Screening Mammography for Women 40 to 49 Years of Age: 
A Clinical Practice Guideline from the American College of Physicians

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Breast cancer is one of the most common causes of death for women in their 40s in the United States. Individualized risk assessment plays an important role when making decisions about screening mammography, especially for women 49 years of age or younger. The purpose of this guideline is to present the available evidence for screening mammography in women 40 to 49 years of age and to increase clinicians’ understanding of the benefits and risks of screening mammography.

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**RECOMMENDATIONS**

**Recommendation 1:** In women 40 to 49 years of age, clinicians should periodically perform individualized assessment of risk for breast cancer to help guide decisions about screening mammography.

A careful assessment of a woman’s risk for breast cancer is important. The 5-year breast cancer risk can vary from 0.4% for a woman age 40 years with no risk factors to 6.0% for a woman age 49 years with several risk factors (1). Factors that increase the risk for breast cancer include older age, family history of breast cancer, older age at the time of first birth, younger age at menarche, and history of breast biopsy. Women 40 to 49 years of age who have any of the following risk factors have a higher risk for breast cancer than the average 50-year-old woman: 2 first-degree relatives with breast cancer; 2 previous breast biopsies; 1 first-degree relative with breast and 1 previous breast biopsy; previous diagnosis of breast cancer, ductal carcinoma in situ (DCIS), or atypical hyperplasia; previous chest irradiation (1); or BRCA1 or BRCA2 mutation (2, 3).

A family history can also help identify women who may have BRCA1 mutations that place them at substantially higher risk for breast and other types of cancer (Table). These women should be referred for counseling and recommendations specific to this population, as recommended by the U.S. Preventive Services Task Force (USPSTF) (4). Risk assessments should be updated periodically, particularly in women whose family history changes (for example, a relative receives a diagnosis of breast or ovarian cancer) and in women who choose not to have regular screening mammography. Although no evidence supports specific intervals, we encourage clinicians to update the woman’s risk assessment every 1 to 2 years.

The risk for invasive breast cancer can be estimated quantitatively by using the Web site calculator provided by the National Institutes of Health (NIH) (http://bcrac.ni.nih.gov/brc/aq1.htm) (1). This calculator is based on the Gail model, which takes into account many of the risk factors previously mentioned. However, clinicians who use the Gail model should be aware of its limitations. Although the model accurately predicts the risk for cancer for groups of women, its ability to discriminate between higher and lower risk for an individual woman is limited (5, 6). This limitation occurs because many women have similar, relatively low absolute risks for invasive breast cancer over 5 years, which makes discrimination among levels of risk difficult for an individual woman.

**Recommendation 2:** Clinicians should inform women 40 to 49 years of age about the potential benefits and harms of screening mammography.

Screening mammography for women 40 to 49 years of age is associated with both benefits and potential harms. The most important benefit of screening mammography every 1 to 2 years in women 40 to 49 years of age is a potential decrease in breast cancer mortality. A recent meta-analysis estimated the relative reduction in the breast cancer mortality rate to be 15% after 14 years of follow-up (relative risk, 0.85 [95% credible interval [CrI], 0.73 to 0.99]) (7). An additional large randomized clinical trial of screening mammography in women 40 to 49 years of age found a similar decrease in the risk for death due to breast...
Table. Family History Patterns Associated with an Increased Risk for BRCA1 or BRCA2 Gene Mutations*

<table>
<thead>
<tr>
<th>Pattern Description</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both maternal and paternal family histories are important</td>
<td></td>
</tr>
<tr>
<td>Women not of Ashkenazi Jewish heritage</td>
<td></td>
</tr>
<tr>
<td>Two first-degree relatives with breast cancer, 1 of whom received the diagnosis at age ≤50 years</td>
<td></td>
</tr>
<tr>
<td>A combination of ≥3 first- or second-degree relatives with breast cancer regardless of age at diagnosis</td>
<td></td>
</tr>
<tr>
<td>A combination of both breast and ovarian cancer among first- and second-degree relatives</td>
<td></td>
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<tr>
<td>A first-degree relative with bilateral breast cancer</td>
<td></td>
</tr>
<tr>
<td>A combination of ≥2 first- or second-degree relatives with ovarian cancer regardless of age at diagnosis</td>
<td></td>
</tr>
<tr>
<td>A first- or second-degree relative with both breast and ovarian cancer at any age</td>
<td></td>
</tr>
<tr>
<td>A history of breast cancer in a male relative</td>
<td></td>
</tr>
<tr>
<td>Women of Ashkenazi Jewish heritage</td>
<td></td>
</tr>
<tr>
<td>Any first-degree relative (or 2 second-degree relatives on the same side of the family) with breast or ovarian cancer</td>
<td></td>
</tr>
</tbody>
</table>

* Adapted from data from the U.S. Preventive Services Task Force (4).

The relative balance of benefits and harms depends on women’s concerns and preferences and on their risk for breast cancer. Clinicians should help women to judge the balance of benefits and harms from screening mammography. Women who are at greater-than-average absolute risk for breast cancer and who are concerned that breast cancer would have a severely adverse effect on quality of life may derive a greater-than-average benefit from screening mammography. Women who are at substantially lower-than-average risk for breast cancer or who are concerned about potential risks of mammography may derive a less-than-average benefit from screening mammography.

If a woman decides to forgo mammography, clinicians should readdress the decision to have screening every 1 to 2 years.

Recommendation 4: We recommend further research on the net benefits and harms of breast cancer screening modalities for women 40 to 49 years of age.

Methodological issues associated with existing breast cancer screening trials, such as compliance with screening, lack of statistical power, and inadequate information about inclusion or exclusion criteria and study population, heighten the need for high-quality trials to confirm the effectiveness of screening mammography in women in this age group. Furthermore, harms of screening in this age group, such as pain, radiation exposure, and adverse outcomes related to false-positive results, should also be studied.

INTRODUCTION

Breast cancer is the second leading cause of cancer-related death among women in the United States. In 2005, an estimated 211 240 new cases of invasive breast cancer will be diagnosed, and 40 410 women will die of the disease (9). Screening mammography reduces breast cancer mortality in women 50 to 70 years of age. Although 25% of all diagnosed cases are among women younger than 50 years of age (9), screening mammography in this age group has remained a topic of debate because of the difficulty in determining the benefit of mammography in this age group. A meta-analysis performed for the USPSTF estimated that screening mammography every 1 to 2 years in women 40 to 49 years of age resulted in a 15% decrease in breast cancer mortality rate after 14 years of follow-up (7). However, the 95% credible interval for this estimate is wide and indicates that the reduction could be as much as 27% or as little as 1%. This relative risk reduction corresponds to about 5.6 deaths prevented per 10 000 women screened (95% CrI, 0.9 to 13.1 deaths prevented per 10 000 women screened). Because screening mammography is also associated with potential harms, a discussion of risks (biopsies, surgery, radiation exposure, false-positive results, and false reassurance), benefits (early detection of breast cancer), and patient preferences should be the basis for screening decisions.

The purpose of this guideline is to present the avail-
Guidelines for Screening Mammography in Women Age 40 to 49 Years

CLINICAL GUIDELINES

This issue of Annals of Internal Medicine presents a series of clinical guidelines. The current guideline focuses on screening mammography in women aged 40 to 49 years.

1. **What are the benefits of screening mammography in women 40 to 49 years of age?**
2. **What are the risks associated with screening mammography in women 40 to 49 years of age?**
3. **Does the balance of risks and benefits vary according to the individual woman’s characteristics?**
4. **What are the methodological issues that affect the interpretation of the results of previous meta-analyses?**

**Benefits**

Of the 8 currently published meta-analyses, 7 estimated that screening women 40 to 49 years of age reduced breast cancer mortality rates, but only 3 of these found a statistically significant reduction (7). The most recent meta-analysis found that screening mammography every 1 to 2 years in women 40 to 49 years of age results in a 15% decrease in breast cancer mortality rate after 14 years of follow-up (relative risk, 0.85 [95% CI, 0.73 to 0.99]) (7). However, concerns about study quality and whether some of the observed benefit may be due to screening that occurred after the women turned 50 years of age complicate interpretation of the evidence. The use of death due to breast cancer as an end point can be criticized because cause of death could have been misclassified, and therefore some authors have suggested using overall mortality as the primary end point. However, estimation of the effect of screening mammography on total mortality would require very large study samples to detect any differences between screened and unscreened groups. Finally, the benefit of screening mammography in younger women remains controversial because of concerns about the quality of the trials that showed this result. Some of the trials had inadequate and inconsistent reporting of randomization, differences in baseline characteristics between study groups, and women in the control group who were screened outside the study protocol. Depending on how stringently the quality criteria were applied, meta-analyses could vary from the 2001 Cochrane meta-analysis that included only 2 of the 8 trials that targeted women between 40 and 49 years of age (10) to the recent USPSTF report that included all trials but the Edinburgh trial (7). A recent study (11) based on 7 model-based analyses concluded that screening mammography resulted in a 7.5% to 22.7% reduction in the breast cancer mortality rate but did not specifically evaluate the effect of screening mammography in women 40 to 49 years of age. On balance, however, we concurred with authors of the meta-analysis for the USPSTF guideline, who concluded that the limitations of the trials were not sufficient to exclude them (7). We believe the weight of the evidence supports a modest reduction in breast cancer mortality rate with mammography screening of approximately 15% in women 40 to 49 years of age, but the wide CIs for this estimate reflect that the reduction could be larger or nearly zero.

Some uncertainty exists in measuring the absolute impact of screening on morbidity associated with breast cancer and its treatment. Early diagnosis through screening is more likely to be associated with breast-conserving surgery. An observational study found that screening is associated with an absolute increase in lumpectomy (0.7 per 1000 women) and a decrease in absolute risk for mastectomy (0.5 per 1000 women) (12).

In summary, evidence demonstrates that screening mammography in women age 40 to 49 years, compared with women who do not get screened, decreases breast cancer mortality. However, the reduction in the mortality rate is smaller than the 22% (95% CI, 0.70 to 0.87) reduction seen in women who are screened when they are older than 49 years of age (6, 7). In addition, the estimate of the mortality rate reduction may be affected by biases in the trials or the effects of screening after the age of 49 years.

**Risks**

Risks of mammography include false-positive results, diagnosis of cancer that would not have become clinically evident during the patient’s lifetime, radiation exposure, false reassurance, and procedure-associated pain. Women 40 to 49 years of age may have a higher risk for a false-positive result, and false-positive rates vary widely among several studies. Mushlin and colleagues’ meta-analysis (13) of the sensitivity and specificity of screening mammography showed false-positive rates of 0.9% and 6.5%, respectively. However, other analyses have demonstrated cumulative rates of false-positive mammograms of 38% after 10 mammograms (14) and 21% after 10 mammograms (15). Some studies show no difference in the false-positive rates between women 40 to 49 years age and those older than 49 years of age (16–19). Outcomes associated with false-positive screening mammograms included small increases in general anxiety and depression, anxiety specific to breast cancer, and perceived increased susceptibility to breast cancer; however, anxiety generally resolved quickly after evaluation (6).

Use of mammography has been associated with increased diagnosis of DCIS. The natural history of DCIS is unknown, as is the percentage of these tumors that will progress to more serious disease. In 1999, 33% of women...
in whom DCIS was diagnosed had mastectomy, 64% had lumpectomy, and 52% had radiation (20). Not all DCIS cases may have required aggressive treatment, but reliable predictors of biological aggressiveness are difficult to categorize.

No direct evidence links cancer risk with radiation exposure from mammography. Reported pain varied from 28% of women in 1 study to 77% of women in another study. However, pain associated with the mammographic procedure was described by few women as a disincentive from having any future screening (21–24).

**Estimating Individualized Benefits and Harms**

Current evidence shows variation among women in terms of benefits and harms associated with screening mammography between 40 and 49 years of age (6). The decision to have screening mammography should be guided by the balance of benefits and harms for an individual woman. This balance will be affected by a woman’s view about how breast cancer and the outcomes associated with screening mammography will influence her quality of life and by her risk for breast cancer. Although the balance will favor screening for many women, it is less certain in women who are very concerned about the potential harms of mammography and who are at substantially lower-than-average risk for breast cancer.

The main benefit of screening mammography every 1 to 2 years in women 40 to 49 years of age is a decrease in breast cancer mortality. Harms of screening mammography include false-positive results, radiation exposure, false reassurance, pain related to the procedure, and possible treatment for lesions that would not have become clinically significant. The probability of false-positive mammograms was also higher in women with dense breasts, if the interval since the last mammography was long, and in women who had previous breast biopsy (25, 26). In addition, women place substantially different value on a false-positive mammogram, a negative mammogram, and the reduction in the rate of mortality associated with breast cancer (27).

A woman’s risk for breast cancer is influenced by age, family history of breast cancer, reproductive history, age at menarche, and history of breast biopsy. For example, the risk for breast cancer is higher for women 40 to 49 years of age if they have a history of breast cancer in a first-degree relative: 4.7 cases per 1000 examinations among women with family history versus 2.7 cases per 1000 examinations among those without family history. Older age, younger age at menarche, older age at the time of first birth, and history of breast biopsy also increase the risk for breast cancer.

The absolute risk for breast cancer for a woman at a given age and with certain risk factors can be estimated by using the Web site calculator provided by the NIH that is based on the Gail model (1). However, the accuracy of the Gail model is better when predicting the average level of risk in a group of women who are at similar risk than when discriminating between women who will and will not develop breast cancer. In addition, a clinician may be unable to assess the risk for breast cancer because of a lack of family history or in women who were adopted.

**Summary**

Screening mammography probably reduces breast cancer mortality in women 40 to 49 years of age modestly. However, the reduction in this age group is smaller than that in women 50 years of age or older, is subject to greater uncertainty about the exact reduction in risk, and comes with the risk for potential harms (such as false-positive and false-negative results, exposure to radiation, discomfort, and anxiety).

Because of the variation in benefits and harms associated with screening mammography, we recommend tailoring the decision to screen women on the basis of women’s concerns about mammography and breast cancer, as well as their risk for breast cancer. Assessment of an individual woman’s risk for breast cancer is important because the balance of harms and benefits will shift to net benefit as a woman’s baseline risk for breast cancer increases, all other factors being equal. For many women, the potential reduction in risk for death due to breast cancer associated with screening mammography will outweigh other considerations.

**Recommendations of Other Organizations**

The 2006 American Cancer Society guideline (28) recommends yearly mammograms starting at age 40 and continuing for as long as a woman is in good health.

The 2003 American College of Obstetricians and Gynecologists guideline (29) recommends that women aged 40 to 49 years have screening mammography every 1 to 2 years.

The 2002 USPSTF guideline (30) recommends screening mammography, with or without clinical breast examination (CBE), every 1 to 2 years for women aged 40 and older.

The 2001 Canadian Task Force on Preventive Health Care (31) says that current evidence regarding the effectiveness of screening mammography does not suggest the inclusion of the maneuver in, or its exclusion from, the periodic health examination of women 40 to 49 years of age who are at average risk for breast cancer. Upon reaching 40 years of age, Canadian women should be informed of the potential benefits and risks of screening mammography and assisted in deciding at what age they wish to initiate the maneuver.

From the American College of Physicians and Drexel University College of Medicine, Philadelphia, Pennsylvania; Beth Israel Deaconess Medical Center, Boston, Massachusetts; Hines Veterans Affairs Hospital and
Guidelines for Screening Mammography in Women Age 40 to 49 Years

Clinical Guidelines

Northwestern University, Chicago, Illinois; and Veterans Affairs Palo Alto Health Care System and Stanford University, Stanford, California.

Note: Clinical practice guidelines are guides only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians’ judgment. All ACP clinical practice guidelines are considered automatically withdrawn or invalid 5 years after publication or once an update has been issued.

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