

# Screening Mammography in Women 40 to 49 Years of Age: A Systematic Review for the American College of Physicians

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**Background:** The risks and benefits of mammography screening among women 40 to 49 years of age remain an important issue for clinical practice.

**Purpose:** To evaluate the evidence about the risks and benefits of mammography screening for women 40 to 49 years of age.

**Data Sources:** English-language publications in MEDLINE (1966–2005), Pre-MEDLINE, and the Cochrane Central Register of Controlled Trials and references of selected studies through May 2005.

**Study Selection:** Previous systematic reviews; randomized, controlled trials; and observational studies.

**Data Extraction:** Two independent reviewers.

**Data Synthesis:** In addition to publications from the original mammography trials, 117 studies were included in the review. Meta-analyses of randomized, controlled trials demonstrate a 7% to 23% reduction in breast cancer mortality rates with screening mammography in women 40 to 49 years of age. Screening mammography is associated with an increased risk for mastectomy but a decreased

risk for adjuvant chemotherapy and hormone therapy. The risk for death due to breast cancer from the radiation exposure involved in mammography screening is small and is outweighed by a reduction in breast cancer mortality rates from early detection. Rates of false-positive results are high (20% to 56% after 10 mammograms), but false-positive results have little effect on psychological health or subsequent mammography adherence. Although many women report pain at the time of the mammography, few see pain as a deterrent to future screening. Evidence about the effect of negative screening mammography on psychological well-being or the subsequent clinical presentation of breast cancer is insufficient.

**Limitations:** Few randomized, controlled trials assessed the risks of screening, and the literature search was completed in 2005.

**Conclusions:** Although few women 50 years of age or older have risks from mammography that outweigh the benefits, the evidence suggests that more women 40 to 49 years of age have such risks.

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Several decades after the first guidelines for breast cancer screening were published, the routine use of mammography among asymptomatic women remains a topic of considerable debate (1, 2). This debate surfaces occasionally on screening women 50 years of age or older but persists regularly for screening women in their 40s (3, 4). The persistence of this controversy suggests a level of unease with our current understanding of the benefits and risks of mammography and with how this understanding has been translated into screening recommendations.

Understanding the risks and benefits of screening mammography among women in their 40s is important because of the critical position that breast cancer holds in that age group. In the United States, breast cancer is one of the most common causes of death for women in their 40s. In 2002, almost 5000 women between 40 and 49 years of age died of breast cancer, compared with the 6800 women who died of heart disease or 1500 women who died of HIV (5). However, despite the relative importance of breast cancer in this age group, the burden of breast cancer among women in their 40s is low for a population-based screening program. More than 98% of women will not develop breast cancer between 40 and 50 years of age, but they will be subject to the risks of population-based screening. Of the 44 000 women who die of breast cancer each year, fewer than one fifth received their diagnoses between the ages of 40 and 49 years (6, 7).

We describe the results of a systematic review of the benefits and risks for screening mammography among women 40 to 49 years of age. Currently, 8 published meta-

analyses discuss the effect of mammography screening in women 40 to 49 years of age on breast cancer mortality rates (8–16). All but 1 demonstrate a reduction in mortality rates from screening mammography. Thus, we did not perform another meta-analysis of the effect of screening mammography on breast cancer mortality rates, but we reviewed briefly the benefits of mammography screening derived from published screening trials and meta-analyses. In addition, we focused on 2 areas that are less well-studied but may affect recommendations about screening mammography among women in this age group: 1) risks of mammography screening and 2) variation in the risks and benefits of mammography according to an individual woman's characteristics.

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## METHODS

### Data Sources

We created a framework of the potential risks and benefits of screening mammography to guide the literature search (Figure). On the basis of the framework, we searched MEDLINE, Pre-MEDLINE, and the Cochrane Central Register of Controlled Trials for English-language publications. We conducted the initial searches in spring 2004 and updated them in May 2005. General search strategies included Medical Subject Headings (MeSH) terms *mammography* or *breast neoplasms* and *mass screening*, as well as the keywords *mammography*, *screening*, and *breast cancer*. We conducted additional searches for each individual risk or benefit by using appropriate keywords and MeSH terms. We reviewed the references of all selected articles to identify additional relevant articles.

### Study Selection

Although previous systematic reviews have largely focused on randomized, controlled trials of mammography screening to quantify the benefit of screening on breast cancer mortality rates, most evidence about risks and other benefits of mammography is derived from observational studies, primarily prospective cohort studies (Table). Thus, we included a wide range of study designs in our review, with the included studies depending on the question and the available evidence. We used meta-analyses to assess the effect of mammography screening on breast cancer mortality rates and the risk for a false-positive mammogram at a single screening; randomized, controlled trials and prospective cohort studies to assess the effect of mammography on breast cancer treatment and the cumulative risk for a false-positive mammogram; and both prospective and cross-sectional observational studies to assess the other risks of mammography. We excluded case series and ecological designs for all risks except for ductal carcinoma in situ (DCIS), because most published data on DCIS outcomes are derived from these study designs. In addition, we reviewed the available publications from the 8 original mammography trials and the published simulation models of the effect of radiation from mammography screening. When possible, we focused on evidence from studies of screening mammography in women in their 40s or analyses of this age group within larger cohorts. When this was not possible, we used studies of screening mammography in older women. In the case of multiple publications from the same study, we included only the most recent publication in our analysis.

For study selection, a study investigator reviewed abstracts of all primary research articles to determine whether the full-text article should be retrieved. We retrieved 873 full-text articles, and 2 investigators reviewed them. In addition to the publications from the original trials, 117 of these articles met inclusion criteria.

### Key Summary Points

Meta-analyses of randomized, controlled trials demonstrate a 7% to 23% reduction in breast cancer mortality rates from screening mammography in women 40 to 49 years of age.

Screening mammography is associated with an increased risk for mastectomy but a decreased risk for adjuvant chemotherapy and hormone therapy.

The risk for radiation is small (30 to 200 breast cancer deaths occurred in an annual screening of 100 000 women 40 to 49 years of age).

Rates of false-positive mammograms are high (20% to 56% after 10 mammograms), but false-positive results have little effect on psychological health or subsequent mammography adherence.

Although many women report pain at the time of mammography, few see pain as a deterrent to future screening.

Breast cancer risk varies among women in their 40s and affects the absolute reduction in rates of breast cancer mortality and the absolute risk for false-positive results on screening mammography.

### Data Extraction and Quality Assessment

Two investigators abstracted information about the study design, setting, study sample, measures, analysis, and results. When needed, we contacted authors to clarify questions about study design or results. We evaluated study quality by using the approach proposed by the Centre for Evidence-Based Medicine ([www.cebm.net/levels\\_of\\_evidence.asp](http://www.cebm.net/levels_of_evidence.asp)) (Appendix Table 1, available at [www.annals.org](http://www.annals.org)). The lead investigator adjudicated any disagreements between the reviewers about article content and quality.

### Role of the Funding Source

The review was conducted under contract with the American College of Physicians. The funding source had no role in the collection, analysis, or interpretation of the data or in the decision to submit the article for publication.

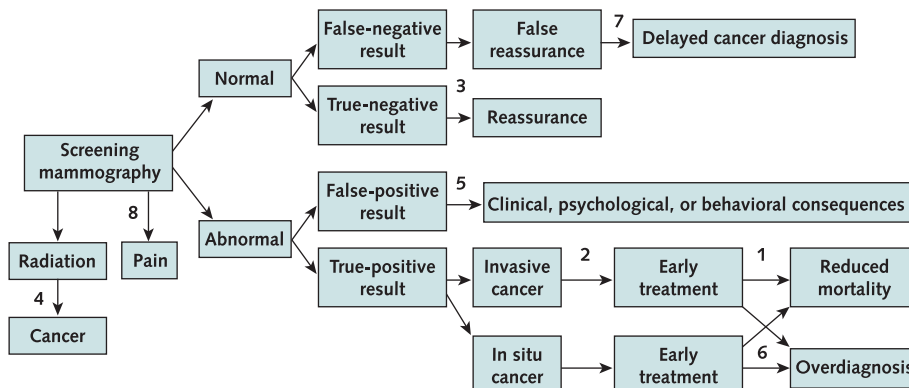
## RESULTS

### Benefits

#### Breast Cancer Mortality

Many meta-analyses have combined the results of major mammography screening trials to assess the effect of screening on breast cancer mortality rates. The latest meta-analysis demonstrated 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 after 14 years of

Figure. Risks and benefits of screening mammography.



Numbers correspond to the risks and benefits outlined in the Table.

follow-up (relative risk, 0.85 [95% CI, 0.73 to 0.99]) (12). This effect size is very similar to that reported by most previous meta-analyses of women 40 to 49 years of age (8, 10, 13, 14, 16). It is smaller than the 22% reduction seen among women 50 years of age or older (relative risk, 0.78 [CI, 0.70 to 0.87]) (12). The meta-analysis did not include the recently published results of the United Kingdom trial of annual mammography screening in 160 921 women in their 40s (relative risk, 0.83 [CI, 0.66 to 1.04]) (17). However, this estimate is so similar to the results of the meta-analyses that the findings are unlikely to substantively change. Nevertheless, the effect of mammography screening on breast cancer mortality rates for women in their 40s remains controversial for several reasons. These reasons in-

clude concern about the quality of the trials that found mammography to have the largest benefit, the interval until the mortality rate reduction began, and the validity of death due to breast cancer as the primary end point (2). We review each issue in the following sections.

Study quality is important because high-quality studies are more likely to provide accurate estimates of the effect size. However, judging study quality is difficult because of imperfect reporting and lack of consensus on criteria for evaluating studies. Furthermore, high-quality studies are relatively uncommon. In the setting of screening mammography for women 40 to 49 years of age, previous meta-analyses differ in their assessment of study quality and study inclusion. The Cochrane meta-analysis (2) excluded all but 2 of the 8 trials that provided information about this age group (the Canadian trial and the Malmö trial). The most recent meta-analysis, which was from the U.S. Preventive Services Task Force (12), included all trials but the Edinburgh trial. Other meta-analyses have included all 8 trials (10, 11, 13, 14, 16). To a great extent, these differences arise from different levels of concern about inadequate or inconsistent information in study publications, including variation in the numbers of participants in sequential reports; differences in baseline characteristics among groups; and lack of information about randomization procedures, date of trial entry, and other study characteristics. Although many of these concerns cannot be fully resolved, recent analyses and critical reviews support the argument that none of the trials is sufficiently biased to necessitate exclusion from meta-analyses, with the possible exception of the Edinburgh trial, for which substantive evidence of failure of randomization persists (18–21).

The reduction in breast cancer mortality rates with mammography screening does not begin for some time after initiation of screening. This delay occurs because breast cancer is not immediately fatal and women who do not undergo screening must begin to die of cancer before a

Table. Risks and Benefits of Screening Mammography

Variable*	Data Sources
<b>Benefits</b>	
1. Mortality rate reduction	Primary end point in randomized, controlled trials and meta-analyses
2. Morbidity rate reduction	Secondary end point in randomized, controlled trials and observational cohort studies
3. Reassurance	No direct or indirect evidence
<b>Risks</b>	
4. Radiation-induced cancer	No direct evidence; indirect evidence from prospective and retrospective cohort studies of radiation exposure from other sources
5. False-positive consequences	Cross-sectional and prospective and retrospective cohort studies
6. Overdiagnosis	No direct evidence; indirect evidence from time trend and cross-sectional studies
7. False reassurance	No direct or indirect evidence
8. Pain or discomfort	Cross-sectional and prospective cohort studies

\* Numbers correspond to those in the Figure.

reduction in mortality rates can be seen. For women 40 to 49 years of age at the initiation of screening, the reduction in breast cancer mortality rates can be measured after 6 years of follow-up and the effect size increases over time (8, 12). Thus, some women who begin screening in their 40s are older than 50 years of age when the reduction in breast cancer mortality rate begins. Although the precise contributions of screening in women 40 to 49 years of age and screening after a woman turned 50 years of age are difficult to determine, several analyses suggest that the most benefit is attributable to screening when women are between 40 and 49 years of age (8, 12).

Concern has been raised about the validity of death due to breast cancer as the primary end point in screening trials. Because differential misclassification of cause of death may bias study results and breast cancer treatment may increase rates of cardiovascular mortality, some investigators have suggested that overall death should be the primary end point (2). However, because the relative reduction in overall mortality rates with mammography will be much smaller than that in breast cancer mortality rates, trials of more than 1 million women would be necessary to detect a difference in overall mortality rates. Existing screening trials use strategies for minimizing misclassification of cause of death, including blinded review of deaths and sensitivity analyses using alternative sources for death classification (19).

The existing mammography screening trials have several other potential limitations for estimating the effect of mammography in community practice (22). Some biases may have resulted in an underestimate of the benefit of current screening programs, whereas others may have led to an overestimate. Mammography technology has improved since the 1960s, when the first trial was begun. However, differences in technology among trials have not been shown to be associated with the magnitude of benefit, and some of the larger estimates come from the earliest trials. Screening intervals and techniques were often less intensive in the trials than those that are currently recommended in the United States. Because most trials tested the effect of an invitation to screening rather than screening itself, many women in the intervention group did not undergo screening. In addition, some women in the control group had screening outside of the study protocol. This crossover biases the results of the trials toward showing no benefit of screening. Case-control studies, which measure the actual use of screening, and observational studies of screening programs generally find higher estimates of the benefit of mammography (23, 24). Women in the intervention group may have been more likely to undergo treatment at referral centers because these centers were connected to the screening programs, which may have led to improved treatment outcomes.

In summary, the body of evidence indicates that women who undergo screening mammography between 40 and 49 years of age are less likely to die of breast cancer

than women who do not undergo screening mammography, although the magnitude of the effect is smaller than that among women 50 years of age or older. The mortality benefit is unlikely to be completely explained by biases in mammography screening trials or the effects of screening after the age of 49 years.

### **Breast Cancer Treatment Morbidity**

Early detection may reduce the morbidity associated with breast cancer treatment by enabling the use of less aggressive therapies, for example, lumpectomy instead of mastectomy. However, more cases of cancer are detected in women who undergo screening than in women who do not undergo screening. Thus, the absolute effect of screening on breast cancer treatment is uncertain.

Five of the 8 screening trials reported data about breast cancer treatment in intervention and control groups (25–29). In addition, 9 other studies assessed the effect of screening on breast cancer treatment (30–39). Overall, these studies demonstrate that, because screening detects earlier-stage cancer, screen-detected cancer is more likely to be eligible for breast-conserving surgery and is less likely to be eligible for adjuvant chemotherapy and hormone therapy than cancer that is detected in some other way. However, differences in eligibility for breast-conserving surgery or chemotherapy do not always translate into differences in treatment (24, 38, 39). In addition, when considering the overall population of women who undergo screening, invitation to mammography screening is associated with absolute increases in the probabilities of mastectomy, lumpectomy, and radiation therapy because more cases of cancer are found (15). For example, in the Malmö trial, women in the screening group were 25% more likely to have a mastectomy and 24% more likely to have radiation therapy than women in the control group (15). However, rates of chemotherapy and hormone therapy remain lower in the screening group than in the control group.

### **Reassurance**

Although clinical experience suggests that many women perceive the reassurance provided by a negative mammogram as a substantial benefit, we found few empirical data to support this effect. Studies exploring the overall psychological impact of screening generally found relatively little effect across the population, with a few studies suggesting improved psychological well-being after screening (40–43).

### **Risks**

#### **Radiation**

No studies directly measure the risk for cancer caused by radiation exposure from mammography screening. Any effect of screening radiation on breast cancer incidence is small and is difficult to separate from the effect of screening on breast cancer detection. Estimates of the risk for

radiation from mammography are derived from cohort studies of other forms of radiation exposure, including high-dose exposures (over a short or prolonged period of time) and low-dose exposures from other sources (44–68). In general, studies of low-dose exposures have been inconclusive, with some demonstrating a small increase in risk and others finding no association (44, 47, 54, 57). However, studies of high-dose exposures have found that women who were exposed to high levels of radiation have a statistically significantly increased risk for breast cancer, with relative risks ranging from 1.33 to 11.39 for exposures of 0.3 to 43.4 Gy (46, 52, 55, 59, 65, 67, 68). High-dose exposures that have been studied include radiation treatment, diagnostic radiography, and atomic bombs. The increase in risk seems to be larger with higher doses of exposure, younger age at exposure, and longer follow-up.

The mean glandular dose from 2-view mammography is approximately 4 to 5 mGy. A recent analysis of radiation dose in the United Kingdom trial of mammography screening in women 40 to 48 years of age found a mean glandular dose of 2.5 mGy for an oblique film and 2.0 mGy for a craniocaudal film (69). However, dosage varies among facilities and increases with breast density. If women 40 to 49 years of age are screened every year and an estimated 20% experience a false-positive test result requiring additional radiographies, the average cumulative exposure from screening during the decade will be around 60 mGy.

**Appendix Table 2** (available at [www.annals.org](http://www.annals.org)) details evidence from these studies on the risk for radiation.

### Overdiagnosis

Overdiagnosis occurs when screening identifies cancer that would not have become clinically evident during a patient's lifetime. Although some proportion of invasive cancer diagnosed by mammography may never have presented clinically, the proportion is likely to be very small for women 40 to 49 years of age. Thus, concern about overdiagnosis from mammography screening focuses on the possibility that some proportion of DCIS detected by mammography would not have progressed to clinically evident invasive carcinoma within the life expectancy of a woman 40 to 49 years of age. Because we found no studies that evaluated this question directly, we examined 3 embedded questions: 1) Does the use of screening mammography increase the probability of a DCIS diagnosis? 2) What proportion of DCIS will progress to clinically evident invasive cancer, and over what period? 3) What are the clinical and quality-of-life consequences of a DCIS diagnosis?

The use of mammography screening has been associated with the incidence of DCIS in ecological and other analyses (70–73). The identification of DCIS increased 7-fold from 1980 (when screening mammography programs were introduced) to 2001 (70). More than 25% of

cases of cancer diagnosed among women in their 40s are DCIS, and 86% of DCIS cases are detected by screening (71).

Relatively few studies have examined the natural history of DCIS. Although some older studies suggest that approximately 40% of women who had a local excision or no treatment for DCIS may develop breast cancer in the same breast, these studies provide little information to evaluate study quality and generally included very few women (74–81). The largest series of 80 women with untreated DCIS found that 14% had a cancer diagnosis after several decades of follow-up (75). Studies of women with treated DCIS have found that 3% to 8% had invasive breast cancer at 5 years and 2% had died of breast cancer at 10 to 15 years (82).

The diagnosis of DCIS has significant clinical consequences. Small cross-sectional studies suggest that women diagnosed with DCIS experience some emotional duress, such as sleeplessness and anxiety (83, 84), but how long these symptoms persist or their effect on overall quality of life is not known. In 1999, 28% of U.S. women diagnosed with DCIS had mastectomy, 64% had lumpectomy, and 52% of those who had lumpectomy had radiation (85).

**Appendix Table 3** (available at [www.annals.org](http://www.annals.org)) details evidence from these studies on the risk for overdiagnosis.

### False-Positive Test Results

Women who undergo screening mammography are at risk for a false-positive result and associated adverse consequences. A recent meta-analysis of the sensitivity and specificity of mammography found that the probability of a false-positive mammogram was between 0.9% and 6.5%, with most studies falling between 2% and 4% (85). Although relatively few studies provided data stratified by age, the rate of false-positive results did not differ between women 40 to 49 years of age and women 50 years of age or older in the Canadian National Breast Screening Study (86, 87), the San Francisco Demonstration Project (88), or the Nijmegen case-control study (89). Other studies have examined the cumulative risk for a false-positive mammogram over time. In an analysis of data from the Harvard Pilgrim Health Care study, the cumulative risks for a false-positive mammogram for women 40 to 49 years of age was 30% after 5 mammograms and 56% after 10 mammograms (90). Other analyses have demonstrated cumulative rates of false-positive mammograms of 21% (91) and 38% (92) after 10 mammograms. Relatively few studies describe diagnostic evaluations among women with abnormal mammograms. Among the 631 false-positive mammograms in the Harvard Pilgrim Health Care study, 162 resulted in additional outpatient visits, 560 resulted in additional diagnostic imaging, and 128 resulted in biopsy. An analysis of the Stockholm trial demonstrated that false-positive mammograms (among 231 women 40 to 49 years

of age) resulted in 648 physician visits, 244 fine-needle aspirations, 92 additional mammographies, and 55 excisional biopsies (93).

We included 22 studies that investigated the outcomes of false-positive screening mammograms (94–115). These outcomes included general anxiety and depression, anxiety specific to breast cancer, perceived susceptibility to breast cancer, adherence to screening mammography, and frequency of breast self-examination.

Overall, these studies found that false-positive mammograms were associated with a small increase in generalized anxiety and depression during the evaluation period, which resolved quickly after the evaluation was completed. In 1 study, these increases were seen only in comparison with women who had a negative test result and not in comparison with women who had not undergone screening (114). Several studies documented a more sustained increase in anxiety specific to breast cancer; however, such increases tended to be small and were confined to few women (92, 106, 109, 110) and several studies found no such increase (99, 101, 115). Two studies (98, 105) reported that increased anxiety specific to breast cancer recurred at the next screening. In general, psychological consequences were greater among women who underwent biopsy than women who had further imaging only.

Most studies found that women who had a false-positive mammogram were just as likely to undergo subsequent mammography screening as women who did not have a false-positive mammogram (100, 105–107, 112, 113). Two studies found slightly lower rates of subsequent screening among women who had a false-positive mammogram (98, 108). Having had a false-positive mammogram was associated with an increase in the frequency of breast self-examination (99–105) and of breast- and non-breast-related health care visits (96).

**Appendix Table 4** (available at [www.annals.org](http://www.annals.org)) details evidence from these studies on the risk for false-positive test results.

### **False Reassurance**

Some proportion of women who have a negative mammogram will develop breast cancer before their next screening. Concern about the risk for false reassurance centers on the possibility that a negative mammogram may lead women to delay seeking attention for a subsequent breast abnormality. If delay in presentation is associated with progressive disease, false reassurance might result in advanced-stage cancer. We identified 2 studies that estimate the probability of these events after a negative mammogram. A survey of 516 women in the Dutch screening program found that more than 99% of women would be concerned about breast cancer if they felt a breast lump and would pursue medical evaluation within a week (116). This probability was not affected by having previous negative screenings. In a study of 336 women with newly

diagnosed breast cancer in Finland, 29% of women with a negative mammogram delayed treatment, compared with 0% of women with screen-detected cancer (117). However, the study did not provide information about the extent or clinical significance of the delay.

### **Pain from the Mammography Procedure**

We included 22 studies that investigated pain and discomfort associated with mammography (43, 118–138). The prevalence of pain varied widely. For example, 1 study found that 77% of women experienced pain, whereas another study reported that 28% of women had considerable pain. This difference could be due to the distinction between “pain” and “considerable pain.” It also could be attributed to differences in the instruments used to measure pain, but it persisted across studies using the same instruments or response scales. In studies that measured whether pain was a deterrent to having future mammography, few women agreed that the pain caused by mammography would prevent them from attending future screening. The degree of pain was associated with the stage of menstrual cycle (126, 135, 136), anxiety (121, 132), and premammography anticipation of pain (43, 121, 134, 138).

**Appendix Table 5** (available at [www.annals.org](http://www.annals.org)) details evidence from these studies on the risk for pain on mammography.

### **Individualizing Risks and Benefits**

Considerable evidence indicates that the risks and benefits of screening mammography vary among women. This variation exists across age groups but has particular clinical relevance for women younger than age 50 years. Lower rates of disease in this age group make individual variation more important. This variation arises in 3 main domains. First, clinical characteristics have been demonstrated to affect mammography performance, including age, family history of breast cancer, and breast density. Second, the absolute benefit of mammography is correlated with the predicted breast cancer risk, both because the relative decrease in breast cancer mortality rate translates into a larger absolute decrease when the baseline risk without screening is higher and because the rate of false-positive results greatly depends on the prevalence of breast cancer in the population. Third, individual values and risk preferences determine the effect that positive and negative mammography outcomes will have on quality of life.

Women with a history of breast cancer in a first-degree relative are more likely to have screen-detected cancer than are women without a family history of breast cancer (139–141). For women 40 to 49 years of age, 4.7 cases are detected per 1000 examinations among women with a family history compared with 2.7 cases per 1000 examinations among women without a family history. For women 50 to 59 years of age, the rates are 6.6 and 4.6 cases per

1000 examinations, respectively (140, 141). In general, the rate of cancer detection among women with a family history of breast cancer matches that among women without a family history who are a decade older. The incidence of false-positive and false-negative mammograms seems to be slightly higher among women with a family history of breast cancer than among women without a family history of breast cancer (139–141).

Several studies suggest that the sensitivity of screening mammography is lower among women with dense breasts. In an analysis of almost 330 000 women, sensitivity was 62.2% in women with extremely dense breasts compared with 88.2% in women whose breasts were almost entirely fat (142). Specificity also changes with breast density. Among women 40 to 44 years of age, 9.7% of women with extremely dense breasts had a false-positive mammogram compared with 4.2% of women with breasts that were almost entirely fat (143). False-positive mammograms are also more common if it has been longer since the last screening and if a woman has had a previous breast biopsy (143).

Information about breast cancer risk can be based on the presence or absence of individual risk factors or on the output of prediction models that incorporate data about several risk factors. The most commonly used individual risk factors for assessing breast cancer risk are age and family history of breast cancer. Breast cancer risk increases steadily with age, from a 5-year risk of 0.28% for a 35-year-old woman to a 5-year risk of 2.35% for a 75-year-old woman (144). Family history also has a substantial effect on risk, with the presence of a first-degree relative conferring a 2- to 3-fold increase in risk and the presence of a second-degree relative conferring a 30% to 50% increase in risk (145). The most commonly used risk prediction model is the Gail model, which was used for enrollment in the initial trial of tamoxifen for breast cancer prevention and is now included in guidelines for tamoxifen use (146–148). This model includes age, family history, age at menarche, age at first live birth, age at menopause, breast biopsy history, and race. Validation studies have demonstrated that the Gail model accurately predicts the number of cases of breast cancer that will develop in a given population but is much less accurate in determining which individual women will develop breast cancer (148–151). In these studies, the Gail model has a c-statistic (area under the receiver-operating characteristic curve) of 0.58 to 0.67, indicating that it provides only modest discriminatory power over chance alone (c-statistic, 0.5).

Although relatively few studies have measured values and preferences about mammography screening, the evidence suggests that women vary substantially in the value they place on a false-positive test result, a negative mammogram, and the reduction in breast cancer mortality rate from screening. In a survey of 479 U.S. women, 63% would tolerate 500 or more false-positive results for every life saved by screening mammography (152). Only 38% would include information about false-positive results in

their decision about screening, although 60% reported that information about nonprogressive breast cancer would influence their decisions. Other studies have demonstrated that most women overestimate their short- and long-term risk for breast cancer and the absolute benefit, although not the relative risk reduction, from screening mammography (153, 154).

## DISCUSSION

Current evidence indicates that women 40 to 49 years of age who undergo routine mammography screening will decrease their risk for death due to breast cancer but will increase their risks for undergoing unnecessary procedures, breast cancer–related anxiety, discomfort at the time of screening, and exposure to low-dose radiation. Because the incidence of breast cancer and the effectiveness of mammography are lower among women in their 40s than among women 50 years of age or older, mammography screening results in less absolute benefit and greater absolute risk for women 40 to 49 years of age than for women 50 years of age or older. The proportion of women 50 years of age or older whose risks for mammography outweigh the benefits is widely accepted to be clinically insignificant. However, the evidence suggests that this proportion is higher and may be clinically significant for women 40 to 49 years of age. Given this difference, a woman 40 to 49 years of age who had a lower-than-average risk for breast cancer and higher-than-average concerns about false-positive results might reasonably delay screening. Measuring risks and benefits accurately enough to identify these women remains a challenge.

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**Appendix Table 1. Evidence-Based Medicine Review Score: Criteria Used to Assess Study Quality\***

Score	Therapy or Prevention, Etiology or Harm	Prognosis	Symptom Prevalence Study
1a	Systematic review of RCTs	Systematic review of inception cohort studies	Systematic review of prospective cohort studies
1b	Individual RCT (with narrow confidence interval)	Individual inception cohort study with >80% follow-up	Prospective cohort study with >80% follow-up
1c	All or none	All or no case series	All or no case series
2a	Systematic review of cohort studies	Systematic review of either retrospective cohort studies or untreated control groups in RCTs	Systematic review of 2b and better studies
2b	Individual cohort study (including low-quality RCT; e.g., <80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT	Retrospective cohort study or poor follow-up
2c	"Outcomes" research; ecological studies	"Outcomes" research	Ecological studies
3a	Systematic review of case-control studies		Systematic review of 3b and better studies
3b	Individual case-control study	–	Nonconsecutive cohort study or very limited study population
4	Case series (and poor-quality cohort and case-control studies)	Case series (and poor-quality prognostic cohort studies)	Case series or superseded reference standards
5	Expert opinion without explicit critical appraisal or based on physiology, bench research, or "first principles"	Expert opinion without explicit critical appraisal or based on physiology, bench research, or "first principles"	Expert opinion without explicit critical appraisal or based on physiology, bench research, or "first principles"

\* Criteria are from the Centre for Evidence-Based Medicine. RCT = randomized, controlled trial.

Appendix Table 2. Radiation\*

Study, Year (Reference)	EBMR Score	Patients, n	Age at Exposure	Design	Radiation Exposure	Outcome	Results
Beral et al., 1988 (44)	4	22 552 exposed	NA	Prospective cohort	Occupational exposure among nuclear industrial workers; 7.8 mSv	Mortality: mean follow-up, 18.6 y	No increase in risk; RR, 1.51 (95% CI, 0.51 to 4.46)
Boice et al., 1989 (45)	3b	953 cases; 1806 controls	Mean, 52 y	Case-control	Therapeutic irradiation for cervical cancer	Incidence	No increase in risk; RR, 0.88 (95% CI, 0.7 to 1.2)
Boice et al., 1991 (48)	2b	2573 exposed; 2367 controls	Mean, 26 y	Prospective cohort	Diagnostic radiography for tuberculosis; 7.6 cGy	Incidence: mean follow-up, 22 y	Increase in risk after 10–15 y of follow-up; RR, 1.29 (95% CI, 1.1 to 1.5)
Boice et al., 1992 (46)	3b	655 exposed; 1189 controls	Mean, 51.7 y	Case-control	Therapeutic irradiation for breast cancer (effect in other breast); 2.82 Gy	Incidence: mean follow-up, 5 y	Increase in risk after 10 y of follow-up; RR, 1.33 (95% CI, 0.99 to 1.78)
Boice et al., 1995 (47)	3b	528 cases; 2628 controls	Mean, 26 y	Case-control	Occupational exposure among radiation technologists; 5 to >50 mSv	Incidence	No increase in risk; RR, 1.13 (95% CI, 0.79 to 1.64)
Darby et al., 1987 (49)	4	2334 exposed	<25 to >55 y	Prospective cohort	Therapeutic irradiation for ankylosing spondylitis; 0.5 Gy	Incidence: mean follow-up, 23 y	Increase in risk; 26 cases observed; 16.07 cases expected
Doody et al., 1998 (50)	4	143 517 exposed	NA	Prospective cohort	Occupational exposure among radiography technicians	Mortality: mean follow-up, 19.8 y	No increase in risk; SMR, 0.99
Hancock et al., 1993 (51)	4	885 exposed	Mean, 28 y	Prospective cohort	Therapeutic irradiation for Hodgkin disease; 40 Gy	Incidence: mean follow-up, 9.3 y	No increase in risk after 30 y of age; RR, 0.7 (95% CI, 0.2 to 1.8)
Hildreth et al., 1989 (52)	2b	1201 exposed; 2469 controls	0–3 y	Prospective cohort	Therapeutic irradiation for thyruis in infancy; 0.69 Gy	Incidence at mean 36 y	Increase in risk after 36 y; RR, 3.6 (95% CI, 1.8 to 7.3)
Hoffman et al., 1989 (53)	4	1030 exposed	Mean, 12.3 y	Prospective cohort	Diagnostic radiography for scoliosis; 0.13 Gy	Incidence: mean follow-up, 26 y	Increase in risk; SIR, 1.82 (90% CI, 1.0 to 3.0)
Holm et al., 1989 (54)	4	35 074 exposed	45 y	Prospective cohort	Diagnostic doses of <sup>131</sup> I <10 mGy	Incidence: 5–20 y of follow-up	No increase in risk; SIR, 0.98 (95% CI, 0.91 to 1.06)
Howe and McLaughlin, 1996 (55)	4	31 917 exposed	Mean, 26 y	Prospective cohort	Diagnostic radiography for tuberculosis; 1 Sv to >10 Sv	Mortality: mean follow-up, 40 y	Increase in risk; RR, 3.15 (95% CI, 1.66 to 5.98) for 1–1.99 Sv
Li et al., 1983 (56)	4	910 exposed	0–17 y	Prospective cohort	Therapeutic irradiation for childhood cancer	Incidence: mean follow-up, 21 y	Increase in risk; 4 cases observed; 0.3 case expected
Lindberg et al., 1995 (57)	4	11 807 exposed	Mean, 5 mo	Prospective cohort	Therapeutic irradiation for skin hemangioma in infancy; 155 mGy	Incidence: mean follow-up, approximately 30 y	No increase in risk; SIR, 1.15
Lundell et al., 1996 (58)	4	9675 exposed	Mean, 6 mo	Prospective cohort	Therapeutic irradiation for skin hemangioma in infancy; 0.39 Gy	Incidence: 27–66 y of follow-up	Increase in risk after 40–50 y of follow-up; SIR, 1.24 (95% CI, 0.98 to 1.54)
Mattsson et al., 1993 (59)	2b	1216 exposed; 1874 controls	Mean, 40 y	Prospective cohort	Therapeutic irradiation for benign breast disease; 5.8 Gy	Incidence: 37–58 y of follow-up	Increase in risk; SIR, 3.58 (95% CI, 2.77 to 4.63)
Modan et al., 1989 (60)	2b	10 834 exposed; 10 834 population controls; 5392 sibling controls	Mean, 7.1 y	Prospective cohort	Therapeutic irradiation for tinea capitis; 1.6 mGy	Incidence: >30 y of follow-up	Increase in risk; RR, 2.11 (90% CI, 1.05 to 4.24)
Morin Doody et al., 2000 (61)	4	5573 exposed	Mean, 10.6 y	Prospective cohort	Diagnostic radiography for scoliosis	Mortality: mean follow-up, 40.1 y	Increase in risk; SMR, 1.69 (95% CI, 1.3 to 2.1)
Pukkala et al., 1995 (62)	4	1577 exposed	Mean, 24 y	Prospective cohort	Occupational exposure among airline cabin attendants	Incidence: mean follow-up, 13.9 y	Increase in risk after 15 y of follow-up; SIR, 1.87 (95% CI, 1.15 to 2.23)
Shore et al., 1986 (63)	2b	601 exposed; 1239 controls	Mean, 27.4 y	Prospective cohort	Therapeutic irradiation for acute postpartum mastitis; 3.77 rad	Incidence: ≥5 y of follow-up	Increase in risk; RR, 3.2 (95% CI, 2.3 to 4.3)
Storm et al., 1992 (64)	3b	529 cases; 529 controls	Mean, 51 y	Case-control	Therapeutic irradiation for breast cancer (effect in other breast); 2.51 cGy	Incidence: ≥8 y of follow-up	No increase in risk; RR, 1.04 (95% CI, 0.74 to 1.46)
Tokunaga et al., 1994 (65)	2b	70 165 exposed	0 to >80 y	Retrospective cohort	Hiroshima and Nagasaki atomic bombs; 0–6.0 Gy	Incidence: mean follow-up, 35 y	Increase in risk dependent on dose; RR, 1.48 (for 0.25–0.49 Gy) to 11.39 (for 4.0–6.0 Gy)
Wahner-Roedler et al., 2003 (66)	4	653 exposed	Median, 31.8	Prospective cohort	Therapeutic irradiation for Hodgkin lymphoma; 40 Gy	Incidence: mean follow-up, 8.7 y	Increase in risk; SIR, 3.0 (95% CI, 1.9 to 4.3)
Wolden et al., 2000 (67)	4	65 exposed	Median, 24.6	Prospective cohort	Therapeutic irradiation for Hodgkin lymphoma; 43.3 Gy	Incidence: mean follow-up, 21.2 y	Increase in risk; RR, 4.7 (95% CI, 3.4 to 6.0)

\* EBMR = Evidence-based Medicine Review; NA = not available; RR = relative risk; SIR = standardized incidence ratio; SMR = standardized mortality ratio.

Appendix Table 3. Overdiagnosis\*

Study, Year (Reference)	EBMR Score	Patients, n	Age	Design	Exposure	Outcomes	Results
<b>Mammography and DCIS</b>							
Claus et al., 2001 (73)	3b	875 cases; 1997 controls	20–79 y	Case-control	Mammography	DCIS	DCIS patients were more likely than controls to have had a screening mammogram (OR, 2.46 [95% CI, 1.78–3.40])
Ernstler et al., 1996 (70)	2c	16 706	≥30 y	Ecological	Mammography	DCIS	Among women age 40–49 y, annual increase in DCIS incidence was 0.4% between 1973 and 1983 compared with 17.4% between 1983 and 1992
Ernstler et al., 2002 (71)	2c	540 738	40–84 y	Retrospective cohort	Mammography	DCIS	28.2% of cases of screen-detected cancer in women age 40–49 y are DCIS, with a rate of 0.56 screen-detected DCIS cases per 1000 mammograms
Li et al., 2005 (72)	2b	32 990	≥30 y	Ecological	Mammography	DCIS	Incidence of DCIS increased by 7.2-fold in the United States between 1980 and 2001; increase was greater among women age >50 y than among women age 30–49 y
<b>Outcomes of DCIS</b>							
Eusebi et al., 1994 (75)	4	80 cases	NA	Case series	DCIS (untreated)	Invasive breast cancer; mean follow-up, 17.5 y	11 of 80 women (14%) developed invasive breast cancer
Betstill et al., 1978 (74)	4	10 cases	Mean, 48 y	Case series	DCIS (untreated)	Invasive breast cancer; mean follow-up, 21.6 y	6 of 10 women (60%) developed invasive breast cancer
Rosen et al., 1980 (80)	4	15 cases	NA	Case series	DCIS (untreated)	Invasive breast cancer; mean follow-up, 9.7 y	10 of 15 women (66%) developed invasive breast cancer
Mills and Thyne, 1975 (78)	4	9 cases	Mean, 55 y	Case series	DCIS (untreated)	Invasive breast cancer; mean follow-up, 8 y	2 of 9 women (22%) developed invasive breast cancer
Farrow, 1970 (77)	4	25 cases	Mean, 52 y	Case series	DCIS (untreated)	Invasive breast cancer; mean follow-up, 8 y	5 of 25 women (20%) developed invasive breast cancer
Page et al., 1995 (79)	4	28 cases	NA	Case series	DCIS (untreated)	Invasive breast cancer; mean follow-up, 10 y	7 of 28 women (25%) developed invasive breast cancer
Kerlikowske et al., 2003 (81)	4	1036 cases	≥40 y	Case series	DCIS (treated)	Invasive breast cancer; mean follow-up, 5 y	8.2% of women developed invasive breast cancer
Bluman et al., 2001 (83)	4	76 cases	Mean, 56 y	Case series	DCIS	Concerns about recurrence, depression, and quality of life	42% of women were moderately or very concerned about recurrence, 30% said thoughts of recurrence affected their mood, 50% reported adverse sexual consequences, and 15% met criteria for depression
Rakovitch et al., 2003 (84)	2b	64 cases; 164 controls with invasive breast cancer	Mean, 56 y	Cross-sectional	DCIS	Concerns about breast cancer, depression, and general anxiety	Women with DCIS have similar levels of breast cancer–specific concerns, general anxiety, and depression as those of women with invasive breast cancer
Ernstler et al., 2000 (76)	4	7072 cases	≥40 y	Retrospective cohort	DCIS (treated)	Death due to breast cancer; 5 and 10 y of follow-up	0.5% died of breast cancer at 5 y and 2.1% died of breast cancer at 10 y

\* DCIS = ductal carcinoma in situ; EBMR = Evidence-based Medicine Review; NA = not available; OR = odds ratio.

**Appendix Table 4. False-Positive Test Results\***

Study, Year (Reference)	EBMR Score	Patients, <i>n</i>	Age	Design	Outcome Measures	Results
Aro et al., 2000 (94)	2b	296 with false-positive, 721 with normal, 892 with no mammograms	50–59 y	Prospective cohort	Anxiety, depression, and screening behavior at baseline, 2 mo, and 12 mo	Higher breast cancer-specific anxiety at 2 and 12 mo; no association with general mood, anxiety, and intended screening behavior
Barton et al., 2004 (95)	2b	1439 with false-positive, 951 with normal mammograms	≥39 y	Prospective cohort	Impact of Events Scale, Hopkins Symptom Checklist at 3 wk and 3 mo	Higher breast cancer-specific and general anxiety
Barton et al., 2001 (96)	2c	496 with false-positive, 496 with normal mammograms	Mean, 50 y	Retrospective cohort	Documented breast concern, ambulatory care utilization at 12 mo	More breast concerns documented in chart and breast-related visits in the next year
Brett et al., 1998 (97)	2b	164 with false-positive, 51 with normal mammograms	50–64 y	Prospective cohort	Psychological Consequences Questionnaire, perceived risk, screening behavior at 1 and 5 mo	Higher rate of adverse psychological consequences at 1 and 5 mo
Brett and Austoker, 2001 (98)	2b	288 with false-positive, 99 with normal mammograms	50–64 y	Prospective cohort	Psychological Consequences Questionnaire, screening behavior at 3 y	Higher rate of adverse psychological consequences among those who had undergone biopsy; less likely to return for screening (85% vs. 92%)
Bull and Campbell, 1991 (99)	2b	253 with false-positive, 331 with normal mammograms; 541 at invitation	50–70 y	Prospective cohort	Hospital Anxiety and Depression Scale at baseline and 6 wk	No association with general anxiety or depression
Burman et al., 1999 (100)	2c	813 with false-positive, 4246 with normal mammograms	Median, 62 y	Retrospective cohort	Screening behavior at 2 y	More likely to return for screening (adjusted OR, 1.21 overall and 1.22 in women age 40–49 y)
Cockburn et al., 1994 (101)	2b	58 with false-positive, 142 with normal, 52 with no mammograms	50–69 y	Prospective cohort	Psychological Consequences Questionnaire at baseline, 1 wk after cleared, and 8 mo	No association with overall emotional, social, and physical function
Ellman et al., 1989 (102)	2b	266 with false-positive, 287 with normal mammograms	45–71 y	Prospective cohort	GHQ-28 at baseline and 3 mo	No association with general anxiety
Gram et al., 1990 (103)	4	126 with false-positive (30 biopsy-proven), 152 with normal mammograms	Mean, 46 y	Prospective cohort	Anxiety at 6 and 18 mo	Higher breast cancer anxiety at 6 and 18 mo
Lampic et al., 2001 (104)	1b	509 with false-positive, 285 with normal mammograms	Mean, 54 y	Prospective cohort	Hospital Anxiety and Depression Scale at 3 and 12 mo	No association with anxiety at 3 or 12 mo; lower rates of depression at 3 and 12 mo
Lampic et al., 2003 (105)	4	517 with false-positive, 285 with normal mammograms	50–64 y	Prospective cohort	Anxiety, screening behavior at 2 y	Higher anxiety about next screening visit and higher frequency of BSE; no association with return for screening
Lerman et al., 1991 (106)	1b	187 with false-positive, 121 with normal mammograms	50–74 y	Prospective cohort	Breast cancer worry at 3 mo, then monitored subsequent adherence	Higher levels of breast cancer worry; more likely to return to screening (74–78% vs. 68%)
Lipkus et al., 2000 (107)	2b	275 with false-positive, 772 with normal mammograms	Mean, 47 y	Retrospective cohort	Risk perception, worry, depression at ≥2 y	Higher risk perception and breast cancer worry; more likely to return for screening (87% vs. 81%)
McCann et al., 2002 (108)	2c	4792 with false-positive (514 biopsy-proven), 108 617 with normal mammograms	50–62 y	Retrospective cohort	Screening behavior at 2 y	Less likely to return for screening (83% vs. 85%)

**Appendix Table 4—Continued**

Study, Year (Reference)	EBMR Score	Patients, <i>n</i>	Age	Design	Outcome Measures	Results
Olsson et al., 1999 (109)	1b	252 with false-positive, 987 with normal mammograms	Mean, 57 y	Prospective cohort	Psychological Consequences Questionnaire at 1 wk and 6 mo	Higher rate of adverse psychological consequences at 6 mo
Ong et al., 1997 (110)	1b	488 with false-positive (306 biopsy-proven), 1173 with normal mammograms	50–64 y	Prospective cohort	Psychological Consequences Questionnaire at 1 mo	Highest rates of adverse psychological consequences among women undergoing surgical biopsy, then women undergoing early recall, then women with normal mammograms
O'Sullivan et al., 2001 (111)	2c	248 with false-positive, 5401 with normal mammograms	50–64 y	Retrospective cohort	Screening behavior	No association with return for screening
Pinckney et al., 2003 (112)	2c	2469 with false-positive, 26 521 with normal mammograms	≥40 y	Prospective cohort	Screening behavior at 30 mo	More likely to return for screening (adjusted OR, 1.40)
Pisano et al., 1998 (113)	2b	126 with false-positive (43 biopsy-proven), 53 with normal mammograms	Mean, 63.5 y	Retrospective cohort	Breast cancer beliefs, screening behavior at 2–4 y	Higher breast cancer risk perception; more likely to intend to return for screening ( <i>P</i> = 0.036)
Scaf-Klomp et al., 1997 (114)	2b	74 with false-positive, 113 with normal, 238 with no mammograms	50–69 y	Prospective cohort	GHQ-12, Hospital Anxiety and Depression scale, Fear of Cancer Scale at 8 wk and 6 mo	Higher anxiety at 6 mo compared with women with normal mammograms but not women who had not undergone screening; no association with intention to return for screening
Sutton et al., 1995 (115)	2b	10 with false-positive, 296 with normal mammograms	50–64 y	Prospective cohort	Spielberger state-trait anxiety inventory at baseline and 9 mo	No association with anxiety

\* BSE = breast self-examination; EBMR = Evidence-based Medicine Review; GHQ = General Health Questionnaire; OR = odds ratio.

**Appendix Table 5. Pain from the Mammography Procedure\***

Study, Year (Reference)	EBMR Score	Patients, n	Age	Design	Outcome Measures	Results
Aro et al., 1996 (118)	2b	883	≥50 y	Prospective cohort	4-point pain scale, 4-point discomfort scale 1 mo before mammography invitation and 2 mo after mammography	412/883 (47%) "uncomfortable," 429/883 (48%) "pain"
Bakker et al., 1998 (41)	2b	315	Mean, 61 y	Prospective cohort	5-point pain scale immediately after and 3 wk after mammography	126/315 (40%) "mammogram hurt"
Baskin-Smith et al., 1995 (119)	3b	378	Mean, 54 y	Cross-sectional	Open-ended question immediately after mammography	56/378 (15%) pain, 32/378 (8%) discomfort
Brew et al., 1989 (120)	3b	203	NA	Cross-sectional	4-point pain scale immediately after mammography	100/203 (49%) uncomfortable, 8/203 (4%) painful, 1/203 (0.5%) very painful
Bruyninckx et al., 1999 (121)	1b	247	Mean, 54 y	Prospective cohort	10-point pain scale immediately after and several weeks after mammography	180/247 (73%) "some pain"
Cockburn et al., 1992 (122)	1b	95	50–69 y	Prospective cohort	7-point pain scale 2 d and 3 mo after mammography	60/95 (63%) discomfort, 5/95 (5%) moderate pain, 1/95 (1%) severe pain
Dibble et al., 2005 (123)	1b	394	Mean, 55 y	Randomized, controlled trial	NRS, VAS immediately after mammography	99/788 (13%) scored >50 on VAS with no breast cushion; 56/788 (7%) scored >50 on VAS with breast cushion
Domar et al., 2005 (124)	1b	143	Mean, 52 y	Randomized, controlled trial	MPQ, 10-point pain scale immediately after mammography	Mean MPQ score of 11.8–13.7 across groups, mean pain scale score of 3.4–3.8 across groups
Dullum et al., 2000 (125)	2b	1800	Mean, 60 y	Prospective cohort	5-point pain scale 3 wk after mammography	570/1800 (31%) moderate pain, 80/1800 (15%) substantial pain, 83/1800 (4%) extreme pain
Jackson et al., 1988 (126)	3b	356	23–84 y	Cross-sectional	5-point pain scale immediately after mammography	39/356 (10%) very uncomfortable, 11/356 (3%) intolerable pain
Kashikar-Zuck et al., 1997 (127)	3b	125	Mean, 61 y	Cross-sectional	VAS (0–100), MPQ, 6-point pain scale immediately after mammography	Mean VAS score of 29.1, mean MPQ score of 12.1, mean pain scale score of 3.2
Keemers-Gels et al., 2000 (128)	3b	954	Mean, 59 y	Cross-sectional	4-point pain scale immediately after mammography	397/954 (41%) little pain, 204/954 (21%) moderate pain, 88/954 (9%) severe pain
Kornguth et al., 2000 (129)	3b	125	Mean, 60 y	Cross-sectional	VAS scale (0–100), MPQ immediately after mammography	Mean VAS score of 30.8, mean MPQ score of 10.4
Leaney and Martin, 1992 (130)	3b	374	NA	Cross-sectional	4-point pain scale immediately after mammography	115/374 (30%) moderate pain, 3/374 (0.8%) severe pain

**Appendix Table 5—Continued**

Study, Year (Reference)	EBMR Score	Patients, n	Age	Design	Outcome Measures	Results
Markle et al., 2004 (131)	1b	505	Mean, 52 y	Randomized, controlled trial	VAS immediately after mammography	Mean VAS score of 53.9 without cushions, mean VAS score of 30.1 with cushions
Nielsen et al., 1991 (132)	3b	272	Mean, 54 y	Cross-sectional	Descriptive rating scales immediately after mammography	128/272 (47%) pain and discomfort
Roworth et al., 1993 (133)	3b	2580	50–64 y	Cross-sectional	3-point discomfort scale and 2-point pain scale immediately after mammography	276/2580 (10%) pain, 2134/2580 (82%) discomfort
Rutter et al., 1992 (134)	3b	597	50–64 y	Cross-sectional	2-point pain scale, 16 adjectives from McGill pain inventory immediately after mammography	206/597 (37%) discomfort, 37/597 (6%) pain
Sapir et al., 2003 (135)	3b	399	26–75 y	Cross-sectional	5-point pain scale immediately after mammography	307/399 (76%) pain
Sharp et al., 2003 (136)	3b	200	Mean, 59 y	Cross-sectional	10-point pain scale immediately after mammography	56/200 (28%) pain
Stomper et al., 1988 (137)	3b	1847	Median, 50 y	Cross-sectional	6-point pain scale immediately after mammography	720/1847 (38%) mild discomfort, 18/1847 (0.9%) severe discomfort, 18/1847 (0.9%) moderate pain
Walter et al., 2001 (138)	3b	216	Mean, 81 y	Chart review	Chart documentation of pain or psychological distress	91/216 (42%) pain, anxiety, or depression

\* EBMR = Evidence-based Medicine Review; MPQ = McGill Pain Questionnaire; NA = not available; NRS = Numeric Rating Scale; VAS = visual analogue scale.