Breast cancer is the most common noncutaneous cancer and the second leading cause of cancer death among women in the United States. About 40,000 women die of breast cancer in the United States each year. For decades, there has been strong interest in screening strategies that will detect early cancers before they progress, thereby reducing mortality. Some trials have demonstrated that mammography is associated with decreased breast cancer mortality, but these data and increasing evidence about the harms of mammography screening have generated controversy. In 2009, in light of evidence that the benefit-risk ratio is higher during that 10-year period would not have become clinically apparent without screening (overdiagnosis), although there is uncertainty about this estimate. The net benefit of screening depends greatly on baseline breast cancer risk, which should be incorporated into screening decisions. Decision aids have the potential to help patients integrate information about risks and benefits with their own values and priorities, although they are not yet widely available for use in clinical practice.

To maximize the benefit of mammography screening, decisions should be individualized based on patients’ risk profiles and preferences. Risk models and decision aids are useful tools, but more research is needed to optimize these and to further quantify overdiagnosis. Research should also explore other breast cancer screening strategies.

**OBJECTIVES** We reviewed the evidence on the mortality benefit and chief harms of mammography screening and what is known about how to individualize mammography screening decisions, including communicating risks and benefits to patients.

**RESULTS** Mammography screening is associated with a 19% overall reduction of breast cancer mortality (approximately 15% for women in their 40s and 32% for women in their 60s). For a 40- or 50-year-old woman undergoing 10 years of annual mammograms, the cumulative risk of a false-positive result is about 61%. About 19% of the cancers diagnosed during that 10-year period would not have become clinically apparent without screening (overdiagnosis), although there is uncertainty about this estimate. The net benefit of screening depends greatly on baseline breast cancer risk, which should be incorporated into screening decisions. Decision aids have the potential to help patients integrate information about risks and benefits with their own values and priorities, although they are not yet widely available for use in clinical practice.

**CONCLUSIONS AND RELEVANCE** To maximize the benefit of mammography screening, decisions should be individualized based on patients’ risk profiles and preferences. Risk models and decision aids are useful tools, but more research is needed to optimize these and to further quantify overdiagnosis. Research should also explore other breast cancer screening strategies.

**IMPORTANCE** Breast cancer is the second leading cause of cancer deaths among US women. Mammography screening may be associated with reduced breast cancer mortality but can also cause harm. Guidelines recommend individualizing screening decisions, particularly for younger women.

**EVIDENCE ACQUISITION** We searched MEDLINE from 1960-2014 to describe (1) benefits of mammography, (2) harms of mammography, and (3) individualizing screening decisions and promoting informed decision making. We also manually searched reference lists of key articles retrieved, selected reviews, meta-analyses, and practice recommendations. We rated the level of evidence using the American Heart Association guidelines.

**CONCLUSIONS AND RELEVANCE** To maximize the benefit of mammography screening, decisions should be individualized based on patients’ risk profiles and preferences. Risk models and decision aids are useful tools, but more research is needed to optimize these and to further quantify overdiagnosis. Research should also explore other breast cancer screening strategies.

Table 1. Pooled Results from Randomized Clinical Trials on Mortality Reductions With Mammography Screening by Age Group

<table>
<thead>
<tr>
<th>Age, y</th>
<th>No. of Studies</th>
<th>Total Events in Group/Total No.</th>
<th>RR (95% CI) With Mammography Screening</th>
<th>ARR With Mammography Screening</th>
<th>NNI to Screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>39-49</td>
<td>5,10-14</td>
<td>448/152,300</td>
<td>0.85 (0.75-0.96)</td>
<td>0.0005</td>
<td>1904</td>
</tr>
<tr>
<td>50-59</td>
<td>6,11,13-15</td>
<td>361/78,465</td>
<td>0.86 (0.75-0.99)</td>
<td>0.0007</td>
<td>1339</td>
</tr>
<tr>
<td>60-69</td>
<td>2</td>
<td>110/19,093</td>
<td>0.68 (0.54-0.87)</td>
<td>0.0027</td>
<td>377</td>
</tr>
<tr>
<td>70-74</td>
<td>1</td>
<td>42/5073</td>
<td>1.12 (0.73-1.72)</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: ARR, adjusted risk ratio; NA, not available; NNI, number needed to invite; RR, risk ratio.

Methods

We searched MEDLINE for relevant randomized clinical trials (RCTs), meta-analyses, systematic reviews, and observational studies from 1960 to January 19, 2014 (search terms are reported in the eBox in Supplement). We also manually searched the references of key articles, reviews, meta-analyses, and practice recommendations. For describing the breast cancer mortality benefit of mammography we included meta-analyses of RCTs of mammography screening examining breast cancer mortality. From 525 articles identified, 20 meta-analyses met these criteria. We focused on the 5 meta-analyses published after 2006, when the most recent RCT, the Age Trial, was published (eFigure 1 in Supplement).

To describe mammography’s harms we focused on false-positive results, unnecessary biopsies, and overdiagnosis, conducting 2 separate searches. The first included systematic reviews and meta-analyses through December 2008, the period for the review informing the 2009 USPSTF decision. The second included primary studies and reviews published since December 2008. We identified 374 articles, including 14 systematic reviews or meta-analyses published before 2008 and 72 studies or reviews published after 2008 (eFigures 2 and 3 in Supplement).

For studies on (1) individualizing information about risks and benefits and (2) communicating the benefits and risks to patients considering mammography screening, we searched for interventions (including decision aids) providing probabilistic information to women on the benefits and risks of screening, their own individual breast cancer risk, or both. We did not include interventions designed to increase screening rates without considering screening risks or a woman’s baseline breast cancer risk. From 907 citations, we identified 23 studies (eFigure 4 in Supplement). From MEDLINE searches and reviews of citations, we additionally identified 25 articles on breast cancer risk models and using risk profiles to guide mammography decisions.

In Table 1, we provide summary risk ratios and number needed to invite (NNI) to screening from Nelson et al’s meta-analysis conducted for the USPSTF. We also report absolute risk ratios calculated by inverting the NNI. In Table 2, we report estimated benefits and harms of breast cancer screening for 10 000 women undergoing annual mammography during a 10-year period. To estimate the number of women diagnosed with invasive breast cancer or ductal carcinoma in situ (DCIS) (column 1), we used Surveillance, Epidemiology, and End Results (SEER) estimates from a recent review by Welch and Passow. The numbers of breast cancer deaths over 15 years (column 2) use Welch and Passow’s estimates of the 15-year risks of dying of breast cancer in a screened population. The lower number reflects a minimal breast cancer mortality reduction of 5% based on RCTs reporting no benefit, and the upper number reflects a reduction of 36% based on the trial reporting the highest benefit. Column 3 provides Welch and Passow’s upper and lower estimates of the number of deaths averted through screening, based on the same range of RCT results. To estimate the number of invasive breast cancers or DCIS diagnosed that would never become clinically important (overdiagnosis, column 4), we report absolute numbers calculated by Welch and Passow based on the Malmö trial and an epidemiologic study. To estimate the number of women with at least 1 false-positive mammogram or unnecessary biopsy (columns 5 and 6), we report the cumulative incidence (with 95% CIs) from 2 studies using Breast Cancer Surveillance Consortium data multiplied by 10 000.

Results

Benefits of Screening Mammography

Between the 1960s and the 1990s, 8 large RCTs assessed breast cancer mortality associated with screening. Meta-analyses of these trials generally demonstrate a 15% to 20% decrease in the relative risk of breast cancer–specific mortality. The variation in estimates is largely attributable to differences in trial quality and inclusion criteria. The Edinburgh trial has been most consistently excluded because of concerns about its cluster randomization strategy. However in other trials, concerns have been raised about randomization, contamination, and assignment of breast cancer mortality.

In addition, some argue that the RCTs are unlikely to be applicable to women undergoing screening today, because they preceded treatment advances that have powerfully influenced breast
cancer and used older mammography techniques.\textsuperscript{17} However, the RCTs nevertheless provide the best data available.

Two recent meta-analyses examined breast cancer mortality across all age groups.\textsuperscript{25,26} The summary risk ratio (RR) for breast cancer mortality reduction with mammography screening at median 11.4 years follow-up was 0.81 (95% CI, 0.74-0.88) in the meta-analysis for the Canadian Task Force that included all RCTs except the Edinburgh trial.\textsuperscript{26} The Cochrane reviewers reported a summary RR of 0.90 (95% CI, 0.79-1.02) when including only the 3 trials they considered of adequate quality.\textsuperscript{25} When the Cochrane reviewers included all the trials except Edinburgh, with 13 years of follow-up, their results were consistent with the Canadian review (RR, 0.81 [0.74-0.87]).\textsuperscript{25} In February 2014, 25-year follow-up results from 2 Canadian trials were published,\textsuperscript{27} showing no mortality benefit from mammography screening (hazard ratio, 1.05 [95% CI, 0.88-1.22]). These results are consistent with earlier reports from these trials (at 13 years’ follow-up, the mortality rate ratio for women aged 50-59 years was 1.02 [95% CI, 0.78-1.33])\textsuperscript{25} and at 11-16 years’ follow-up among women aged 40-49 years, it was 0.97 (95% CI, 0.74-1.27)\textsuperscript{25} and would be unlikely to substantially change meta-analysis results.

Three meta-analyses assessed mortality reduction within multiple age groups,\textsuperscript{9,25,26} and 2 focused on women aged 40 to 49 years only.\textsuperscript{28,29} For women aged 40 to 49 years, these 5 meta-analyses provided summary RRs ranging from 0.81 to 0.85. Variation in the estimated RRs again resulted from differing decisions about trial quality and inclusion. In 3 analyses excluding the Edinburgh trial alone, summary RRs for women aged 40 to 49 years were 0.84 (95% CI, 0.75-0.96)\textsuperscript{26} and 0.84 (95% CI, 0.73-0.96).\textsuperscript{27} Table 1 shows estimates from the meta-analysis conducted for the USPSTF.\textsuperscript{9}

Despite similar relative benefits across age groups, because baseline breast cancer risk varies, the absolute benefit and NNI to screening to prevent 1 breast cancer death vary by age (Table 1). Based on the meta-analysis by Nelson et al,\textsuperscript{9} about 1904 women aged 39 to 49 would need to be invited to prevent 1 breast cancer death, vs 377 women aged 60 to 69. To address the “psychological magnification” of relative risks and most patients’ limited numeracy, experts recommend using natural frequencies (eg, the number of cancers diagnosed among a certain number screened) to aid comprehension of such findings.\textsuperscript{30,31} Table 2 provides published estimates from Welch and Passow of mammography’s benefits using natural frequencies. Welch and Passow provide a range for number of breast cancer deaths in a screened population using results from RCTs with markedly contrasting results—the Canadian trials, which showed no significant breast cancer mortality benefit (Welch and Passow use a more conservative estimate of 5%)\textsuperscript{30,31} and the Swedish 2-County Trial, which showed about a 36% risk reduction among those attending screening.\textsuperscript{11} Welch and Passow calculated these numbers based on SEER 15-year breast cancer mortality rates (assuming that the benefit of mammography would extend beyond the screening period) and adjusted for self-reported mammography rates in the United States,\textsuperscript{19} providing a range to reflect the uncertainty about the benefit. Based on these estimates, among 10 000 women aged 50 years undergoing annual screening for 10 years, approximately 302 would be diagnosed with invasive breast cancer or DCIS, between 56 and 64 women would die of breast cancer despite screening, and between 3 and 32 breast cancer deaths would be averted through screening depending on the true effect of mammography. Some might argue that the ranges overemphasize extreme RCT results (concerns have been raised about suboptimal randomization in the Swedish trial\textsuperscript{25}) and may be difficult to communicate to patients, and that meta-analyses can at least provide a “best estimate.” If Welch and Passow’s methodology is used but Nelson et al’s meta-analysis results are applied to the adjusted SEER breast cancer death rates, among 10 000 women aged 40 years undergoing annual mammography for 10 years, 31 deaths would occur despite screening and 5 deaths would be averted; among 50-year-olds, 62 deaths would occur despite screening and 5 deaths would be averted; among 60-year-olds, 62 deaths would occur despite screening and 5 deaths would be averted; and among 70-year-olds, 62 deaths would occur despite screening and 5 deaths would be averted.

Table 2. Estimated Benefits and Harms of Mammography Screening for 10000 Women Who Undergo Annual Screening Mammography Over a 10-Year Period

<table>
<thead>
<tr>
<th>Age, y</th>
<th>No. of Diagnosed With Invasive Breast Cancer or DCIS During the 10 y of Screening\textsuperscript{9}</th>
<th>No. of Breast Cancer Deaths in next 15 y</th>
<th>No. of Deaths Averted With Mammography Screening Over Next 15 y</th>
<th>No. of Breast Cancers or DCIS Diagnosed During the 10 y That Would Never Become Clinically Important (Overdiagnosis)\textsuperscript{9}</th>
<th>No. of Deaths With ≥1 False-Positive Result During the 10 y</th>
<th>No. Of Breast Cancers or DCIS With ≥1 Unnecessary Biopsy During the 10 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>190</td>
<td>27-32</td>
<td>1-16</td>
<td>7-104\textsuperscript{4}</td>
<td>6130 (5940-6310)</td>
<td>700 (610-780)</td>
</tr>
<tr>
<td>50</td>
<td>302</td>
<td>56-64</td>
<td>3-12</td>
<td>30-137</td>
<td>6130 (5800-6470)</td>
<td>940 (740-1150)</td>
</tr>
<tr>
<td>60</td>
<td>438</td>
<td>87-97</td>
<td>5-49</td>
<td>64-194</td>
<td>4970 (4780-5150)</td>
<td>980 (840-1130)</td>
</tr>
</tbody>
</table>

Abbreviation: DCIS, ductal carcinoma in situ.

\textsuperscript{9} Number of cancers expected to be diagnosed in the next 10 years from Surveillance, Epidemiology, and End Results (SEER) statistics\textsuperscript{36} and also reported by Welch and Passow.\textsuperscript{17} These numbers are from SEER incidence rates and reflect a combination of screened and unscreened women, so they would be higher in a completely screened population such as these 10 000 women by a number that depends on the magnitude of overdiagnosis.

\textsuperscript{10} Number of women expected to die of breast cancer in the next 15 years among a screened cohort are from Welch and Passow,\textsuperscript{17} who used SEER statistics\textsuperscript{36} adjusted for mammography rates reported in the 2008 National Health Interview Survey.\textsuperscript{16} The lower bound numbers represent death rates under the assumption of a breast cancer mortality risk reduction of 0.64 from mammography screening based on the benefit noted in the Swedish 2-County Trial,\textsuperscript{26} the upper bound represents death rates under the assumption of a breast cancer mortality risk reduction of 0.95 based on the minimal benefit noted in the Canadian Trials.\textsuperscript{30,31}

\textsuperscript{4} Number of deaths averted are from Welch and Passow;\textsuperscript{17} the lower bound represents breast cancer mortality reduction if the breast cancer mortality RR were 0.95 (based on minimal benefit from the Canadian trials\textsuperscript{30,31}), and the upper bound represents the breast cancer mortality reduction if the RR were 0.64 (based on the Swedish 2-County Trial)\textsuperscript{26}.

\textsuperscript{11} Overdiagnosed cases are calculated by Welch and Passow;\textsuperscript{17} the lower bound represents overdiagnosis based on results from the Malmö trial,\textsuperscript{20} whereas the upper bound represents the estimate from Bleyer and Welch.\textsuperscript{21}

\textsuperscript{12} False-positive and biopsy estimates and 95% CIs are 10-year cumulative risks reported in Hubbard et al\textsuperscript{22} and Braithwaite et al.\textsuperscript{23} For 60-year-old women we used estimates of false-positive results or biopsies in women aged 66 to 74 years with a Charlson score of 0.

\textsuperscript{13} The lower bound estimate for overdiagnosis reported by Welch and Passow\textsuperscript{17} came from the Malmö study,\textsuperscript{20} which did not enroll women younger than 50 years.
Harms of Screening Mammography
False-Positive Results
False-positive results raise suspicion for breast cancer and lead to further testing, such as additional imaging or biopsy, but do not result in a cancer diagnosis. Recent evidence from the Breast Cancer Surveillance Consortium suggests that the 10-year cumulative risk of at least 1 false-positive result is 61.3% for women starting screening at ages 40 or 50 years and 49.7% for women aged 66 to 74 years undergoing annual screening. Table 2 shows that among 10,000 women aged 50 years undergoing annual mammography for 10 years, approximately 6,130 (95% CI, 5,800-6,470) will have at least 1 false-positive result.

The risk of false-positive results increases when screening starts at younger ages or occurs annually, leading to more mammograms. This was a key consideration influencing the USPSTF recommendation to pursue biennial screening starting at age 50. The significance of a false-positive result for an individual woman, however, is debated, and likely varies substantially by patient. A review of 23 observational studies concluded that false-positive mammography results increase anxiety and distress related to mammography and breast cancer but do not increase clinically diagnosed anxiety and depression.

Overdiagnosis
Overdiagnosis is the detection of a tumor through screening that would not have become clinically evident in the absence of screening. Overdiagnosis can occur either because of a tumor’s indolent pathological features or because of competing mortality risks attributable to older age or comorbidities. Previously overdiagnosis was considered primarily explained by DCIS, but it is now thought that some invasive cancer diagnoses also represent overdiagnosis; both types of cases are generally included in analyses, since both are considered primarily explained by DCIS, but it is now thought that some invasive cancer diagnoses also represent overdiagnosis. Long-term follow up of all cancers diagnosed during the screening period (and 11% during the entire observation period) were overdiagnosed. This proportion represents the excess incidence of cancers detected in the screened group over long-term follow-up, as a fraction of all cancers diagnosed in the screened group during the screening period (or the entire observation period).

The RCT findings have limitations, including possible underestimation of overdiagnosis because some screening occurred in the control groups (in the Canadian National Breast Screening Study, 26.3% of the control group had at least 1 mammogram outside the study). Overestimation is also possible since women were not followed up until all had died, although in the recent update of the Canadian trials, excess cases still represented 22% of screening-detected cancers. The applicability of the RCTs to women undergoing mammography screening today in the United States is also uncertain. Because the Malmö trial screened women only every 18 to 24 months and used older, less sensitive mammography techniques, Welch and Passow used the Malmö estimate as a “lower bound” estimate of overdiagnosis risk. Published estimates of overdiagnosis from observational studies vary from less than 5% to more than 50% because of differing populations, assumptions, and measurement methods. To identify incidence rates in the absence of screening, observational studies often use historical incidence rates or incidence in an unscreened geographical region. A recent study based on SEER incidence and survival trends using historical incidence rates as a comparison reported that 31% of all breast cancers diagnosed in the United States represented overdiagnosis. Welch and Passow used these data as their “upper bound” estimate of overdiagnosis risk.

In Table 2, we include Welch and Passow’s lower and upper bound estimates to convey the uncertainty and methodological limitations around measuring overdiagnosis, the estimate from the meta-analysis of 3 RCTs (19%) lies between these extremes. It is thus likely that among 10,000 women aged 50 years undergoing annual mammography for 10 years, of 302 cases of cancer or DCIS, between 30 and 137 would reflect overdiagnosis, with a best guess being 57 based on the meta-analysis estimate of 19%.

Individualizing Mammography Screening Decisions
For a woman in the United States, the average lifetime risk of breast cancer is about 12.3%; the 10-year risks of invasive breast cancer at ages 40, 50, and 60 years are 1.5%, 2.3%, and 3.5% respectively. Numerous risk factors have been identified for breast cancer, although up to 60% of breast cancers occur in the absence of known risk factors. Each individual risk factor confers only a modest relative risk increase, and most are common in the general population; therefore, combinations of risk factors are most frequently used in efforts to estimate breast cancer risk. Several risk models attempt to use these risk factors to predict both breast cancer incidence in populations and individuals’ absolute risk. The Gail model, developed in a population of women undergoing annual screening and including age at menarche, age at first birth, number of first-degree relatives with breast cancer, number of previous breast biopsies, and presence of atypical hyperplasia as risk factors, was one
of the first. Several limitations of the Gail model have been described, including its omission of breast density and its limited applicability in certain racial/ethnic groups and high-risk populations. Revisions of the model include more diverse populations and breast density, which is associated with a 1.5- to 2-fold increased risk of breast cancer among women aged 40 to 50 years but raises the challenging question of whether a baseline mammogram should be obtained in all women. Although these models help refine understanding of a woman’s absolute risk for breast cancer and can help communicate risk to women, they are more accurate in predicting incidence in population subgroups and far less useful in identifying which individual women will or will not get cancer. Despite its limitations, the Gail model has been validated in 4 large populations and, as the basis for the National Cancer Institute’s online Breast Cancer Risk Assessment Tool (http://www.cancer.gov/bcrisktool), is commonly used in clinical practice.

Several decision analysis models have attempted to estimate how individual risk profiles influence the benefits and harms of screening. Older age and other factors that increase breast cancer risk also increase the absolute breast cancer mortality benefit with mammography. The risk of false-positive results also generally increases with certain individual characteristics such as breast density. Older age and other comorbidity increase the risk of overdiagnosis because of decreasing life expectancy, as do characteristics of the cancer itself (aggressive tumors are less likely overdiagnosed than indolent tumors because of shorter lead time). A comparative study of 4 microsimulation models found that for women aged 40 to 49 years with a Gail-model breast cancer risk twice average, biennial mammography screening yielded the same ratio of benefits and harms as annual screening for women 50 years or older at average risk. Similarly, a cost-utility model found that biennial screening among women aged 40 to 49 years with high breast density and either a first-degree relative with breast cancer or a history of a breast biopsy had similar ratios of benefits to harms as biennial screening of women in their 50s without those risk factors. Of note, however, none of these models considered overdiagnosis in their main analysis.

If a healthy 40-year-old woman had twice the average risk of breast cancer because of dense breasts, she would be expected to have twice the absolute benefit of annual screening (eg, 10 lives saved per 10,000 instead of 5) (Table 2). She would, however, also have a higher risk of false-positive findings.

**Supporting Informed Decision-Making**

Decisions about mammography should involve discussion of risks, benefits, uncertainties, alternatives, and patient preferences. Although numerous interventions have aimed to increase mammography uptake, including interventions tailored to individuals’ psychological readiness to adopt screening or to individuals’ own risk profiles, fewer studies examine measures of an informed decision as an outcome. A Cochrane review of RCTs examined the effects of personalized risk communication on informed decision making about screening for a range of diseases. Studies focused on mammography screening; those assessing outcomes related to informed decisions generally showed an increase in knowledge, quality of life, and accuracy of risk perception with personalized risk communication. Notably, meta-analysis of 4 studies of interventions providing women with numerical information about their risk showed that among women 40 years or older, there was no association between provision of numerical information and uptake of mammography (odds ratio, 0.84 [95% CI, 0.68-1.03]). Informed decisions require reconciling information about the risks and benefits of screening with a patient’s values. Decision aids using pamphlets, videos, or Internet tools can provide information, elicit preferences, and help patients make decisions. A Cochrane review defined decision aids as “interventions designed to help people make specific and deliberate choices…by providing (at the minimum) information on the options and outcomes relevant to a person’s health status,” and helping patients “to clarify…the value they place on the benefits, harms, and scientific uncertainties.” Overall, decision aids increased knowledge, decreased decisional conflict and anxiety, and had variable effect on uptake of the test or treatment in question. The review’s only mammography study recruited 70-year-old Australian women nearing the upper age cutoff for screening. Exposure to the decision aid led to less indecision about continuing mammography, although there was no difference in screening participation the next month. A more recent study among US women 75 years or older administered a paper decision aid just before a primary care encounter. Women who received the decision aid reported knowing more about benefits and risks and screening, decreased intentions to be screened, and were less likely to undergo mammography in the following 2 years. One RCT since the Cochrane review examined an online decision aid among women aged 38 to 45 years. The decision aid summarized the risks and benefits of mammography and provided a val-

**Table 3. Existing Guidelines for Mammography Screening**

<table>
<thead>
<tr>
<th>Organization and Year of Guidelines</th>
<th>Recommendations Regarding Mammography Screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norwegian Breast Cancer Screening Program, 1996</td>
<td>Screening mammography every 2 y for women between ages 50 y and 69 y</td>
</tr>
<tr>
<td>US Preventive Services Task Force, 2009</td>
<td>Biennial screening mammography for women between ages 50 y and 74 y The decision to start regular, biennial screening mammography before age 50 y should be an individual one and take into account patient context, including the patient’s values regarding specific benefits and harms</td>
</tr>
<tr>
<td>National Health Service Breast Cancer Screening Program (United Kingdom), 2010</td>
<td>Screening mammography every 3 y for women aged 47-73 y</td>
</tr>
<tr>
<td>Canadian Task Force on Preventive Health Care, 2011</td>
<td>Routine screening mammography for women aged 50-74 y</td>
</tr>
<tr>
<td>National Cancer Institute (United States), 2012</td>
<td>Screening mammograms every 1 to 2 y in women ≥40 y</td>
</tr>
<tr>
<td>American Cancer Society (United States), 2013</td>
<td>Yearly mammograms starting at age 40 y</td>
</tr>
</tbody>
</table>

* Prior guidelines had recommended mammography every 3 years for women 50 years and older; in 2010, the age range was extended to include women aged 47 to 73 years.
who would normally consider starting screening at age 50 years, clinicians and patients incorporate such risk factors; for example, guidelines ideally should reflect the net benefit of screening, and inconsistencies among guidelines mean that they have limited utility for guiding patient counseling and decisions. Because risk factors other than age influence the net benefit of screening, guidelines ideally should incorporate such risk factors; for example, clinicians and patients who would normally consider starting screening at age 50 years for an average-risk woman should consider starting at age 40 for a woman with risk factors placing her at twice average risk.96-

Discussion
Evidence suggests that mammography screening is associated with reduced breast cancer mortality, but the benefit is modest. Although better data are needed to estimate the magnitude of overdiagnosis, the risks of mammography screening are significant, decreasing the net benefit of screening. The net benefit is less for younger women, who have a lower absolute risk of breast cancer and greater risk of false-positive findings, and with annual screening, which increases false-positive findings and would also be expected to increase overdiagnosis.73

Table 3 includes current guidelines from the United States, Canada, and Europe. Despite offering clinicians and patients a general framework for evidence-based decisions, because of their limited incorporation of individual risk profiles other than age, variation across guidelines, and inherent population-based approaches, they have limited utility for guiding patient counseling and decisions. Because risk factors other than age influence the net benefit of screening, guidelines ideally should incorporate such risk factors; for example, clinicians and patients who would normally consider starting screening at age 50 years for an average-risk woman should consider starting at age 40 for a woman with risk factors placing her at twice average risk.96-

Harms of Mammography
About half or more of women who have a mammogram yearly for 10 years will have a false-positive mammogram, and up to 20% of these women will need a biopsy. If you decide to have a mammogram, you can anticipate that you will have at least 1 false-positive finding for which you are called back for additional images and perhaps a biopsy. Most of these findings are false alarms.

For some women undergoing regular screening, the mammogram may find an invasive cancer or noninvasive condition (ductal carcinoma in situ) that would never have caused problems (“overdiagnosis”). We cannot tell which these are, so they will be treated just like all other cancers. Experts are uncertain of how frequently this happens, but estimates suggest that if a woman undergoing a screening mammogram is diagnosed with cancer or ductal carcinoma in situ, there is about a 15% chance that the cancer is being overdiagnosed, and she will receive unnecessary treatment.

Making a Decision About Mammography
Experts recommend that women aged 50 to 74 years undergo a screening mammogram every 2 years. Whether you are likely to benefit from starting mammograms earlier or having them more frequently depends on your risks for breast cancer and your values and preferences. Each woman may feel differently about the possibility of having a false-positive result or being diagnosed with and treated for cancer that might not have caused problems. It is important for you to consider what these experiences might mean for you. It is also important to consider how you might feel if you decide not to undergo screening mammography and you are later diagnosed with breast cancer, even if the likelihood that mammography would have made a difference is small.

Discussion
Evidence suggests that mammography screening is associated with reduced breast cancer mortality, but the benefit is modest. Although better data are needed to estimate the magnitude of overdiagnosis, the risks of mammography screening are significant, decreasing the net benefit of screening. The net benefit is less for younger women, who have a lower absolute risk of breast cancer and greater risk of false-positive findings, and with annual screening, which increases false-positive findings and would also be expected to increase overdiagnosis.73

Table 3 includes current guidelines from the United States, Canada, and Europe. Despite offering clinicians and patients a general framework for evidence-based decisions, because of their limited incorporation of individual risk profiles other than age, variation across guidelines, and inherent population-based approaches, they have limited utility for guiding patient counseling and decisions. Because risk factors other than age influence the net benefit of screening, guidelines ideally should incorporate such risk factors; for example, clinicians and patients who would normally consider starting screening at age 50 years for an average-risk woman should consider starting at age 40 for a woman with risk factors placing her at twice average risk.96-

However, a better understanding of overdiagnosis is needed to inform how individual characteristics influence the harms of mammography, and breast cancer risk models with better discriminatory accuracy are needed to more accurately individualize information about the benefits and harms of screening. In the meantime, the online Breast Cancer Risk Assessment Tool from the National Cancer Institute can assist physicians and patients in estimating risk.

The significance of the harms of mammography also depends on individuals’ values and preferences, and eliciting these requires provision of accurate and balanced information and values clarification. In light of the harms and modest benefit of screening, as well as the substantial uncertainty surrounding their relative weight for individual patients, clinicians’ efforts must focus on promoting informed screening decisions. The Box offers some suggestions for such discussions.

Given time constraints in primary care, decision aids may complement the points in the Box, laying the groundwork for discussions between clinicians and patients. Decision aids can facilitate informed decision-making and improve quality of care when there is no clear superior treatment or screening option. Limited evidence suggests that decision aids can improve and standardize informed decision-making in breast cancer screening.78,83 But more research is needed to optimize their use and guide integr-
tion into practice. One challenge is how best to communicate the evidence.\textsuperscript{30} Although natural frequencies are preferred, they are derived from absolute risks and require estimating individuals’ baseline risk.\textsuperscript{76} Research is needed on communicating scientific uncertainty, including regarding overdiagnosis. A recent qualitative study found that the influence of learning about overdiagnosis on screening intentions depended greatly on the magnitude of overdiagnosis presented.\textsuperscript{83} Expert consensus on overdiagnosis, combined with improved understanding of how to describe this complex issue, may strengthen mammography decision aids. Research will also be needed to explore the long-term effects of decision aids for screening decisions, especially since women with more information may actually be less likely to engage in screening.\textsuperscript{76,77} Provisions in the Affordable Care Act establishing shared medical decision making as a marker of quality of care could help speed development, dissemination, and evaluation of decision aids.\textsuperscript{84}

This review has provided a broad overview of key considerations in mammography screening decisions and the related areas of uncertainty. It has several limitations. We have relied on evidence of screening benefits from RCTs conducted decades ago in Europe and Canada, which may not generalize to US women today.\textsuperscript{17,85} Furthermore, reports about overdiagnosis are methodologically heterogeneous and controversial. The review does not address several other important facets of breast cancer screening, including the use of magnetic resonance imaging and newer mammography technologies. It also does not address the complex issue of DCIS.

Conclusions

Although some of the challenges of mammography can be resolved with further research to guide individualized decisions and thoughtful development and dissemination of decision aids, better breast cancer screening tests are needed. More sophisticated tools, for example, could distinguish aggressive vs indolent tumors, reducing the burden of overtreatment.\textsuperscript{86} Mammography screening appears to be associated with reduced breast cancer mortality, but for some patients, the harms may outweigh the benefits. Until better screening methods are available, improved understanding of these harms, enhanced strategies to identify the highest-risk patients, and tools to help patients and clinicians incorporate these in their decisions should be research priorities.

ARTICLE INFORMATION

Author Contributions: Dr Pace and Keating had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Pace, Keating.

Acquisition, analysis, or interpretation of data: Pace, Keating.

Drafting of the manuscript: Pace, Keating.

Critical revision of the manuscript for important intellectual content: Pace, Keating.

Administrative, technical, or material support: Pace.

Study supervision: Keating.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Keating reported receiving research funding from the National Cancer Institute, the American Cancer Society, and the Komen for the Cure Foundation. Dr Pace reported no disclosures.

Funding/Support: Dr Pace’s work on this review was funded by the Global Women’s Health Fellowship at Brigham and Women’s Hospital.

Role of the Sponsor: The funder played no role in the design and conduct of the study; the collection, management, analysis, and interpretation of the data; the preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

Correction: This article was corrected online April 23, 2014, for an incorrectly reported date.

Submissions: We encourage authors to submit papers for consideration as a Review. Please contact Mary McGrae McDermott, MD, at mdm608@northwestern.edu.

REFERENCES


47. Gatzsche PC. Ramifications of screening for breast cancer: overdiagnosis in the Malmö trial was considerably underestimated. BMJ. 2006;332(7435):727.


84. The Patient Protection and Affordable Care Act 2010.
