator based on the
number of women who do not decline screening rather than all women of qualifying age.
Detection

The detection domain includes screening imaging, diagnostic follow-up if applicable, and final assessment. Inherent in this domain are several key concepts such as the performance of imaging modalities (particularly new technologies), variations in interpretive performance, screening adherence, and timeliness of follow-up. Each of these concepts has a rich but incomplete evidence base, especially in terms of how these factors interact with risk to affect outcomes. Process measures for the detection domain should include screening rates based on a denominator of eligible women choosing to participate in screening, modality used in relation to risk, and timeliness of care. Outcome measures for detection are well-established and include sensitivity, specificity, biopsy rate, positive predictive value, cancer detection rate, and recall rate. These outcomes should be assessed for population subgroups such as women at high risk and those with dense breasts, and for new modalities. An important aspect of the detection domain is to provide feedback regarding process (such as referral completion) and outcome (such as a positive mammogram) measures to inform appropriate subsequent care and potentially refine subsequent risk assessments. Similarly, a percentage of screening examinations will lead to recommendations for biopsy, which then transition women into the diagnosis domain.

Diagnosis

The diagnostic phase may yield benign, in situ, or invasive disease, which then stratifies women into risk categories with regard to breast cancer mortality. A benign biopsy may reveal precursor breast lesions that increase risk and can be incorporated into future screening decisions. For example, both atypical ductal and lobular hyperplasia are associated with an increased cancer risk (2.5-fold for atypical ductal hyperplasia and > 5-fold for atypical lobular hyperplasia\textsuperscript{39}). Although the diagnosis of DCIS encompasses a wide range of risk in terms of progression to invasive disease, overall it carries a relatively high risk of progression to invasive cancer.\textsuperscript{40,41} Because of the marked variability in risk, it can be managed clinically in several ways ranging from active surveillance with treatment deferred to bilateral mastectomy.\textsuperscript{42} Patient preferences based on a thorough understanding of risks are critical to elicit and incorporate into management plans as patients move from the diagnostic to treatment phases. Similarly, invasive cancers are stratified into mortality risk based on tumor markers, stage of disease, histology, and other tumor characteristics. Within the diagnostic domain, key process measures include those related to the use of appropriate imaging modalities and biopsy, intensity of diagnostic workup, and timeliness. Important outcome measures in the diagnostic domain are biopsy yield, positive predictive value, stage of disease at diagnosis, extent of disease, and tumor characteristics. The risk profile of a woman’s disease ascertained in the diagnostic phase directly impacts the final key domain in the screening continuum: treatment and survivorship.

Treatment and survivorship

Although breast cancer treatment is somewhat distal to screening, it is an important part of the screening continuum, given the objective of early detection to lower treatment burden and improve survival. In this phase, risk is conceptualized mostly in terms of disease management for mortality reduction. However, patient preferences are still critical to
maximize quality of life when developing a treatment plan, as well as during and after treatment. For example, even though treatment recommendations vary by tumor characteristics, patient preferences also guide decisions, particularly given the clinical equipoise between lumpectomy and mastectomy in many cases.\textsuperscript{42} Timeliness, adherence to treatment, and care coordination are all important process measures of this domain. Key outcomes to measure include quality of life and long-term adverse sequelae of treatment such as cardiomyopathy, disease recurrence, and survival. Survivorship may extend for decades, and women typically reenter the screening awareness domain but with an updated risk profile of having a personal history of breast cancer. Thus the screening process begins anew with additional screening decisions to be made in terms of imaging modality, screening/surveillance interval, and duration of screening/surveillance over the life course. Evidence is notably lacking in this area and represents a gap to fill with experimental and/or rigorous observational studies.

**Summary of the Risk-Based and Preference-Based Conceptual Model**

This model offers a new perspective for screening, aligning processes with individual risk and preferences. A more personalized approach is conceptualized to result in breast cancer screening regimens that minimize harms and maximize benefits for women. The model provides a roadmap for process and outcome measures that may be most useful for monitoring and informing risk-based and preference-based screening. We propose that these measures be developed as validated standardized measures used across the multiple levels of care discussed. New care delivery models should incorporate these measures, which are more meaningful than, for example, the percentage of women aged 40 years to 75 years who are screened. Such a metric is crude and may penalize providers who engage in informed discussions with their patients if these women elect not to screen or to do so at an interval not considered “adherent”. Refined measures that reflect personalized regimens rather than “one-size-fits-all” screening should be the basis for patient population management and larger national policies such as payment tied to performance. The model is also useful to identify evidence gaps for effective and informed screening. Several advances are needed to achieve effective personalized regimens: better risk models, better risk assessment strategies, assessment of new technologies, identification of predictors of disease progression, harnessing of information technology, and standardized data systems to evaluate the screening process in an ongoing manner. For the latter, we also need validated metrics that are feasible to capture within the context of clinical care. A national opportunity to make these advances is currently underway, with the NCI’s PROSPR (Population-Based Research Optimizing Screening through Personalized Regimens) initiative.

**PROSPR**

PROSPR is a unique setting for the development and evaluation of personalized strategies to refine the screening process. This program, initiated by the NCI, will run for at least 5 years (2011–2016) and includes 3 PROSPR breast cancer screening research centers and a single statistical coordinating center. The PROSPR network is unique compared with other breast cancer screening consortiums, and is comprised of diverse types of delivery systems (Table 2).\textsuperscript{10} The PROSPR research centers are using this risk-based and preference-based screening
conceptual model to study personalized approaches to breast cancer screening. Examples of this work include improving care processes within primary care settings, developing standardized measures through electronic health records, evaluating digital breast tomosynthesis, and identifying novel prognostic markers that can guide personalized management strategies for women diagnosed with DCIS. In addition to the ongoing projects at each research center, the statistical coordinating center works with all research centers to develop transnetwork research projects that further examine differences in breast cancer screening practices across centers. The PROSPR network will assess variations at the patient, provider, facility, system, and possibly policy level, and how these impact screening rates and outcomes.

Implications of a Personalized Screening Paradigm

The time has come to shift the breast cancer screening paradigm to risk-based and preference-based screening rather than a “one-size-fits-all” approach for the population. Across all levels of health care delivery systems, personalized screening regimens offer advantages for processes of care and hold the promise of improved screening outcomes. The common objective for all levels (patients, providers, facilities, health care systems, and regional/national organizations) is decreased mortality from breast cancer. Within levels, however, other goals also are of great concern, such as reducing unnecessary burdens of screening, providing efficient and cost-effective care, maintaining quality of life, and refining our knowledge base. However, just as there are objectives to achieve at all levels so too are there factors at each level to understand in terms of their influence on screening processes and outcomes. In this model, we included key characteristics in each domain that are opportunities for personalized care, although we recognize that there are additional factors not presented at the patient, provider, facility, system, and policy level that may affect the care continuum.

Personalized screening regimens represent a paradigm shift in part because they move away from quality measures typically used by health care systems, such as Healthcare Effectiveness Data and Information Set (HEDIS), Medical Home criteria, and pay-for-performance. The broad policies based on these measures are rooted in the “one-size-fits-all (most)” model of current recommendations that relies predominantly on age to guide screening decisions. There is indeed a tension between personalized medicine and population-wide guidelines. When considering how screening has fallen short in the general population, broad-brush guidelines may be the simplest way to push forward population-wide screening uptake, adherence, and monitoring thereof. Those broad-brush guidelines, however, are not likely to maximize benefit and minimize harm because they target average-risk women, not subsets of women who have heterogeneous responses along the care continuum. The issue of DCIS and possible overdiagnosis exemplifies how personalization can help to minimize the harms associated with overdiagnosis and overtreatment. In addition, a personalized approach may help women to clarify their own screening decisions, such as the age at which to initiate and stop screening to realize the most benefit with the least harm. Systems of care need to shift to support providers in personalizing screening regimens rather than complying with a given metric (eg, using metrics such as the percentage of women with risk assessment, percentage of women with screening
discussions, or percentage of women who are current for screening among those women who did not decline screening).

**What Do We Still Need to Know in Breast Cancer Screening?**

We believe that the risk-based personalized breast cancer screening model presented will guide the next era of clinical practice and research. Despite 50 years of research in breast cancer screening and treatment, important gaps in the evidence base remain. As screening and related health care evolve toward new modes of delivery, these gaps must be addressed to achieve the fullest potential of population-based breast cancer screening. Key areas needing attention are found at the individual level and at the level of care delivery (Table 3). As noted by Zapka et al,[6] improving our approach to screening requires that we take into account the complexity of the multilevel environment in health care delivery. A multilevel framework is well-suited to interventional, comparative effectiveness, and translational research paradigms, current paradigms that are useful for further breast cancer screening research. For example, translational research activities may generate evidence at the molecular level to determine the likelihood of DCIS progression, which then may be translated into clinical practice via multilevel interventions and assessed for optimization through a comparative effectiveness research framework. Furthermore, the decades of knowledge and experience gained in breast cancer screening should be brought to bear on other guideline-based screening efforts, such as for colorectal, cervical, and lung cancer. Common themes among these cancers are found in the breast cancer screening evidence gaps. Examples include: 1) when to initiate and stop screening based on evidence of benefits and harms; 2) best practices for risk calculation, risk assessment, risk communication, and shared decision-making; 3) comparative effectiveness of screening modalities; 4) process quality measures; and 5) methodology to better measure overdiagnosis. Progress in these areas for breast cancer screening can facilitate progress for other current or future population-based cancer screening recommendations. A paradigm shift from a relatively crude age-based regimen toward more specific and effective risk-based and preference-based personalized screening regimens would be timely as new models of care delivery are being implemented in the United States.

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**CONFLICT OF INTEREST DISCLOSURES**

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REFERENCES


Figure 1.
A high-level conceptual view of breast cancer screening is presented.
Figure 2.
A conceptual model of care delivery across domains is presented that represents risk-based and preference-based care within multilevel systems. BI-RADS indicates Breast Imaging-Reporting and Data System; 2D, 2-dimensional; MRI, magnetic resonance imaging; chemo, chemotherapy; PPV, positive predictive value; EOD, extent of disease.
### TABLE 1

Breast Screening Guidelines Comparison

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Age at Initiation, Years</th>
<th>Screening Interval, Years</th>
<th>Age at Cessation, Years</th>
<th>Notes</th>
</tr>
</thead>
</table>
| US Preventive Services Task Force<sup>b</sup> | 50 | 2 | 75 | - The decision to initiate screening before age 50 y should be an individual one that takes patient context and values into account.  
- Insufficient evidence to assess benefits and harms among women aged ≥75 y.  
- Breast self-examinations are not recommended. |
| American Cancer Society | 40 | 1 | Conditional | - Screening continues as long as a woman is in good health.  
- Women should practice breast self-awareness.  
- Women should talk with their physician about family/medical history to determine whether other recommendations would be made based on risk, particularly for screening breast MRI based on lifetime breast cancer risk and other risk factors. |
| American College of Radiology<sup>c,d</sup> | 40 | 1 | Conditional | - Screening should stop when life expectancy is <5 to 7 y or when abnormal results would not be acted on due to age or comorbidities.  
- Ultrasound can be considered in high-risk women who cannot undergo MRI or women with dense breasts as an adjunct to mammography.  
- Breast MRI is recommended in women with a >20% lifetime risk of breast cancer, BRCA mutation carriers, untested first-degree relatives of proven BRCA mutation carriers, those with a history of chest irradiation, and women with newly diagnosed breast cancer (contralateral breast). Breast MRI may be considered in women with a 15% to 20% lifetime risk of breast cancer. |
| American College of Obstetrics and Gynecology | 40 | 1 | Not specified | - Women aged ≥40 y should have annual CBEs.  
- Women aged 20 to 30 y should undergo CBE every 1 to 3 y, although it is of unclear benefit.  
- All women should practice breast self-awareness.  
- Women should be informed of the predictive value of screening mammography and informed that their screening results may lead to recommendations for further testing.  
- Enhanced screening may be offered to women with a lifetime risk of breast cancer of ≥20%.  
- Average-risk women are not recommended to receive screening breast MRI.  
- Women testing positive for BRCA1 and BRCA2 are recommended for enhanced screening and risk reduction strategies. |
| Kaiser Permanente Care Management Institute<sup>f</sup> | 50 | 1–2 | 75 | - Women aged ≥75 y should use a shared decision-making approach to assess continued screening.  
- Women aged 40 to 49 y should use a shared decision-making approach to assess whether to screen. |

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Breast Cancer Screening Recommendations for Average-Risk Women

<table>
<thead>
<tr>
<th>Age at Initiation, Years</th>
<th>Screening Interval, Years</th>
<th>Age at Cessation, Years</th>
<th>Notes</th>
</tr>
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- Routine mammography is not recommended for women aged <40 y.
- Screening interval of 1 to 2 y is recommended.

Abbreviations: CBE, clinical breast examination; MRI, magnetic resonance imaging.

\( ^{a} \) National Guideline Clearinghouse (available at guideline.gov/syntheses/synthesis.aspx?id=39251).

\( ^{b} \) The US Preventive Services Task Force and Kaiser Permanente Care Management Institute recommendations are specifically for asymptomatic average-risk women.

\( ^{c} \) The American College of Radiology has published more detailed appropriateness criteria for breast cancer screening (available at acr.org/-/media/ACR/Documents/AppCriteria/Diagnostic/BreastCancerScreening.pdf).

\( ^{d} \) The Society of Breast Imaging issued breast screening recommendations in conjunction with the American College of Radiology.
### TABLE 2
Overview of Cohorts at the PROSPR Breast Cancer Research Centers

<table>
<thead>
<tr>
<th></th>
<th>University of Vermont</th>
<th>Geisel School of Medicine at Dartmouth and Brigham and Women’s Hospital</th>
<th>University of Pennsylvania</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ages included</td>
<td>18 to 89 y.</td>
<td>30 to 89 y.</td>
<td>18 to 89 y.</td>
</tr>
<tr>
<td>Cohort definition</td>
<td>Women who have undergone imaging at participating Vermont facilities.</td>
<td>Women who are seen in primary care within the Dartmouth-Hitchcock Regional Primary Care Collaborative or within the Brigham and Women’s Primary Care Practice-Based Research Network.</td>
<td>Women who have undergone breast cancer screening at Penn Medicine imaging sites.</td>
</tr>
<tr>
<td>Research foci</td>
<td>• Develop prognostic markers for personalized management of DCIS.</td>
<td>• Map screening processes within health systems.</td>
<td>• Evaluate digital breast tomosynthesis.</td>
</tr>
<tr>
<td></td>
<td>• Identify markers of progression from DCIS to invasive disease.</td>
<td>• Develop electronic health record tools to personalize and improve screening processes.</td>
<td>• Assess an imaging biomarker of breast tissue composition.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Compare the effectiveness of care processes.</td>
<td>• Evaluate risk communication strategies.</td>
</tr>
</tbody>
</table>

Abbreviations: DCIS, ductal carcinoma in situ; PROSPR, Population-Based Research Optimizing Screening through Personalized Regimens.
### TABLE 3
Evidence Gaps in Population-Based Personalized Breast Cancer Screening

- Benefits and harms of screening in women aged ≥75 y.
- Optimal approaches for risk assessment, risk communication, and shared decision-making.
- Performance of breast MRI for subgroups of women, over time, and by indication.
- Appropriate performance measures to optimize the screening process.
- Comparative assessment of tomosynthesis.
- Understanding risk of DCIS progression to invasive cancer.
- Methods for measuring overdiagnosis.
- Process measures validated for efficient, high-quality screening.
- Refined breast cancer risk models including factors such as breast density, genetic markers, and prior imaging results.

Abbreviations: DCIS, ductal carcinoma in situ; MRI, magnetic resonance imaging.