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Screening for Breast Cancer: A Systematic Review to Update the 2009 U.S. Preventive Services Task Force Recommendation

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Structured Abstract

Background: In 2009, the U.S. Preventive Services Task Force (USPSTF) recommended biennial screening mammography for women age 50 to 74 years, and based decisions for earlier screening on individual patient context and values. Evidence was insufficient to recommend screening beyond age 75.

Purpose: To systematically update the 2009 USPSTF review on screening for breast cancer in average risk women age 40 years and older.

Data Sources: The Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews (through December 2014), Ovid MEDLINE (through December 2014), and reference lists were searched for relevant studies. Additional data were obtained from investigators of randomized trials and from the Breast Cancer Surveillance Consortium.

Study Selection: Randomized controlled trials and observational studies of breast cancer screening in asymptomatic women age 40 and older reporting breast cancer mortality, all-cause mortality, advanced breast cancer, treatment morbidity, and the harms of screening.

Data Extraction: One investigator abstracted data and a second investigator confirmed accuracy. Investigators independently dual-rated study quality and applicability using established criteria. Discrepancies were resolved through a consensus process.

Data Synthesis: A meta-analysis of screening trials with updated data from the Canadian (CNBSS-1 and CNBSS-2), Swedish Two-County Study, and Age trials indicated breast cancer mortality reductions for age 39 to 49 years (relative risk [RR] 0.88; 95% confidence interval [CI], 0.73 to 1.003; 9 trials; 4 deaths prevented/10,000 over 10 years); 50 to 59 years (RR 0.86 [95% CI, 0.68 to 0.97]; 7 trials; 8/10,000); 60 to 69 years (RR 0.67 [95% CI, 0.54 to 0.83]; 21/10,000); and 70 to 74 years (RR 0.80 [95% CI, 0.51 to 1.28]; 3 trials; 13/10,000). Risk reduction was 25 to 31 percent for women age 50 to 69 years across several observational studies, with similar reductions for women age 40 to 49 in two studies. Trials indicated no statistically significant reductions in all-cause mortality with screening. Risk for higher-stage breast cancer was reduced for age 50 years and older (RR 0.62 [95% CI, 0.46 to 0.83]; 3 trials), but not for age 39 to 49 years (RR 0.98 [95% CI, 0.74 to 1.37]; 4 trials). The majority of cases from screening were ductal carcinoma in situ and early stage, and screening resulted in more mastectomies (RR 1.20 [95% CI, 1.11 to 1.30]; 5 trials) and radiation (RR 1.32 [95% CI, 1.16 to 1.50]; 2 trials).

Younger women and those with risk factors had more false-positive results and recommendations for additional imaging and biopsies. Cumulative rates for false-positive mammography results over 10 years were 61 percent for annual and 42 percent for biennial screening; rates for biopsy were 7 to 9 percent for annual and 5 to 6 percent for biennial screening. Estimates of overdiagnosis ranged from 11 to 22 percent in trials; and 1 to 10 percent in observational studies. Some women with false-positive results or pain experienced distress and were less likely to return for their next mammogram. Tomosynthesis with mammography reduced recalls (16/1000), but increased biopsies (1.3/1000) and cancer detection (1.2/1,000).

The number of deaths due to radiation induced cancer from screening with digital mammography was estimated through modeling as between 2 to 11 per 100,000 depending on age at onset and screening intervals.

Limitations: Limited to English-language articles; the number, quality, and applicability of studies varied widely. Trials of mammography screening reflect imaging technologies and cancer treatment therapies that are not currently in use. Studies are lacking on screening effectiveness based on risk factors, intervals, and modalities; and on screening modalities relevant to women who are not high-risk.

Conclusions: Breast cancer mortality is reduced with mammography screening, although estimates are of borderline statistical significance, the magnitudes of effect are small for younger ages, and results vary depending on how cases were accrued in trials. Higher stage tumors are also reduced with screening for age 50 years and older. False-positive results are common in all age groups, and are higher for younger women and those with risk factors. Approximately 11 to 22 percent of cases may be overdiagnosed. Observational studies indicate that tomosynthesis with mammography reduces recalls, but increases biopsies and cancer detection. Mammography screening at any age is a tradeoff of a continuum of benefits and harms.

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Chapter 1. Introduction

Purpose and Previous U.S. Preventive Services Task Force Recommendation

This report will be used by the U.S. Preventive Services Task Force (USPSTF) to update their 2009 recommendation on screening for breast cancer.[1] In 2009, the USPSTF recommended biennial screening mammography for women ages 50 to 74 years (B recommendation). They determined that the decision to start regular, biennial screening mammography before the age of 50 years should be an individual one and take patient context into account, including the patient's values regarding specific benefits and harms (C recommendation). The USPSTF concluded that evidence was insufficient to assess the additional benefits and harms of screening mammography in women age 75 years or older (I Statement).

The USPSTF also recommended against teaching breast self-examination (BSE) as a cancer screening strategy (D recommendation), and concluded that evidence was insufficient to assess the additional benefits and harms of clinical breast examination (CBE) beyond screening mammography in women age 40 years or older (I Statement). The USPSTF concluded that the evidence was insufficient to assess the additional benefits and harms of either digital mammography or magnetic resonance imaging (MRI) instead of film mammography as screening modalities for breast cancer (I Statement).

This report updates evidence on the effectiveness of mammography in decreasing breast cancer mortality, all-cause mortality, and advanced breast cancer among women who are not at high risk for breast cancer; harms of screening; and how effectiveness and harms vary by age, risk factors, screening intervals, and screening modalities. This report includes studies relevant to current medical practice in the United States and highlights gaps as well as strengths in evidence. Additional reviews and analyses for the USPSTF are provided in separate reports including systematic reviews of the performance characteristics of screening methods and the accuracy of breast density determination and use of supplemental screening technologies, and a model of radiation exposure.

Condition Definition

Breast cancer is a proliferation of malignant cells that arises in the breast tissue, specifically in the terminal ductal-lobular unit, and represents a continuum of disease ranging from noninvasive to invasive carcinoma.[2] Noninvasive carcinoma, or an in situ lesion, does not invade the surrounding stroma and does not metastasize. Noninvasive lesions are confined to either the duct (ductal carcinoma in situ [DCIS]),[3] or to the lobule (lobular carcinoma in situ [LCIS], now categorized as lobular intraepithelial neoplasia [LIN]).[3] LCIS is considered a marker for increased risk of invasive ductal or lobular breast cancer,[4] while some forms of DCIS are considered precursor lesions for invasive ductal carcinoma. DCIS is heterogeneous and has varying clinical behavior and pathologic characteristics.[5]

Unlike noninvasive lesions, invasive breast cancer invades the basement membrane into the adjacent stroma, and therefore, has metastatic potential. The most common sites of metastasis include adjacent lymph nodes, lung, liver, and bone.[2] Approximately 70 to 80 percent of invasive breast cancer cases are invasive or infiltrating ductal carcinoma and approximately 10 percent are invasive lobular carcinoma.[2] Other less common histologic subtypes of invasive breast cancer include apocrine, medullary, metaplastic, mucinous, papillary, and tubular.[2]

Prevalence and Burden of Disease

Breast cancer is the second most common cancer in women in the United States after non-melanoma skin cancer, and is the second leading cause of cancer death after lung cancer.[6,7] In 2015, an estimated 231,840 women in the United States will be diagnosed with breast cancer and 40,290 will die, representing 14 percent of all new cancer cases and 6.8 percent of all cancer deaths.[8] Incidence rates have been stable over the last 10 years and death rates have been falling approximately 1.9 percent each year between 2002 and 2011. According to lifetime risk estimates for the general population, 12.3 percent of women will develop breast cancer during their lives, and 2.8 percent will die from the disease.[9] The overall 5-year relative survival rate for breast cancer in 2006 was 90.6 percent, and an estimated 2,899,726 women were living with breast cancer in the United States in 2011.[8]

Etiology and Natural History

Current research on the etiology of breast cancer focuses on clarifying the role of both inherited and acquired mutations in oncogenes and tumor suppressor genes and the consequences these mutations may have on the cell cycle, as well as investigating various prognostic biological markers. The contribution of external influences, such as environmental exposures, have on regulatory genes is unclear. Currently, no single environmental or dietary exposure has been found to cause a specific genetic mutation that causes breast cancer. Exposure to both endogenous and exogenous estrogen is important in tumorigenesis and growth. Other potential causes of breast cancer include inflammation and virally mediated carcinogenesis.[10]

Whether DCIS is a precursor lesion or a marker of risk is uncertain. With the widespread use of screening mammography in the United States, nearly 90 percent of DCIS cases are now diagnosed only on imaging studies, most commonly by the presence of microcalcifications. These represent approximately 23 percent of all breast cancer cases.[11] Although DCIS is the most common type of noninvasive breast cancer, its natural history is poorly understood. Older studies of palpable DCIS lesions indicated that 14 to 53 percent of untreated DCIS progressed to invasive cancer over 8 to 22 years.[12-14] The rate of progression of mammography detected DCIS is not known. Characteristics associated with subsequent invasive breast cancer include young age, black race, indication for biopsy, tumor characteristics such as high nuclear grade, comedo-type necrosis, tumor size;[15] and high breast density.[16]

Risk Factors

Although many risk factors have been associated with breast cancer in epidemiologic studies, most relationships are weak or inconsistent.[17] Most women who develop breast cancer have no identifiable risk factors beyond sex and age. However, a small number of clinically significant risk factors are associated with high risks for breast cancer and can be used to identify women who may be eligible for screening outside routine screening recommendations. These include women with *BRCA1* or *BRCA2* mutations and their untested first-degree relatives,[18] and other hereditary genetic syndromes associated with more than a 15 percent lifetime risk, including Li-Fraumeni syndrome, Cowden syndrome, or hereditary diffuse gastric cancer.[19] Previously diagnosed high-risk breast lesions, including LCIS, atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), flat epithelial atypia, papillary atypia, and apocrine atypia significantly increase risk for breast cancer.[20] Estimated 10-year breast cancer risks associated with breast lesions include 17.3 percent with ADH, 20.7 percent with ALH, 23.7 percent with LCIS, and 26.0 percent with severe ADH.[20] Also, women with a history of high-dose radiation therapy to the chest between the ages of 10 to 30 years, such as for treatment of Hodgkin lymphoma, are also considered at high risk.[19]

Family history of breast cancer, particularly among first-degree relatives, is also an important risk factor. Approximately 5 to 10 percent of women with breast cancer have a mother or sister with breast cancer, and up to 20 percent have either a first-degree or a second-degree relative with breast cancer.[21-25] The degree of risk associated with family history varies according to familial patterns of disease. Estimates of lifetime risk of breast cancer determined by kindred analysis of over 15 or 20 percent are considered high.

Additional factors that increase risk to lower degrees than described above include older age; current use of menopausal hormone therapy using combined estrogen and progestin regimens;[26] current use of oral contraceptives;[17] nulliparity;[17] high body mass index (BMI) for postmenopausal women only;[27] and higher breast density.[28] Breast density is a radiographic measure of breast tissue that is associated with increased risk for breast cancer and reduced mammography sensitivity. Breast density is currently described by four categories: almost entirely fat, scattered fibroglandular densities, heterogeneously dense, and extremely dense.[29] Approximately 40 percent of women have heterogeneously dense breasts and 10 percent have extremely dense breasts. Increased breast density is more common among younger women.[30] Compared with women with scattered fibroglandular densities, hazard ratios for breast cancer are 1.6 for premenopausal women with heterogeneously dense breasts and 2.0 for those with extremely dense breasts.[28]

Empiric models that incorporate several of these risk factors have been developed to predict breast cancer risk for individual women.[31] All of the models include age and number of first-degree relatives with breast cancer into their calculations, but vary in their complexity. Studies of their diagnostic accuracy indicate that the models are poor predictors of an individual's risk.[31] It remains unclear how to apply these models to selecting candidates for breast cancer screening.

Rationale for Screening and Screening Strategies

Breast cancer has a known asymptomatic phase that can be identified with mammography and could be more effectively treated in early stages than when clinical signs and symptoms present. While screening may not reduce mortality for some aggressive cancer types,[32] and has less impact on slowly progressive types,[33,34] survival may be improved for other types of cancer when they are identified at localized stages.

Interventions and Treatment

Current treatment for breast cancer in the United States involves a combination of therapies including surgery, radiation, hormonal therapy, and chemotherapy based on stage (0 to IV) and status of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2).[35] Clinical staging using the American Joint Committee on Cancer (AJCC) TNM system guides treatment and informs prognosis (**Table 1**).[36] In this system, stage grouping is based on tumor size (T), lymph node involvement (L), and presence of metastasis (M). Main categories are expressed as DCIS (stage 0), localized (Stage I, IIA, IIB, or T3, N1, M0), locally advanced or regional (Stage III), and metastatic disease (Stage IV). Survival varies by stage, and the 5-year relative survival rates for breast cancer in the United States are 99 percent with localized, 84 percent with regional, and 23 percent with metastatic disease.[9]

Treatment regimens are highly individualized according to each patient's clinical status and preferences (**Table 2**). In addition, many patients are recruited to clinical trials of new regimens. Surgical therapies for DCIS and localized and regional invasive cancer include lumpectomy or total mastectomy with or without reconstruction. Surgery also involves sentinel lymph node biopsy for selected cases of DCIS, axillary node staging for localized disease, and axillary node dissection for regional disease. Surgical therapy is performed in only selected cases of metastatic disease. Radiation therapy generally follows surgery. Whole breast radiation may be added to lumpectomy for DCIS, localized, and regional disease. Radiation to the lymph nodes and chest wall, if involved, may be indicated for localized and regional disease.

Endocrine treatment is recommended for ER-positive patients at all stages. Usual regimens include 5 years of tamoxifen for DCIS, 10 years of extended adjuvant hormonal therapy (tamoxifen with or without aromatase inhibitors) for localized and regional disease, and additional regimens for metastatic disease.[35,37] Premenopausal ER-positive patients with metastatic disease may also consider ovarian ablation or suppression.

Systemic neoadjuvant/adjuvant chemotherapy for invasive cancer is determined by ER, PR, and HER2 status, and predictive tests for chemotherapy benefit.[38,39] Chemotherapy is given after surgery for localized disease. Patients with regional disease generally receive chemotherapy before or after breast surgery and incorporate one year of trastuzumab (Herceptin). Chemotherapy for metastatic disease involves more complicated regimens depending on receptor status, tumor biology, and initial responses.[35,38-40]

Current Clinical Practice

Mammography screening in the United States is generally opportunistic, unlike the many screening programs organized as public health services in other countries. Mammography is provided by radiology units of hospitals and outpatient facilities as well as by stand-alone imaging centers. Services range from imaging alone to comprehensive services that may be integrated within breast centers. As such, there is considerable variation in current clinical practice depending on the patient population, provider practice, community, and institutional policy, although national accreditation and professional groups define practice standards and quality benchmarks to assure consistency of care.

While there is general consensus that mammography screening is beneficial for many women, conflicting screening recommendations have led to practice variability. Issues lacking consensus include the optimal ages to begin and end routine screening; optimal screening intervals; defining and balancing the benefits of screening with potential harms; appropriate use of various imaging modalities including supplemental technologies; values and preferences of women regarding screening; and how all of these considerations vary depending on a woman's risk for breast cancer.

Despite variation in clinical practices and guidelines, rates of screening mammography in the United States are generally high and have remained relatively stable for the past decade.[41,42] Data from the HEDIS® Health Plan measure set indicate that mammography screening between 2009 and 2011 was performed by 71 percent of eligible women covered by commercial plans, 69 percent for Medicare plans, and 51 percent for Medicaid plans.[43] The Patient Protection and Affordable Care Act mandates insurance coverage for annual screening mammography beginning at age 40 years with no co-pay or deductible charges. However, this coverage applies to only the annual screening mammogram, and subsequent related services are not similarly covered.

Breast cancer screening for women without risk factors indicating high risk is conducted using periodic mammography (**Figure 1**). Digital mammography has generally replaced film in the United States, and newer technologies, such as digital tomosynthesis, are rapidly disseminating. Imaging modalities are further described in **Table 3**. In general, approximately 90 percent of women in a screening round have normal mammography results and are advised to return in 1 or 2 years, while 10 percent are recalled for additional imaging to visualize areas of concern identified on the screening mammogram.[44] Additional imaging may involve special mammographic views, ultrasound, MRI, or tomosynthesis. Approximately 10 percent of women having additional imaging are identified with suspicious breast lesions requiring biopsies.[44]

Additional imaging after screening mammography has traditionally been reserved to further visualize incompletely evaluated breast lesions. However, in response to public concerns about breast density, 21 states have passed breast density notification legislation requiring that reports of patients' breast density be provided to them with their mammography results.[45] Most laws encourage patients to have a discussion of additional screening options with their primary physicians and some mandate insurance coverage for supplemental imaging, including screening MRI, ultrasound, and tomosynthesis. Descriptive studies of supplemental imaging for patients

with dense breasts, in addition to other risk factors in some studies, suggest increased rates of cancer detection, but also increased false-positive results with MRI and ultrasound.[46-50] Randomized trials of the effectiveness of supplemental imaging have not been reported.[51]

Screening MRI is recommended for certain high-risk groups, including women with *BRCA1* or *BRCA2* mutations and their untested first-degree relatives, women with greater than 20 percent lifetime risk of developing breast cancer as defined by risk prediction models, and women who have received high-dose radiation therapy to the chest between the ages of 10 and 30 years.[52] Use of MRI for screening women who are not at high risk for breast cancer is not recommended,[52] and experts suggest that MRI should not be performed in settings where the capacity for MR-guided biopsy does not exist. Currently, there are no studies investigating MRI use in women who are not at high risk, and none showing decreased mortality with MRI screening for women at any risk level.

If tissue sampling is recommended, a biopsy is performed (**Figure 2**). The type of biopsy is based on the characteristics of the lesion as well as patient and physician preferences. Current biopsy techniques include fine-needle aspiration (FNA), stereotactic core biopsy (for nonpalpable, mammographic lesions), ultrasound-guided or MRI-guided core biopsy, non-image-guided core biopsy (for palpable lesions), incisional biopsy, or excisional biopsy. These techniques vary in the level of invasiveness and amount of tissue acquired, impacting their yield and patient experience. Although more invasive than FNA, core biopsies, as well as incisional and excisional biopsies, offer the pathologist a sample with intact cellular architecture, and thereby allow additional pathologic examination of the breast tissue. Testing includes examination of cellular receptors (e.g., ER/PR, HER2/neu receptor), as well as identification of tumor type and grade.[53,54] Ultrasound of the ipsilateral axilla has become a common practice when malignancy is suspected on imaging, and can help guide FNA or core biopsy of abnormal axillary lymph nodes. This additional information contributes to appropriate treatment planning for a patient who is newly diagnosed with breast cancer, and often allows for definitive surgery to be completed with a single-stage procedure.[55]

Recommendations of Other Groups

The American Cancer Society recommends yearly mammograms starting at age 40 and continuing for as long as the woman is in good health. BSEs are optional for women beginning in their 20s, while CBEs are recommended about every 3 years for women in their 20s and 30s.[56]

The American Academy of Family Physicians (AAFP) recommends the decision to conduct screening mammography prior to age 50 should be individualized and take into consideration the patient's context and risk factors. For women between ages 50 and 74, the AAFP recommends biennial screening in addition to recommending against clinicians teaching women BSE.[57]

The American Congress of Obstetrics and Gynecologists (ACOG) recommends that mammography screening be offered annually to women beginning at age 40. ACOG recommends annual CBE for women ages 40 and older, and every 1 to 3 years for women ages 20 to 39. ACOG also endorses educating women ages 20 and older regarding breast self-

awareness.[58]

The American College of Radiology (ACR) recommends annual screening mammography for asymptomatic women 40 years of age and older.[59] The decision as to when to stop routine mammography screening should be made on an individual basis by each woman and her physician based on a woman's overall health.

The National Comprehensive Cancer Network (NCCN) recommends annual screening mammography, clinical breast exam, and breast awareness for asymptomatic, average risk women age 40 years and older.[60]

Chapter 2. Methods

Key Questions and Analytic Framework

Using the methods developed by the USPSTF,[61,62] the USPSTF and the Agency for Healthcare Research and Quality (AHRQ) determined the scope and key questions for this review. Investigators created an analytic framework outlining the key questions and included patient populations, interventions, and outcomes (**Figure 3**).

The target population for the USPSTF recommendation served as the focus of the systematic review. This population includes women age 40 years and older and excludes women with physical signs or symptoms of breast abnormalities and those at high-risk for breast cancer whose surveillance and management are beyond the scope of the USPSTF's recommendations for prevention services. Women at high-risk are those with risk factors known to increase their risks of breast cancer to levels that make them eligible for screening or followup services outside of recommendations for women without these risk factors. Women at high-risk include those with pre-existing breast cancer; *BRCA1* or *BRCA2* mutations and their untested first-degree relatives[18] and other hereditary genetic syndromes associated with more than a 15 percent lifetime risk of developing breast cancer (including Li-Fraumeni syndrome, Cowden syndrome, or hereditary diffuse gastric cancer);[19] previously diagnosed high-risk breast lesions (DCIS, LCIS, ADH, ALH); and high-dose radiation therapy to the chest between the ages of 10 and 30. Women with lower risks for breast cancer are generally eligible for routine screening and are relevant to the USPSTF's recommendations.

Key Questions

1. What is the effectiveness of routine mammography screening in reducing breast cancer–specific and all–cause mortality, and how does it differ by age, risk factors, and screening intervals?
2. What is the effectiveness of routine mammography screening in reducing the incidence of advanced breast cancer and treatment-related morbidity, and how does it differ by age, risk factors, and screening intervals?
3. How does the effectiveness of routine breast cancer screening in reducing breast cancer–specific and all-cause mortality vary by different screening modality?
4. How does the effectiveness of routine breast cancer screening in reducing the incidence of advanced breast cancer and treatment-related morbidity vary by different screening modality?
5. What are the harms of routine mammography screening, and how do they differ by age, risk factors, and screening intervals?
6. How do the harms of routine breast cancer screening vary by different screening modality?

Risk factors considered in this review are common among women who are not at high-risk for breast cancer as defined above. These include family history of breast cancer (not including genetic syndromes described above), breast density, race/ethnicity, menopausal status, current

use of menopausal hormone therapy or oral contraceptives, prior benign breast biopsy, and BMI for women older than age 50 years.

Outcomes related to benefits included in this review are reduced breast cancer mortality, all-cause mortality, advanced breast cancer, and morbidity related to breast cancer treatment. Other outcomes, such as increased breast cancer awareness and peace of mind with screening, are not included. Treatment-related morbidity includes physical adverse effects of treatment, quality of life measures, and other measures of impairment. Screening modalities include mammography (digital, tomosynthesis), MRI, ultrasound, and CBE (alone or in combination). Only breast imaging technologies approved for screening by the U.S. Food and Drug Administration are included in this review, consistent with the scope of the USPSTF.

Harms include false-positive and false-negative mammography results, false reassurance, anxiety and worry, overdiagnosis and resulting overtreatment, and radiation exposure. Overdiagnosis refers to women receiving a diagnosis of DCIS or invasive breast cancer who had abnormal lesions that were unlikely to become clinically evident during their lifetimes in the absence of screening. Overdiagnosis may have more effect on women with shorter life expectancies because of age or comorbid conditions.

Contextual Questions

Three contextual questions were also requested by the USPSTF to provide additional background information. Contextual questions are not reviewed using systematic review methodology but are addressed using the strongest, most relevant evidence. These include the following.

1. What are the rates of specific adverse effects of current treatment regimens for invasive breast cancer and DCIS in the United States?
2. What are the absolute incidence rates of DCIS and localized and advanced invasive breast cancer in screened and nonscreened populations in the United States?
3. How do women weigh the harms and benefits of screening mammography and how do they use this information in their decisions to undergo screening?

Search Strategies

In conjunction with the systematic review investigators, a research librarian searched the Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Ovid MEDLINE (all searches through December 2014) for relevant studies and systematic reviews. Reference lists of articles were also reviewed. Search dates varied because some key questions (Key Questions 1, 3, 5, 6) were included in the 2009 systematic review and required only updates of studies published since the previous search in 2008. Other key questions were not addressed by the previous review and required searches that covered longer time periods (Key Questions 2 and 4, and cohort studies for Key Questions 1 and 3). These searches extended to 1996 because this corresponds to the last time the USPSTF evaluated similar data, and represents a period when practice was shifting to digital mammography in the United States. The contextual questions have a shorter time period for searches because they require the most

current data to be clinically relevant. Search strategies are available in **Appendix A1**.

In addition, unpublished data from the Breast Cancer Surveillance Consortium (BCSC) on screening with digital mammography were evaluated. The BCSC is a collaborative network of mammography registries with linkages to pathology databases and tumor registries across the United States supported by the National Cancer Institute (NCI).[63,64] These data draw from community samples that are representative of the larger, national population and may be more applicable to current practice in the United States than other published sources.

Also, unpublished updated data from the Canadian and Swedish Two-County randomized controlled trials (RCTs) were obtained from the trial investigators.

Study Selection

At least two reviewers independently evaluated each study to determine inclusion eligibility. Studies were selected on the basis of prespecified inclusion and exclusion criteria developed for each key question (**Appendix A2**). The selection of studies is summarized in a flow diagram (**Appendix A3**). **Appendix A4** lists excluded studies with reasons for exclusion.

Studies of women at high-risk for breast cancer as defined above or with previously diagnosed breast cancer were not included. Studies most clinically relevant to practice in the United States were selected over studies that were less relevant. Relevance was determined by practice setting, population, date of publication, use of technologies and therapies in current practice, and other factors. Also, studies of higher-quality and those with designs ranked higher in the study design-based hierarchy of evidence, such as RCTs over observational studies, were emphasized because they are less susceptible to bias.

To determine the effectiveness of screening, RCTs, observational studies of screening cohorts, and systematic reviews of screening with mammography (film, digital, tomosynthesis) and other modalities (MRI, ultrasound, CBE alone or in combination) were included. Valid comparisons evaluated outcomes of groups of women exposed to screening versus nonscreening, not comparisons of detection methods that do not capture a woman's longitudinal screening experience (e.g., rates of screen-detected vs. nonscreen-detected cancer).

Outcomes included breast cancer specific and all-cause mortality (Key Questions 1 and 3) and advanced breast cancer and treatment-related morbidity (Key Questions 2 and 4). While advanced breast cancer is classified as metastatic disease (Stage IV) by the AJCC TNM system,[36] most screening studies defined advanced breast cancer at much lower thresholds, including Stage IIA or higher, lymph node positive disease, or tumor size of 20 mm or larger.[65] Studies providing outcomes specific to age, risk factors, screening intervals, and modalities were preferred over studies providing general outcomes, when available. Risk factors conferring a moderate, as opposed to high, level of risk were included as listed previously.[17,66]

The harms of screening were determined from several study designs and data sources. For mammography, searches focused on recently published systematic reviews and meta-analyses of

radiation exposure, pain during procedures, patient anxiety and other psychological responses, consequences of false-positive and false-negative mammography results, and overdiagnosis. Specific searches for primary studies published more recently than the included systematic reviews and meta-analyses were also conducted.

Performance characteristics of screening methods (e.g., sensitivity, specificity, positive predictive value); accuracy of breast density determination; use of supplemental screening technologies; and a new model of radiation exposure are presented in separate reports. Studies of cost-effectiveness of screening were not addressed in this update.

Data Abstraction and Quality Rating

Details of the study design, patient population, setting, screening method, interventions, analysis, followup, and results were abstracted by one investigator and confirmed by a second. Two investigators independently applied criteria developed by the USPSTF[61,62] to rate the quality of each study as good, fair, or poor for studies designed as RCTs, cohort studies, case-control studies, and systematic reviews (**Appendix A5**). USPSTF criteria to rate other study designs included in this review are not available. Discrepancies were resolved through consensus. Only data from RCTs rated fair- or good-quality were included in the meta-analyses.

Meta-Analysis of Mammography Screening Trials

Several meta-analyses were conducted to determine more precise summary estimates for the effectiveness of breast cancer screening when adequate data were reported by trials. Clinical and methodological diversity and statistical heterogeneity were considered to determine the appropriateness of meta-analysis. All outcomes (breast cancer mortality, all-cause mortality, and advanced cancer occurrence) were binary. A random-effects model was used to combine relative risks (RRs) as the effect measure of the meta-analyses, while incorporating variation among studies. A profile-likelihood model was used to combine studies in the primary analyses.[67] The presence of statistical heterogeneity among the studies was assessed by using the standard Cochran's chi-square test, and the magnitude of heterogeneity by using the I^2 statistic.[68]

To account for clinical heterogeneity and obtain clinically meaningful estimates, the analyses were stratified by age group (39 to 49 years, 50 to 59 years, 60 to 69 years, 70 to 74 years, or ≥75 years), whenever possible. Investigators of two recently published updates of trials provided additional age-stratified data for the meta-analysis.[69,70] Two definitions were used to evaluate advanced breast cancer outcomes (stage and tumor size).

For breast cancer mortality, two methods of including cases in estimates were used because each offers advantages and disadvantages, and may provide additional insights to the interpretation of results. The long case accrual method counts all of the breast cancer cases contributing to breast cancer deaths. In this method, the case accrual time is equivalent to or close to the followup time. The short case accrual method includes only deaths that occur among cases of breast cancer diagnosed during the screening intervention period, and in some trials, within an additional

defined case accrual period. These methods are further described in the results section.

To facilitate the interpretation of the combined RR for breast cancer mortality, the absolute rate reduction for 100,000 women-years of followup (i.e., 10,000 women followed for 10 years) was calculated for each age group based on the combined RR and the combined cancer rate of the control group. The combined cancer rate of the control group was obtained using a random effects Poisson model for each age group using data from the trials. All analyses were performed using Stata/IC 13.1 (StataCorp, College Station, TX).

Analysis of BCSC Data

Background information and additional details about methods of the BCSC are described in **Appendix A6**. Data were obtained from the BCSC Statistical Coordinating Center for 405,191 women ages 40 to 89 years who had routine screening with digital mammography during 2003 to 2011 at participating facilities at six BCSC breast imaging registries. Results were stratified by age in decades to determine age-specific outcomes. Routine screening required at least one mammography examination within the previous 2 years (defined as 30 months). For women with several mammography examinations during this time period, one result was randomly selected to be included in the calculations. These data comprise a defined subset of BCSC data intended to represent the experience of a cohort of regularly screened women without histories of breast cancer or current breast symptoms.

Screening mammography examinations were those designated as such by the radiologist or radiology technologist performed more than 9 months after a previous imaging examination in women without histories of breast cancer, breast augmentation, or mastectomies. This approach eliminated the possibility that a woman's first mammogram was included because first mammograms are more likely to be read as false positives. Unilateral exams were also excluded. Mammography information included Breast Imaging Reporting and Data System (BI-RADS) breast density, assessment scores, and recommendations for further workup. In addition, prior to each mammography examination, women completed questionnaires that included demographic and medical history information, including previous mammography information.

Data include the numbers of positive and negative mammography results and, of these, the numbers of normal screening and false-negative results based on followup data within 1 year of mammography screening and before the next screening examination. Positive versus negative initial and final results were defined according to standardized terminology and assessments of the American College of Radiology BI-RADS 4th edition atlas[71] and BCSC standard definitions.[72] Each screening mammography examination was given an initial BI-RADS assessment based on the screening views only. Positive initial results included four assessment categories: needs additional imaging evaluation (category 0), probably benign (category 3) with a recommendation for immediate work-up (these were treated as a category 0 based on the recommendation), suspicious abnormality (category 4), or highly suggestive of malignancy (category 5).[73] Negative results included assessments of negative (category 1) or benign findings (category 2), or category 3 without a recommendation for immediate work-up.

For women who had positive screening mammography results, data were evaluated on the number of women receiving a recommendation for additional imaging, the number receiving a recommendation for biopsy, and diagnoses including invasive breast cancer, DCIS, and no cancer. Recommendation for biopsy was defined as a positive final result after all imaging including work-up of an abnormal screening examination. Positive final results included BI-RADS assessments of 4 or 5 or 0 with a recommendation for biopsy.[73] Negative final results included an assessment of 1, 2, or 3 or 0 with a recommendation for normal or short-interval followup or clinical exam.

From these data, age-specific rates (numbers per 1,000 women per screening round) of invasive breast cancer, DCIS, false-positive and false-negative mammography results, recommendations for additional imaging, and recommendations for biopsies were calculated.

Age groups were further divided into sub-categories to determine whether outcomes differed by time since last mammography screening or risk factors. Two measures of time since last mammography screening were evaluated to represent broad and narrow estimates of one versus two years (9 to 18 versus 19 to 30 months; 11 to 14 versus 23 to 26 months).

Risk factors included those mostly commonly associated with breast cancer.[17] These included first-degree relatives with breast cancer (none, ≥1); breast density (almost entirely fat, scattered fibroglandular densities, heterogeneously dense, extremely dense); benign breast biopsy (none, previous); race/ethnicity (white, black, Asian, Hispanic, other); menopausal status (pre, peri, postmenopausal); menopausal hormone therapy use (none, combination [estrogen with progestin], estrogen only); oral contraceptive use (no current use, current use), and body mass index (BMI) (<25, 25 to <30, ≥30 kg/m^2). Since the BCSC data do not include information on types of menopausal hormone therapy, the analysis assumes that a woman with a uterus uses combination therapy, while a woman without a uterus uses estrogen-only therapy. The main analysis analyzed three categories of breast density, combining almost entirely fat and scattered fibroglandular densities into one group. As a sensitivity analysis, density was analyzed in three additional ways: (1) three categories, combining heterogeneously dense and extremely dense into one group; (2) four separate BI-RADS categories; and (3) two categories that combine almost entirely fat and scattered fibroglandular densities into one group and heterogeneously dense and extremely dense into another group.

From these data, age-specific rates (numbers per 1,000 women per screening round) of false-positive and false-negative mammography results, recommendations for additional imaging, and recommendations for biopsies were calculated and comparisons by age, time since last mammography screening, and risk factors were determined. To account for correlation among mammograms interpreted at the same radiology facility, robust standard errors from logistic regression were estimated using generalized estimating equations with an independence working correlation matrix. Differences between groups were assessed by 2-sided P-values with 95% confidence intervals (CIs).

Data Synthesis

The aggregate internal validity (quality) of the body of evidence for each key question was assessed ("good," "fair," "poor") using methods developed by the USPSTF, based on the number, quality and size of studies, consistency of results between studies, and directness of evidence.[61,62]

External Review

The draft report was reviewed by content experts from multiple disciplines, USPSTF members, AHRQ Project Officers, and collaborative partners and revised prior to finalization (**Appendix A7**).

Response to Public Comment

A draft version of the evidence report was posted for public comment on the USPSTF website from April 18 to May 18, 2015. Comments from 13 contributors were directly relevant to the systematic review, while comments from other contributors were outside its scope, or concerned the recommendation statement, CISNET model, or other evidence reports. Most comments addressed four major issues detailed below, while additional comments suggested adding studies that were either already included or were previously considered, but did not meet prespecified inclusion criteria; or correcting minor errors that have since been corrected.

Inclusion of Observational Studies

The evidence report includes nearly 200 observational studies of breast cancer screening including 83 studies of benefits. Results of studies of the effectiveness of screening in reducing breast cancer mortality are reported for both observational studies and RCTs. For women age 50 to 69 years, the trials indicated statistically significant reductions in breast cancer mortality ranging from 0.78 to 0.81 depending on whether short or long case accrual methods were used. Observational studies indicated reductions of 0.69 to 0.75. For women age 40 to 49, few data from observational studies were available because most European countries collecting these data do not screen younger women. For women age 70 and older, data from both RCTs and observational studies were not available.

RCTs are the least biased study design for determining efficacy/effectiveness, and provide a stronger body of evidence than observational studies. When RCTs and studies of other designs have similar results, such as breast cancer mortality reduction for women age 50 to 69 years, the body of evidence is stronger. Observational studies are subject to important biases that limit their use in determining effectiveness. Most importantly, they lack comparability of comparison groups that is only attainable through randomization. Many observational studies that compare characteristics of breast cancer diagnoses between screened and unscreened women provide comparisons between screen-detected and nonscreened-detected cases. This approach categorizes all cancer cases identified outside of a screening mammogram as nonscreen-detected,

even though a woman may have had prior screening mammography.

In RCTs, intension-to-screen analysis is essential to determining efficacy/effectiveness, and is comparable to intension-to-treat analysis for drug trials. Data from trials not using intension-to-screen analysis, or from observational studies, provide outcomes for women who self-select screening. While outcomes from women who self-select screening may be useful for planning health care services, they do not provide valid measures of efficacy/effectiveness. This is a major difference between how evidence-based guideline groups and some professional societies interpret the research literature.

Inclusion of RCTs

The evidence review describes the RCTs of screening and their limitations in detail. No trials met criteria for good quality (all RCTs in the meta-analysis were fair-quality; a poor-quality trial was excluded).

The meta-analyses of RCTs for breast cancer mortality outcomes use two methods in order to more precisely explain the results of the trials and provide a range of outcomes. There are advantages and disadvantages to these methods, and these are described in the evidence review. While both methods have been used for individual trials and for some of the Swedish trials collectively, no other systematic reviews have taken this rigorous approach across all trials. Results of some of the trials appear in both estimates because the trial investigators only published short case accrual results. Rather than eliminate trials from the meta-analysis, the "longest followup available" from each trial was included and those based on short case accrual are clearly indicated (this was also the approach in the 2009 meta-analysis[44]).

Regarding outcomes related to advanced breast cancer, most of the diagnostic outcomes of the trials were based on early stages of disease (Stage IIA or localized), not advanced. To address the key question about prevention of advanced disease, the meta-analysis used the most advanced disease categories available from the trials. These results indicated reduced risk with screening for women age 50 and older. The connection between being diagnosed with advanced breast cancer and dying is not a key question of this evidence review. This link is acknowledged in the analytic framework.

Screening Intervals

None of the RCTs were designed to evaluate screening intervals. The observational data, including studies from the BCSC, are based on women who self-select screening and adhere, or not, to specific periods of time between screening. Comparisons between women who electively screen annually versus biennially are inherently biased because these women differ in many ways. Estimates from BCSC data are approximations that reflect opportunistic screening in a fluctuating population of women whose information was collected by the participating registries. The BCSC data need to be interpreted with these limitations in mind.

Harms

The studies on overdiagnosis are described in detail in the evidence review and the general conclusion is that they are too methodologically heterogeneous to provide reliable estimates. Until a consensus definition with common metrics is determined, these estimates are uncertain.

Chapter 3. Results

Overview of the RCTs of Screening

Eight main RCTs of mammography screening provide outcomes that address several key questions for this review. Trials involving over 600,000 women have been conducted in the United States, Canada, United Kingdom, and Sweden. These include the Health Insurance Plan of Greater New York (HIP) trial,[74] Canadian Breast Cancer Screening Study 1 (CNBSS-1),[75,76] Canadian Breast Cancer Screening Study 2 (CNBSS-2),[77,78] United Kingdom Age trial,[79] and four from Sweden, including the Stockholm trial,[80] Malmö Mammographic Screening Trial (referred to separately as MMST I and MMST II),[81] Gothenburg trial,[82] and Swedish Two-County Study (referred to separately as Östergötland and Kopparberg).[83] All of these trials met criteria for fair quality and were included in this report. An additional trial, the Edinburgh trial,[84,85] was not included in this review because of its inadequate randomization, introducing high risk of bias and limiting any inferences.

Updates of three trials provided new data for this report,[69,70,86] although only the Canadian and Age trials provided published results that were stratified by age groups.[69,86] Age-stratified results for the Swedish Two-County Study were provided by the trial investigators (Dr. László Tabár personal communication).

Trials varied in their recruitment of participants, screening protocols, control groups, and sizes (**Table 4**). The HIP trial used direct-exposure film mammography, while all of the other trials used screen-film mammography, and none evaluated digital mammography or tomosynthesis. Five trials examined the effectiveness of screening among women between the ages of 40 and 74 years;[74,80-84] two trials enrolled only women in their 40s;[75,79] and one enrolled only women in their 50s.[77] The four trials from Sweden and the Age trial from the United Kingdom evaluated mammography alone, and the other trials evaluated the combination of mammography and CBE. Overviews of the Swedish trials providing outcome data have also been published.[87,88] The overviews addressed several important study limitations of the Swedish trials including reassessing causes of death in the Swedish Two-County Study with a blinded independent end point committee.

Five trials were randomized at the individual participant level (CNBSS-1, CNBSS-2, HIP, Age, Stockholm, and Malmö); one trial used individual (82%) and cluster (18%) randomization (Gothenburg); and two trials used cluster randomization by community (Swedish Two-County). Breast cancer mortality was the main outcome measure, and all trials evaluated differences between the screening and control groups on an intention-to-screen basis. Seven studies randomized women to an invitation to screening or control group receiving "usual care" at the time the study was conducted. Usual care generally did not include screening mammography, or only at specific age thresholds.

The two Canadian trials enrolled volunteers who underwent a pre-examination with CBE before randomization to the intervention or control groups. The Swedish trials randomized women according to communities. The Age trial recruited women from general practice lists, and the

HIP trial recruited women enrolled in a health insurance plan.

The Gothenburg, Stockholm, Malmö, Swedish Two-County, Age, and HIP trials included DCIS in their breast cancer case reporting, while the Canadian trials included only invasive breast cancer in the latest update. All of the trials provided information on the stage, size, or lymph node involvement of cases; however, these outcomes were reported differently across the trials using various descriptions and levels of severity.

Trials differed in their methods of accrual of breast cancer cases and deaths, influencing the analysis of outcomes. Two methods are provided in this report to help explain discrepancies between estimates (**Figure 4**). The long case accrual method counts all of the breast cancer cases contributing to breast cancer deaths diagnosed during the screening intervention period plus the followup period. This method has been referred to as the "followup" method of analysis by some investigators. While this method includes the most cases, it has the potential to dilute a true benefit because participants from the control group are also screened after the study intervention period ends.

The short case accrual method includes only deaths occurring among cases of breast cancer diagnosed during the screening intervention period, and in some trials, within an additional defined case accrual period. This has been referred to as the "evaluation method" of analysis by some investigators. This method always involves the evaluation of fewer breast cancer cases for mortality outcomes because the duration of case accrual is shorter than for the long case accrual period. This method reduces the risk of contamination in the control group after the screening phase of a trial is completed, but in the absence of concurrent screening, it can introduce bias.

The applicability of the screening trials to current populations and practice has likely decreased over time. All of the trials were conducted in the past when imaging technologies and breast cancer therapies were markedly different than today.[34] Only the HIP trial enrolled women in the United States, however, this trial began 50 years ago. Only women in the Canadian and Age trials, and some women in the Malmö trial, had access to current adjuvant chemotherapies for breast cancer.

In general, women who enroll in trials and attend screening interventions differ from those who do not, underscoring the importance of intention-to-screen analysis to evaluate outcomes. Two trials (HIP, Stockholm) evaluated the differences between women randomized to the intervention group who chose to be screened (attendees) compared with those who did not. In these trials, attendees had higher risks of breast cancer and lower risks of all-cause mortality than non-attendees.[89,90] In the Canadian trials that recruited volunteers from several communities, participants were more educated, had lower parity, and had overall higher risks of breast cancer compared with the general population.[75,77] These findings indicate that women at higher risk of breast cancer but lower risk of all-cause mortality may choose to participate in screening. These are important differences that could influence outcomes.

Key Question 1. What Is the Effectiveness of Routine Mammography Screening in Reducing Breast Cancer–Specific and All-Cause Mortality, and How Does It Differ by Age, Risk Factor, and Screening Interval?

Summary

Randomized Trials of Screening

- Updated results from the CNBSS-1, CNBSS-2, Age, and Swedish Two-County Study trials provided breast cancer mortality outcomes with longer followup than the previous review.
- For women age 39 to 49 years, a meta-analysis of trials comparing mammography screening with nonscreening indicated a combined RR of 0.88 (95% confidence interval [CI], 0.73 to 1.003; 9 trials) using the long case accrual method; and 0.84 (95% CI, 0.70 to 1.002; 9 trials) with short case accrual. The absolute mortality reduction (deaths prevented) with screening was 4 per 10,000 women over 10 years.
- For age 50 to 59 years, the combined RR was 0.86 (95% CI, 0.68 to 0.97; 7 trials) with long case accrual; and 0.86 (95% CI, 0.69 to 1.007; 7 trials) with short case accrual. The absolute mortality reduction with screening was 5 to 8 per 10,000 women over 10 years.
- For age 60 to 69 years, the combined RR was 0.67 (95% CI, 0.54 to 0.83; 5 trials) with long case accrual; and 0.67 (95% CI 0.55 to 0.91; 5 trials) with short case accrual. The absolute mortality reduction (deaths prevented) with screening was 12 to 21 per 10,000 women over 10 years.
- Breast cancer mortality for women age 70 to 74 years was not statistically significantly different between randomized groups in the screening trials, but estimates were limited by low numbers of events from trials that had smaller sample sizes of women in this age group.
- All-cause mortality did not differ between randomized groups in meta-analyses of trials, regardless of whether trials were analyzed in combined or separate age groups.
- No RCTs evaluated breast cancer mortality or all-cause mortality outcomes on the basis of risk factors besides age.
- There are no head-to-head trials of different screening intervals and existing trials do not provide enough information to determine the specific effects of screening intervals.

Observational Studies

- Observational studies of the effectiveness of population-based mammography screening on breast cancer mortality reported a wide range of reductions in breast cancer death. Most studies were conducted in Europe or the United Kingdom and included women age 50 to 69 years.
- Meta-analyses from recent reviews from the EUROSCREEN Working Group indicated 25 to 31 percent mortality reduction for women invited to screening in the screening programs. This compares to 19 to 22 percent reduction for women age 50 to 69 years in the meta-analysis of screening RCTs that used intention-to screen analysis.

- The only U.S observational study of breast cancer mortality reduction is a record review that indicated no differences in breast cancer deaths between screened versus non-screened women older than age 80 years.[91]
- A large fair-quality study of the Mammography Screening of Young Women Cohort in Sweden indicated reduced risk for breast cancer deaths for women age 40 to 49 years invited to screening compared with women not invited (RR 0.74; 95% CI, 0.66 to 0.83).
- An observational study of Canadian women age 40 to 79 comparing screening program participants versus nonparticipants indicated reduced breast cancer mortality of 40 percent among participants.
- Two observational studies of screening intervals indicated no breast cancer mortality differences between annual and biennial screening for women 50 years or older, or between annual and triennial screening among women age 40 to 49 years.

Evidence

Previous Reports

The 2002 evidence review for the USPSTF included a meta-analysis of the eight published RCTs of mammography screening and breast cancer mortality that were rated fair-quality.[92,93] For all age groups combined, results of the meta-analysis indicated a RR for breast cancer mortality of 0.84 (95% credible interval [CrI], 0.77 to 0.91) for women randomly assigned to screening over 14 years of followup. For women age 40 to 49 years specifically, results indicated a RR of 0.85 (95% CrI, 0.73 to 0.99), while for women age 50 years and older, results indicated a RR of 0.78 (95% CrI, 0.70 to 0.87).

The 2009 evidence review for the USPSTF included new results from the Age trial and updated results from the Gothenburg trial in addition to the previous trials, and provided meta-analysis estimates for breast cancer mortality according to four age groups.[44,94] For women age 39 to 49 years, the combined RR was 0.85 (95% CrI, 0.75 to 0.96); for 50 to 59 years, 0.86 (95% CrI, 0.75 to 0.99); for 60 to 69 years, 0.68 (95% CrI, 0.54 to 0.87); and for 70 to 74 years, 1.12 (95% CrI, 0.73 to 1.72).

Previous evidence reviews for the USPSTF did not address the effectiveness of screening in reducing all-cause mortality, or how mortality reduction differs by risk factors and screening intervals.

New Studies

Breast Cancer Mortality

RCTs with long case accrual methods. Seven RCTs provided breast cancer mortality outcomes by age using long case accrual methods. These included the Swedish Two-County (Kopparberg and Östergötland),[83] Age,[79] Gothenburg,[82] HIP,[95] and Canadian (CNBSS-1 and CNBSS-2)[69] trials. The Malmö I, Malmö II, and Stockholm trials reported breast cancer mortality outcomes by age using only short case accrual.[87] However, these results were included in the combined meta-analysis because they are the most inclusive results available. Quality ratings of these trials

are described in previous reports. [92,93,94] Across all trials with long case accrual, the mean or median screening intervention time ranged from 3.5 to 14.6 years, case accrual time from 7.0 to 17.4 years, and followup time from 11.2 to 21.9 years.

For women age 39 to 49 years, a meta-analysis of nine RCTs using the longest case accrual available indicated a combined RR of 0.88 (95% CI, 0.73 to 1.003; I^2=25.4%; p=0.218; **Figure 5**).[69,82,83,86,87,95] The CIs of all nine trials crossed 1.0 as did the combined estimate.

For age 50 to 59 years, a meta-analysis of seven trials using the longest case accrual available indicated a combined RR of 0.86 (95% CI, 0.68 to 0.97; I^2=38.0%; p=0.139), consistent with a statistically significantly lower death rate in the screening group.[69,82,83,87,95] Estimates from the Kopparberg[83] and Stockholm[87] trials indicated statistically significant differences between randomized groups favoring screening, while the CIs from the five other trials crossed 1.0.

For age 60 to 69 years, a meta-analysis of five trials using the longest case accrual available indicated a combined RR of 0.67 (95% CI, 0.54 to 0.83; I^2=0%; p=0.739), consistent with a statistically significantly lower death rate in the screening group.[83,87,95] In this age group, estimates from three Swedish trials (Kopparberg,[83] Östergötland,[83] and Malmö I[87]) indicated statistically significant differences between randomized groups favoring screening, while the CIs from the two other trials crossed 1.0. Combining results across the two age groups of women age 50 to 69 years indicated a RR of 0.78 (95% CI, 0.68 to 0.90; I^2=41.0%; p=0.118).

Only three Swedish trials, Östergötland,[83] Kopparberg,[83] and Malmö I,[87] provided outcomes for women age 70 to 74 years. The numbers of events in these trials were much lower than for other age groups, and none of the trials indicated statistically significant differences between randomized groups. A meta-analysis of the three trials using the longest case accrual available indicated a combined RR of 0.80 (95% CI, 0.51 to 1.28; I^2=0%; p=0.962).

A sensitivity analysis that included results of a combined analysis of the Swedish trials (Malmö I, Malmö II, Stockholm, Östergötland, Gothenburg, Stockholm) that used a long case accrual ("followup") method[87] indicated reduced point estimates that diminished the effect of screening, although the statistical significance of the estimates did not change.

Results of the meta-analysis were used to determine absolute rates of breast cancer mortality reduction per 10,000 women screened for 10 years (**Table 5**). Using RRs from the long case accrual meta-analysis, the numbers of deaths reduced (prevented) included 4.1 (95% CI, -0.1 to 9.3) for age 39 to 49 years; 7.7 (95% CI, 1.6 to 17.2) for age 50 to 59 years; 21.3 (95% CI, 10.7 to 31.7) for age 60 to 69 years; and 12.5 (95% CI, -17.2 to 32.1) for age 70 to 74 years. Absolute reduction for the combined group of women age 50 to 69 was 12.5 (95% CI 5.9 to 19.5).

RCTs with short case accrual methods. Meta-analysis estimates from trials with short case accrual methods differed only slightly from those with long case accrual (**Figure 6**). Across all trials with short case accrual, the mean or median screening intervention time ranged from 3.5 to 14.6 years, case accrual time from 5.0 to 15.5 years, and followup time from 10.7 to 25.7 years. Including the same trials as the previous analysis, but with short case accrual, the combined RR for women age 39 to 49 years was 0.84 (95% CI, 0.70 to 1.002; I^2=35.8%; p=0.143; 9

trials).[69,82,83,86,87,95] The Gothenburg trial was the only trial with statistically significant differences between groups.[82]

Results for age 50 to 59 years indicated a RR of 0.86 (95% CI, 0.69 to 1.007; I^2=33.9%; p=0.182; 7 trials), and only the Stockholm trial reported statistically significant differences between groups.[83,87] Results for age 60 to 69 and 70 to 74 years differed slightly from the previous analysis (60 to 69 years; RR 0.67; 95% CI 0.55 to 0.91; I^2=0%; p=0.476; 5 trials; and 70 to 74 years; RR 0.90; 95% CI, 0.46 to 1.78; I^2=0%; p=0.923; 3 trials). Combining results across the two age groups of women age 50 to 69 years, indicated a RR of 0.81 (95% CI, 0.69 to 0.95; I^2=43.7%; p=0.114).

Results of the meta-analysis were used to determine absolute rates of breast cancer mortality reduction per 10,000 women screened for 10 years (**Table 5**). Using RRs from the short case accrual meta-analysis, the numbers of deaths reduced (prevented) included 3.5 (95% CI, -0.1 to 7.4) for age 39 to 49 years, 4.5 (95% CI, -0.2 to 9.8) for age 50 to 59 years, 12.1 (95% CI, 3.4 to 20.7) for age 60 to 69 years, and 12.2 (95% CI, -37.7 to 26.9) for age 70 to 74 years. Absolute reduction for the combined group of women age 50 to 69 years was 6.1 (95% CI 1.2 to 10.9).

Observational studies. Observational studies of mammography screening provide additional information about screening effectiveness in contemporary populations and settings. However, observational studies are subject to important biases that limit their use in determining effectiveness. Most importantly, they lack comparability of comparison groups that is only attainable through randomization.

Recent comprehensive systematic reviews of observational studies summarize most of the relevant research.[96-99] Included studies were designed as time-trend, incidence-based mortality, or case-control studies. Time-trend studies compare changes in breast cancer mortality among populations in relation to the introduction of screening. Incidence-based mortality studies compare mortality rates of women screened or invited to screen with women not screened or invited. To reflect the incidence of breast cancer, rather than prevalence, these studies include only breast cancer cases diagnosed during a specific time period that follows the initial screen. Case-control studies compare histories of screening between women dying of breast cancer with women not dying of breast cancer. Examples of limitations of these specific study designs include incorrect assumptions for comparison groups in time-trend studies, high risk of lead and length time bias in incidence-based mortality studies, and self-selection bias in case-control studies. Additional limitations are described in **Table 6**.

Three good-quality reviews were recently conducted by the EUROSCREEN Working Group to assess the effectiveness of population-based mammography screening on breast cancer mortality (**Appendix B1**).[96-98] Inclusion criteria included studies with original data from population-based screening programs in Europe and the United Kingdom that reported breast cancer mortality outcomes; were published in English; included women age 50 to 69 years; evaluated current screening programs; and were designed as time-trend, incidence-based mortality, or case-control studies. Studies with overlapping data or data that were updated by newer results were not included. Although quality criteria were not prespecified, the studies appeared to undergo critical review according to design-specific factors. However, individual studies were not given quality

ratings. Studies included in these reviews are listed in **Appendix A8**.

A EUROSCREEN review evaluated 12 time-trend studies reporting changes in breast cancer mortality in relation to the introduction of screening.[97] These studies described trends over time or evaluated change using regression analysis. No combined estimates of effectiveness were provided because of dissimilarities of comparisons and outcome measures. Five studies reporting outcomes as reductions per year indicated breast cancer mortality reductions of 1 to 9 percent per year for approximately 10 years after the introduction of screening (i.e., 10% to 90%).[100-104] Seven studies reporting before/after changes indicated 0 to 36 percent reductions in mortality after screening was introduced compared with before screening.[105-111] Three of these studies that were considered to have adequate followup reported mortality reductions ranging from 28 to 35 percent.[106,107,110]

Another EUROSCREEN review included 20 incidence-based mortality studies that evaluated breast cancer mortality rates in relationship to screening.[96,98] The least biased studies estimated breast cancer mortality from a cohort of women not invited for screening, or from historical and current control groups; and used long case accrual periods that were the same as the study followup periods. A meta-analysis[98] of these studies indicated a RR of 0.75 (95% CI, 0.69 to 0.81; p=0.23; 7 studies)[34,107,112-116] for invitation to screening; and 0.62 (95% CI, 0.56 to 0.69; p=0.40; 7 studies)[34,107,112-116] for actual screening.

The third EUROSCREEN review included eight case-control studies that provided odds ratios (ORs) for breast cancer mortality adjusted for self-selection bias using various methods.[98] A meta-analysis of studies indicated an OR of 0.69 (95% CI, 0.57 to 0.83; p=0.005; 7 studies)[117-122] for invitation to screening; and 0.52 (95% CI, 0.42 to 0.65; p=0.17; 7 studies) [117-122] for actual screening.

A good-quality systematic review conducted outside of the EUROSCREEN Working Group included time-trend, cohort, and hybrid studies (**Appendix B1**).[99] Hybrid studies were defined as studies that identified a cohort, but used population-based data on mammography exposure. Studies were restricted to those with women age 50 to 69 years that captured over 10 years of screening experience. Several studies included in this review were also included in the EUROSCREEN reviews. Study quality was evaluated by prespecified criteria that included concepts of the USPSTF criteria and emphasized control groups, adjustment for potential confounders, and ascertainment of mortality outcomes. Of 17 studies meeting inclusion criteria and rated fair-quality, five reported RR reductions for breast cancer death of 0 to 12 percent; eight reported 13 to 33 percent; and four reported more than 33 percent, although not all results reached statistical significance.[99]

The results of these systematic reviews indicated a wide range of estimates of breast cancer mortality reduction with screening for women age 50 to 69 years. Meta-analyses from the EUROSCREEN reviews indicated 25 to 31 percent mortality reduction for women invited to screening in the screening programs. In comparison, the meta-analysis of screening RCTs using intention-to screen analysis for women age 50 to 69 years indicated reductions of 19 to 22 percent, as described in the previous section of this report.

Six additional studies were not included in the published systematic reviews described above because they were published in 2011 or later, included women in countries outside Europe and the United Kingdom, or focused on ages older or younger than 50 to 69 years (**Table 7**). The only U.S study was a record review of older women who died of breast cancer. Results indicated no differences in breast cancer deaths between screened versus non-screened women older than age 80 years.[91]

One study included only women in their 40s. A large fair-quality study of the Mammography Screening of Young Women Cohort in Sweden indicated reduced risk for breast cancer deaths for women age 40 to 49 years invited to screening compared with women not invited (RR 0.74; 95% CI, 0.66 to 0.83).[123] The estimated NNS during a 10-year period (corresponding to about 6 mammography episodes) to save 1 life was calculated as 1252 women (95% CI, 958 to 1915 women).[123]

A study of over 2 million women age 40 to 79 in Canada compared screening program participants versus nonparticipants. [124] Results were expressed as standardized mortality ratios (i.e., the ratio of the observed breast cancer mortality of screening participants to province-specific breast cancer mortality based in nonparticipant incidence and survival rates). [124] Results indicated reduced breast cancer mortality of 35 to 44 percent that varied by age. Although the analysis considered the influence of self-selection bias using historical trend data for women age 35 to 39, the validity of this approach is unclear.

Additional studies provided updated data from screening programs in Norway[125,126] and the Netherlands[127] with results consistent with the EUROSCREEN report showing reduced mortality with screening for women age 50 to 69 years.

All-Cause Mortality

All included RCTs of mammography screening reported all-cause mortality outcomes. However, not all trials reported them according to age groups, and the two Canadian trials reported results by combining age groups (40 to 49 years and 50 to 59 years) as one trial. Results reflecting the longest followup times available for each trial were selected for inclusion in the meta-analysis.

For combined age groups, a meta-analysis of nine RCTs indicated a combined RR of 0.99 (95% CI, 0.97 to 1.003; I^2=0%; p=0.577, **Figure 7**).[69,79,87,128] Results were similar for each age group (**Figure 8**), including age 39 to 49 years (RR 0.99; 95% CI, 0.94 to 1.06; I^2=0%; p=0.478; 7 trials); 50 to 59 years (RR 1.02; 95% CI, 0.94 to 1.10; I^2=0%; p=0.588; 3 trials); 60 to 69 years (RR 0.97; 95% CI, 0.90 to 1.04; I^2=0%; p=0.650; 2 trials); and 70 to 74 years (RR 0.98; 95% CI, 0.86 to 1.14; I^2=72.4%; p=0.057; 2 trials).

Breast Cancer–Specific and All-Cause Mortality Differences by Risk Factors and Screening Intervals

Screening trials did not provide results according to risk factors other than age. No head-to-head comparisons of trials by screening intervals are available. The HIP, Age, and Canadian trials used mammography screening intervals of 12 months, and none showed age-specific mortality

reductions. The Swedish Two-County trial had screening intervals ranging from 24 to 36 months that varied by age group, and reported breast cancer mortality reductions for age 50 to 69 years. However, these trials differed by many other factors (inclusion, randomization, adherence, etc.) and they did not provide enough information to determine the specific effects of screening intervals.

Observational studies provide additional information about screening intervals (**Table 7**). A time-trend study of 658,151 Canadian women age 40 to 79 years compared breast cancer mortality rates before and after the change from annual to biennial screening for women 50 years or older, while annual screening remain unchanged for age 40 to 49 years.[129] Results indicated no significant reductions for age 40 to 49 or 50 years and older. A registry-based study in Finland indicated no breast cancer mortality differences between annual and triennial screening among women age 40 to 49 years.[130]

Key Question 2. What Is the Effectiveness of Routine Mammography Screening in Reducing the Incidence of Advanced Breast Cancer and Treatment-Related Morbidity, and How Does It Differ by Age, Risk Factor, and Screening Interval?

Summary

RCTs

- The RCTs of mammography screening provided several measures of intermediate breast cancer outcomes. However, most comparisons between screening and control groups using these categories provided differences between the two groups in relatively early stages of disease, rather than advanced stages.
- Combining estimates based on definitions corresponding to Stage II disease or higher (Stage II+, size ≥20 mm, 1+ positive lymph node) in a meta-analysis indicated no significant reductions in advanced disease for women age 39 to 49 or 50 years and older.
- When thresholds were defined by the most severe disease categories available from the trials (Stage III + IV disease, size ≥50 mm, 4+ positive lymph nodes), meta-analysis indicated no reductions for age 39 to 49 years (RR 0.98; 95% CI, 0.74 to 1.37); but reduced risk of advanced cancer in the screening group for age 50 years and older (RR, 0.62; 95% CI, 0.46 to 0.83).
- In a Cochrane review that included five screening RCTs, women randomized to screening were significantly more likely to have surgical therapy (mastectomies, lumpectomies) and radiation therapy, and less likely to have hormone therapy than controls. Use of chemotherapy was similar between groups.
- No RCTs evaluated the incidence of advanced breast cancer outcomes and treatment on the basis of risk factors or screening intervals.

Observational Studies

- Six observational studies compared advanced breast cancer outcomes between women in populations participating in screening versus nonparticipating. Of these, two studies indicated statistically significantly more Stage III and IV breast cancer among unscreened women; three reported more lymph node positive disease; and three reported more tumors greater than 20 mm in size.
- Four case series studies indicated less extensive survey, such as fewer total mastectomies and more breast conservation therapies, and less chemotherapy among women who had previously had screening mammography compared with those who did not, but these studies included women with DCIS and early stage cancer as well as advanced cancer.
- An analysis of BCSC data indicated a lower proportion of Stage III + IV disease among women age 40 to 49 years screened annually versus biennially, but not for women age 50 to 59 years.
- A second analysis of BCSC data indicated that women age 40 to 49 years with extremely dense breasts had increased risks for advanced stage cancer (IIB+) and large-size tumors (>20 mm) with biennial compared with annual screening. Differences were not significantly different for positive lymph nodes, other density categories, other age groups, or between biennial and triennial screening.

Evidence

Previous Reports

Previous evidence reviews for the USPSTF did not address this question.

New Studies

Incidence of Advanced Breast Cancer

RCTs. Intermediate outcomes of screening trials can be evaluated to determine if screening reduces the risk for advanced breast cancer, thereby leading to better prognosis and potentially less aggressive treatment and morbidity. The RCTs of mammography screening provided several measures of intermediate outcomes for screening and control groups. The most commonly used measures included clinical stage (Stage 0 to IV),[80,81,131,132] number of involved lymph nodes (0, 1 to 3, 4+),[75,77,82,83,133] and tumor size (mm),[76,78,83] although these measures varied across trials. Most comparisons between screening and control groups using these categories provided differences between the two groups in relatively early stages of disease, rather than advanced stages.

A published analysis of trials defined advanced breast cancer as Stage II disease or higher, size 20 mm or greater, or having one or more positive lymph nodes (**Table 8**).[65] These outcomes are all consistent with Stage IIA disease (i.e., localized) or higher according to the AJCC TNM system.[36] Combining estimates based on these definitions of advanced cancer in a meta-analysis produced a RR for women age 39 to 49 years of 0.90 (95% CI, 0.79 to 1.04; I^2=23.1%; p=0.267; 5 trials),[65,82,83,131] and for age 50 years and older, 0.85 (95% CI, 0.65 to 1.13; I^2=80.5%; p=0.002;

4 trials; **Figure 9**),[65,82,83,131] indicating no statistically significant overall differences between the screening and control groups.

To evaluate these relationships using a higher level of disease to define advanced breast cancer, thresholds were redefined to the most severe disease categories available from the trials, recognizing that these definitions do not represent equivalent disease stages. These include Stage III + IV disease (i.e., regional + metastatic), size 50 mm or greater, or having four or more positive lymph nodes. Combining estimates based on these definitions of advanced cancer in a meta-analysis indicated no difference for women age 39 to 49 years (RR 0.98; 95% CI, 0.74 to 1.37; I^2=0%; p=0.556; 4 trials);[76,83,131,133] but reduced risk of advanced cancer in the screening group for age 50 years and older (RR, 0.62; 95% CI, 0.46 to 0.83; I^2=0%; p=0.692; 3 trials; **Figure 10**).[78,83,131]

Observational studies. Although many observational studies have been published comparing characteristics of breast cancer diagnoses between screened and unscreened women, most provide comparisons between screen-detected and nonscreened-detected cases. This approach categorizes all cancer cases identified outside of a screening mammogram as nonscreen-detected, even though a woman may have had prior screening mammography. This type of comparison does not provide accurate estimates of the effectiveness of participation in a screening program compared with nonparticipation. Instead, comparisons between rates of advanced breast cancer outcomes between women in populations participating in screening versus nonparticipating would more appropriately address this Key Question.

Six case series studies compared advanced breast cancer outcomes for women who had previous mammography screening with those who did not (**Table 9**).[134-139] These studies were based on screening populations from the Malmö trial,[139] Kaiser Permanente,[135] and screening programs in the United Kingdom,[134] Denmark and Sweden,[137] Spain,[136] and Canada.[138]

Two studies indicated statistically significantly more Stage III and IV breast cancer among unscreened women,[137,138] three reported more lymph node positive disease,[134,136,139] and three reported more tumors greater than 20 mm in size.[134,136,138,139] A study of 242 women age 42 to 49 years at Kaiser Permanente found no statistically significant differences in stage between screened and nonscreened women.[135]

Treatment-Related Morbidity

Although outcomes related to treatment are reported by some of the screening trials, their interpretation and application to current practice is problematic. Treatment approaches have changed over time, are subject to local practice standards, and increasingly involve patient choices.

A Cochrane review compared treatments between randomized groups in five screening trials providing these outcomes, including the CNBSS-1, CNBSS-2, Malmö, Kopparberg, and Stockholm trials.[140] In this analysis, women randomized to screening were significantly more likely to have surgical therapy, analyzed as mastectomies and lumpectomies combined (RR 1.35; 95% CI, 1.26 to 1.44; I^2=0%; p=0.80; 5 trials) and mastectomies alone (RR 1.20; 95% CI, 1.11

to 1.30; I^2=0%; p=0.86; 5 trials). These women were also more likely to have radiation therapy (RR 1.32; 95% CI, 1.16 to 1.50; I^2=0%; p=0.36; 2 trials), and less likely to have hormone therapy (RR 0.73; 95% CI, 0.55 to 0.96; I^2=78%; p=0.03; 2 trials). Use of chemotherapy was similar between groups (RR 0.96; 95% CI, 0.78 to 1.19; I^2=71%; p=0.06; 2 trials).

Four case series studies compared breast cancer treatments for women who had previous mammography screening with those who did not, but these studies included women with DCIS and early stage cancer as well as advanced cancer (**Table 10**).[135-138] Studies also provided information on advanced cancer outcomes described above, and were based on screening populations from Kaiser Permanente,[135] and screening programs in Denmark and Sweden,[137] Spain,[136] and Canada.[138] Results indicated statistically significantly less extensive survey, such as fewer total mastectomies and more breast conservation therapies;[135-138] and less chemotherapy[135,136,138] among women who had previously had screening mammography.

Differences by Risk Factors and Screening Intervals

Five observational studies compared advanced breast cancer outcomes by screening intervals (**Table 9**),[141-145] including four studies based on BCSC data.[141,143-145] A recent analysis of data from 4,492 women in the BCSC compared annual with biennial mammography screening and the adjusted proportion of cancer stage at diagnosis.[143] Results indicated a lower proportion of Stage III + IV disease among women age 40 to 49 years screened annually versus biennially (10.1% vs. 14.0%; adjusted difference 4.8%; 95% CI, 1.3% to 8.4%), but not among women age 50 to 59 years.[143] An older study of 7,840 women in the BCSC indicated no differences between annual and biennial screening for detecting Stage III + IV cancer or tumor size greater than 20 mm among women age 40 to 89 years.[145]

A separate analysis of BCSC data compared annual with biennial and triennial mammography screening and risks for advanced stage disease (Stage IIB+), large tumor size (>20 mm), and positive lymph nodes.[144] Results indicated that women age 40 to 49 years with extremely dense breasts had increased risks for advanced stage cancer (OR 2.39; 95% CI, 1.06 to 3.39) and large tumors (OR 2.39; 95% CI, 1.37 to 4.18) with biennial compared with annual screening. Differences were not statistically significantly different for positive lymph nodes, other density categories, other age groups, or between biennial and triennial screening. Another BCSC study reported no statistically significant differences in stage, tumor size, or lymph node involvement for average weight, overweight, and obese women screened annually compared with biennially.[141]

A study based on data from the Vermont Breast Cancer Surveillance System also reported no differences in cancer stage, size, or lymph node status between women screened annually compared with biennially.[142]

Key Question 3. How Does the Effectiveness of Routine Breast Cancer Screening in Reducing Breast Cancer–Specific and All-Cause Mortality Vary by Different Screening Modality?

Summary

- RCTs of mammography with or without CBE do not compare relative mortality reduction across different modalities.
- No study of tomosynthesis, ultrasound, or MRI address this question.

Key Question 4. How Does the Effectiveness of Routine Breast Cancer Screening in Reducing the Incidence of Advanced Breast Cancer and Treatment-Related Morbidity Vary by Different Screening Modality?

Summary

- Cancer detection rates were higher, but there were no differences in tumor size, stage, or node status between women screened with tomosynthesis and digital mammography and with those receiving mammography alone in two case series studies.
- No other studies evaluated the effectiveness of CBE, ultrasound, or MRI in reducing the incidence of advanced breast cancer or treatment related morbidity.

Evidence

Previous Reports

Previous evidence reviews for the USPSTF did not address this question.

New Studies

Two case series studies comparing digital mammography versus tomosynthesis and digital mammography reported detection rates by cancer stage using various categories of cancer staging (**Table 11**).[146,147] A study of patients seen at a multisite community-based breast center in the United States evaluated diagnostic outcomes of 18,202 women receiving mammography and 10,878 receiving mammography and tomosynthesis.[146] Results indicated no differences in cancer size, stage, or node status. A second case series of 12,631 women age 50 to 69 years in Norway also found no differences between groups for tumor size or node status[147] but found a 27 percent adjusted increase in cancer detection rates (p=0.001) with the addition of tomography.

Key Question 5. What Are the Harms of Routine Mammography Screening, and How Do They Differ by Age, Risk Factor, and Screening Interval?

Summary

False-Positive and False-Negative Mammography Results, Recommendations for Additional Imaging, and Recommendations for Biopsies

- Data from the BCSC for regularly screened women using digital mammography based on results from a single screening round indicated:
  - False-positive mammography rates were highest among women age 40 to 49 years (121.2 per 1,000 women; 95% CI 105.6 to 138.7) and declined with age; rates of false-negative results tended to increase with age, but were not statistically significantly different across age groups.
  - Rates of recommendations for additional imaging were highest among women age 40 to 49 years (124.9 per 1,000 women; 95% CI 109.3 to 142.3) and decreased with age, while rates of recommendations for biopsy did not differ between age groups.
  - For every case of invasive breast cancer detected by mammography screening in women age 40 to 49 years, 464 women had screening mammography, 58 were recommended for additional imaging, and 10 were recommended for biopsies. These estimates declined with age.
  - Results did not differ by time since last mammography screening regardless of whether broad or narrow estimates of one versus two years were used.
  - Family history of breast cancer, high breast density, and previous benign breast biopsy were associated with higher rates of false-positive and false-negative results and recommendations for additional imaging and biopsy across most age groups. Premenopausal status, use of menopausal hormone therapy, and lower BMI were associated with some of the outcomes for specific age groups only.
  - Rates for all outcomes were lowest for women with almost entirely fat breasts, and highest for women with heterogeneously dense breasts or for those in the combined category of heterogeneous and extreme density.
- Published data from the BCSC using film and digital mammography provided 10-year cumulative rates.
  - Rates of false-positive mammography results were 61 percent for annual and 41 percent for biennial screening, while rates of false-positive biopsy were 7 to 9 percent for annual and 5 to 6 percent for biennial screening. Women older than age 50 years had higher false-positive biopsy rates.
  - Rates of false-positive mammography results and biopsy were highest among women receiving annual mammography, those with heterogeneously dense or extremely dense breasts, and those either 40 to 49 years old or who used combination hormone therapy.

Overdiagnosis

- A meta-analysis of three RCTs, a systematic review of 13 observational studies, and 18

individual studies of overdiagnosis were identified for the current update. Studies of overdiagnosis were primarily based on screening trials, screening programs and registries, or modeled data. Studies differed by their characteristics, methods, and measures. These differences influenced their estimates of overdiagnosis, limited comparisons, and prohibited combined estimates.

- The Malmö I and Canadian National Breast Screening Study (CNBSS-1 and CNBSS-2) trials provide data with reduced bias for estimates of overdiagnosis because they did not provide screening of controls at the end of the trial, had randomized comparison groups, and followup times extended sufficiently beyond the screening period to differentiate earlier diagnosis from overdiagnosis. Combined results indicated 10.7 percent (long case accrual method) to 19.0 percent (short case accrual method) overdiagnosis for invasive cancer + DCIS.
- Data from RCTs where women in the control groups were offered screening at the end of the screening periods are susceptible to over- or underestimating overdiagnosis. Two new publications from these RCTs indicate no or minimal overdiagnosis.
- Unadjusted estimates from 13 observational studies included in the EUROSCREEN review indicated overdiagnosis rates ranging from 0 to 54 percent. For six studies that adjusted overdiagnosis estimates for breast cancer risk and lead time, rates varied from 1 to 10 percent.
- Additional observational studies not included in the EUROSCREEN review reported overdiagnosis estimates of 3 to 50 percent, with most between 14 to 25 percent.
- Although several statistical models of overdiagnosis have been published, these studies have been less acceptable to guideline development groups because of the many assumptions that were used to construct them. Models indicated estimates ranging from 0.4 to 50 percent.

Anxiety, Distress, and Other Psychological Responses

- Women with false-positive results were more distressed than women with normal screening results, particularly those who had biopsies, FNA, and early recall.
- Women with false-positive results had more anxiety, psychological distress, and breast cancer specific worry after screening compared with those with normal screening results in most studies. Anxiety improved over time for most women, but persisted for over 2 years for some.
- Two studies reported that women with false-positive results were less likely to return for their next mammogram; two other studies reported no differences; however, when women were given letters tailored to their last screening result they were more likely to re-attend.
- Results of studies of anxiety and depression are mixed. Some studies indicate that women with false-positive results have more anxiety and depression than those with normal screening results, particularly among non-white women, but other studies show no differences.

Radiation Exposure

- Models calculate the number of deaths due to radiation induced cancer using estimates for digital mammography is between 2 per 100,000 in women age 50 to 59 years screened biennially, and up to 11 per 100,000 in women ages 40 to 59 years screened annually.

Pain During Procedures

- Although many women may experience pain during mammography (1% to 77%), the proportion of those experiencing pain who do not attend future screening varies (11% to 46%).

Evidence

False-Positive and False-Negative Mammography Results, Recommendations for Additional Imaging, and Recommendations for Biopsies

Previous Reports

Data from the BCSC that was based on a single screening round and included film and digital mammography indicated that false-positive mammography results were common in all age groups. The rate was highest among women age 40 to 49 years (97.8 per 1,000 women per screening round) and declined with each subsequent age decade.

The rate of false-negative mammography results was lowest among women age 40 to 49 years (1.0 per 1,000 women per screening round) and increased slightly with subsequent age decades. Rates of additional imaging were highest among women age 40 to 49 years (84.3 per 1,000 women per screening round) and decreased with age. Biopsy rates were lowest among women age 40 to 49 years (9.3 per 1,000 women per screening round) and increased with age. The BCSC data indicated that for every case of invasive breast cancer detected by mammography screening in women age 40 to 49 years, 556 women had screening mammography, 46 to 48 additional diagnostic imaging, and five to eight biopsies. These numbers declined with age for mammography and additional imaging, and only slightly for biopsies.

The cumulative risk for false-positive mammography results was reported in published studies as 21 to 49 percent after 10 mammography examinations for women in general,[148-150] and up to 56 percent for women age 40 to 49.[149] For all ages, the cumulative risk of a false-positive biopsy after 10 screening mammograms was calculated as 19 percent of all women screened.[149]

New Studies

BCSC Data.

Differences by age. Data for regularly screened women based on results from a single screening round using digital mammography indicated that false-positive screening mammography results were common in all age groups (**Table 12**). The rate was highest among women age 40 to 49 years (121.2 per 1,000 women; 95% CI 105.6 to 138.7) and declined with age ($p<0.001$). Rates of false-negative mammography results tended to increase with age, but were not statistically significantly different across age groups, and ranged from 1.0 to 1.5 per 1,000 women.

In current practice, women with an initial positive mammography result are recommended for

additional diagnostic imaging as a second step in the screening process. In the BCSC data, rates of recommendations for additional imaging were highest among women age 40 to 49 years (124.9 per 1,000 women; 95% CI 109.3 to 142.3) and decreased with age ($p<0.001$). Rates of recommendations for biopsy were not statistically significantly different across age groups, and ranged from 15.6 to 17.5 per 1,000 women.

Rates of invasive breast cancer were lowest among women aged 40 to 49 years (2.2 per 1,000 women; 95% CI 1.8 to 2.6) and increased across age groups ($p<0.001$). Rates of DCIS were also lowest among women aged 40 to 49 years (1.6 per 1,000 women; 95% CI 1.3 to 1.9) and increased with age ($p=0.05$). Women aged 70 to 79 had the highest rates of invasive cancer (7.2 per 1,000 women; 95% CI 6.4 to 8.1) and DCIS (2.3 per 1,000 women; 95% CI 1.7 to 3.0), and the yield of screening was more favorable for older women. For every case of invasive breast cancer detected by mammography screening in women aged 40 to 49 years, 464 women had mammography, 58 were recommended for additional imaging, and 10 were recommended for biopsies. In comparison, for women aged 70 to 79, for every case of invasive breast cancer detected by screening, 139 women had mammography, 11 were recommended for additional imaging, and 3 were recommended for biopsies.

Differences by time since last mammography screening. Rates of false-positives, false-negatives, and recommendations for additional imaging did not differ in comparisons of times since last mammography screening regardless of interval durations (9 to 18 versus 19 to 30 months; 11 to 14 versus 23 to 26 months) (**Table 13**). Biopsies were recommended at a higher rate for women aged 60 to 69 years who had their last mammogram 23 to 26 months previously compared to 11 to 14 months (18.8 versus 15.2 per 1,000 women; $p=0.03$).

Additional published BCSC data about screening intervals indicated that sensitivity, recall rates, and cancer detection rates increased as the months since previous mammography increased, whereas specificity decreased.[151]

Differences by risk factors. Rates of false-positive mammography results were statistically significantly higher for women with specific risk factors compared with women without them (**Table 14**). These included women with first-degree relatives with breast cancer compared with no relatives for women aged 40 to 69 years. Women with heterogeneously dense breasts had higher false-positive rates than those with almost entirely fat and scattered fibroglandular densities, or extremely dense breasts, for all ages except aged 80 to 89 years. Rates were also higher among women with previous benign breast biopsies for aged 40 to 79 years. Comparisons based on race and ethnicity indicated the lowest rates among Asians for all age groups.

Premenopausal women had the highest false-positive rates for women aged 40 to 59 years compared with perimenopausal and postmenopausal women. Women using menopausal hormone therapy had the highest rates for aged 70 to 79 years, while comparisons for other age groups were not statistically significant. Women with lower body mass (BMI <30) had higher false positive rates for aged 40 to 59 years.

Rates of false-negative results were higher for women with first-degree relatives with breast cancer for aged 40 to 79 years, although results were of borderline statistical significance for

aged 50 to 69 years (**Table 15**). Women with almost entirely fat and scattered fibroglandular densities had lower rates than those with other types of breast density for ages 40 to 69 years. Rates were higher among women with previous benign breast biopsies for aged 50 to 89 years, and women with lower body mass (BMI <30) for ages 50 to 59 years. Other comparisons between groups were not statistically significant.

Risk factors associated with differences in rates of recommendations for additional imaging were similar to those for false positive mammography results (**Table 16**). Rates were highest among women with first-degree relatives with breast cancer for all ages, heterogeneously dense breasts (ages 40 to 79), previous benign breast biopsies (ages 40 to 79), premenopausal status (ages 40 to 50), use of menopausal hormone therapy (age 70 to 79), and lower BMI (ages 40 to 49). Comparisons based on race and ethnicity indicated the lowest rates among Asians for all age groups.

Rates of recommendations for biopsy were statistically significantly higher for women aged 40 to 69 years with first-degree relatives with breast cancer, and for women aged 40 to 79 years with previous breast biopsies (**Table 17**). Women aged 40 to 59 years with heterogeneously dense or extremely dense breasts had higher rates than women with less dense breasts, while for women aged 60 to 79 years, rates were highest for women with heterogeneously dense breasts only. Higher rates were also associated with premenopausal status for age 50 to 59 years; no current use of oral contraceptives for age 40 to 49 years; lower BMI for age 40 to 49, but higher BMI for age 70 to 79. Other comparisons between groups were not statistically significant.

Rates of false-positives, false-negatives, recommendations for additional imaging, and recommendations for biopsies were lowest for women with almost entirely fat breasts for all ages. False-negative rates were highest for women with extremely dense breasts for all ages, except those aged 60 to 69 years (**Table 18**). Rates of false-positives, recommendations for additional imaging, and recommendations for biopsies were highest for women with heterogeneously dense breasts or for the combined category of heterogeneously and extremely dense breasts, except for women aged 40 to 49 years where rates of recommendations for biopsies were highest among women with extremely dense breasts.

Two studies published since the 2009 review estimated the cumulative probability of false-positive results after 10 years of mammography screening based on data from the BCSC.[143,144]

Data collected from film and digital screening mammography performed between 1994 and 2006 indicated that when screening began at age 40 years, the cumulative probability of receiving at least one false-positive mammography result after 10 years was 61 percent (95% CI, 59% to 63%) with annual, and 41 percent (95% CI, 41% to 43%) with biennial screening.[143] Estimates were similar when screening began at age 50 years. The cumulative probability of receiving a false-positive biopsy recommendation after 10 years of screening was 7 percent (95% CI, 6% to 8%) with annual versus 5 percent (95% CI, 4% to 5%) with biennial screening for women who initiated screening at age 40 years; and 9 percent (95% CI, 7% to 12%) with annual versus 6 percent (95% CI, 6% to 7%) with biennial for women who began at age 50 years.

A study of BCSC data collected between 1994 and 2008 also evaluated 10-year cumulative

probability estimates for false-positive mammography and biopsy results, but stratified results by age, breast density, and use of menopausal hormone therapy.[144] Rates of false-positive mammography results were highest among women receiving annual mammography that had extremely dense breasts and were either 40 to 49 years old (65.5%) or used combination hormone therapy (65.8%). Rates were lower among women 50 to 74 years receiving biennial or triennial mammography that had scattered fibroglandular densities (39.7% and 21.9%, respectively) or almost entirely fat breasts (17.4% and 12.1%, respectively). These rates were similar regardless of menopausal estrogen use. The highest rates were among women age 40 to 49 years undergoing annual screening that had heterogeneously dense (68.9%) or extremely dense (65.5%) breasts. The highest rates of false-positive biopsy were related to similar characteristics and ranged from 12 to 14 percent.

Overdiagnosis

Previous Reports

A review of eight RCTs of mammography screening[152] and eight additional studies[153-160] in the previous report provided estimates of overdiagnosis that ranged from non-existent to nearly 50 percent of diagnosed breast cancer cases. Methods for estimating overdiagnosis varied in many ways, particularly by the type of comparison groups, assumptions about lead time, and the denominator used to calculate the rates.[161,162] The different methodologies led to wide variations in estimates and a lack of agreement as to the true rate of overdiagnosis from mammography screening.

New Studies

A meta-analysis of three RCTs,[163,164] a systematic review of 13 observational studies,[161] and 17 individual studies[69,165-180] of overdiagnosis were identified for the current update (**Table 20**). Estimates of overdiagnosis were primarily based on screening trials, screening programs and registries, or modeled data. Studies differed by patient populations of various ages and with different risks for breast cancer; screening and followup times; screening policies, uptake, and intensity; and underlying cancer incidence trends. Estimates differed in their numerators and denominators; whether they included both invasive cancer and DCIS; assumptions about lead time and progression of invasive cancer and DCIS; and whether they reported relative or absolute changes.

Various methods were used to estimate overdiagnosis. The most common methods determined the differences between the incidence of cancer in the presence and in the absence of screening (observed excess incidence approach); or made inferences about the lead time or natural history of breast cancer and estimated the corresponding frequency of overdiagnosis (lead-time approach).[162] In addition, at least seven different measures of overdiagnosis were reported in published papers.[168] How differences in study characteristics, methods, and measures effect estimates of overdiagnosis have been well described,[162-164,168,181,182] yet there is currently no consensus about the most appropriate approach.[164]

Estimates from RCTs. Data from three RCTs that did not provide screening of controls at the

end of the trial were considered to be the least biased estimates of overdiagnosis in a comprehensive review commissioned by Cancer Research U.K. and the Department of Health in England.[163,164] The Malmö I and Canadian National Breast Screening Study (CNBSS-1 and CNBSS-2) trials provided randomized comparison groups, and followup times that extended sufficiently beyond the screening period to differentiate earlier diagnosis from overdiagnosis.[163]

Using results of the Malmö I[159] and two Canadian trials,[76,78] the excess incidence of breast cancer (both invasive cancer and DCIS) in the screening population was compared with the incidence in the absence of screening (**Table 21**). For the short case accrual method that includes cases identified only during the screening period, overdiagnosis was estimated to be 19.0 percent (95% CI, 15.2% to 22.7%; I^2=64.8%; p=0.058; 3 trials). For the long case accrual method that includes cases identified throughout the screening and followup periods, overdiagnosis was 10.7 percent (95% CI, 9.3% to 12.2%; I^2=22.3%; p=0.276; 3 trials). Estimates for women age 40 to 49 years in the CNBSS-1 trial were higher (22.7% for short case accrual; 12.4% for long case accrual) than for women age 50 to 59 years in the CNBSS-2 trial (16.0% and 9.7%, respectively), and women age 55 to 69 years in the Malmö trial (18.7% and 10.5%, respectively).

However, overdiagnosis estimates from the trials included in this meta-analysis used different denominators. The Malmö I trial included all breast cancer cases, not just those identified with screening, while the Canadian trials included only cancer cases detected by screening. If these were calculated similarly, results from Malmö would be 23 percent instead of the 11 percent estimate used.[81] In addition, more recently published long-term followup of the two Canadian trials 15 years after enrollment indicated a 22 percent overdiagnosis rate for combined age groups.[69]

Data from the other RCTs are susceptible to over- or underestimating overdiagnosis because women in the control groups were offered screening at the end of the screening periods.[163,164] If cases from screened control groups were included in the estimate of overdiagnosis, differences between comparison groups would be reduced and overdiagnosis would be underestimated. If these cases were excluded, overdiagnosis estimates would be inflated because the control group would not have been followed up long enough to determine accurate estimates. New publications of overdiagnosis reported from trials that screened control groups indicated none or minimal overdiagnosis, including the Swedish Two-County trial[110,178] and Screening for Young Women Trial.[170]

Estimates from screening programs and registries. A systematic review for the EUROSCREEN Working Group included 13 observational studies providing estimates of overdiagnosis in European population-based screening programs.[161] Five newer studies in this review are included in this update,[110,167,171,173,176] and three older studies were included in the previous report (**Table 20**).[153,156,160] These studies differed by many of the study characteristics, methods, and measures previously described that limited comparisons and prohibited combined estimates. In particular, for studies comparing screening and nonscreening populations from different time periods, adjustments for breast cancer risk were dependent on correct estimates of temporal trends. Also, denominators defining the populations at risk were inconsistent across studies (e.g., breast cancer diagnosis in an entire population versus women of a specific age who attended screening). Importantly, most studies used denominators that included all breast cancer

cases, rather than screen-detected cases, leading to lower estimates.

Unadjusted estimates from the 13 observational studies included in the EUROSCREEN review indicated overdiagnosis rates ranging from 0 to 54 percent.[161] For six studies that adjusted overdiagnosis estimates for breast cancer risk and lead time, rates varied from 1 to 10 percent.

European studies published since the EUROSCREEN systematic review include three studies of the Norwegian Breast Cancer Screening Program (NBCSP),[169,172,179] and one from Denmark.[171,175] The Norwegian studies reported overdiagnosis rates of 13.9 to 16.5 percent of invasive cancer + DCIS, and 9.6 to 11.3 percent of invasive cancer only, when comparing women screened with those never invited or nonattenders;[169] 15 to 25 percent of invasive cancer depending on region and lead time assumptions when comparing populations in regions with versus without screening;[172] and 50 percent of invasive cancer + DCIS when comparing screening versus discontinuation of screening that assumes that all increases in incidence were due to overdiagnosis.[179] The Danish study estimated overdiagnosis as the cumulative incidence of breast cancer + DCIS in regions with screening compared with expected cumulative incidence. For women followed for at least 8 years, the estimates were 3 percent in Copenhagen and 0.7 percent in Funen.[175] These results contrast with the estimate of 33 percent overdiagnosis in an earlier study of the same regions that used ratios of incidence between screened and nonscreened areas for the screened age group.[171]

An analysis of the Canadian British Columbia Cancer Registry between 1970 and 2009 provided two estimates of overdiagnosis in women age 40 to 89 years.[166] Rates were 17.3 percent of invasive cancer + DCIS and 5.4 percent for invasive cancer only when using cumulative incidence rates of women involved in active screening compared with women who were never screened or not actively screened. A second estimate compared the observed and expected cumulative population incidence rates between two time periods, resulting in estimates of 6.7 percent of invasive cancer + DCIS and -0.7 percent for invasive cancer only.

The only study conducted in the United States was not based on screening programs, but on comparisons of the expected increase in the incidence of early-stage cancer detected with mammography screening with the actual decrease in late-stage cancer incidence in women over a 40-year period using Surveillance, Epidemiology, and End Results (SEER) data.[165] Overdiagnosis rates based on different incidence trend assumptions were estimated from 22 to 31 percent.

Estimates from models. Although several statistical models of overdiagnosis have been published, these studies have been less acceptable to guideline development groups because of the many assumptions that were used to construct them.[163,164] Results of the models are heavily dependent on estimates of lead time and of progression rates from DCIS to invasive cancer. The longer the lead time, the more the estimate decreases with time. Assignment of these assumptions can be subjective. Six new studies of models of screening populations in The Netherlands,[167,168] United Kingdom,[180] France,[177] Spain,[173] and Australia,[174] met inclusion criteria for this update (**Table 20**).

A microsimulation model for estimating overdiagnosis in screening programs in The Netherlands

provided 1-year estimates across different time periods that ranged from 1.0 to 11.4 percent.[168] Another microsimulation model of screening programs in The Netherlands provided estimates based on assumptions of the progression from DCIS to invasive cancer.[167] These included overdiagnosis estimates of 1.4 to 7.7 percent of all breast cancer, and 5.0 to 25.2 percent of screen-detected breast cancer.

A Markov simulation model estimated overdiagnosis for different screening strategies in the United Kingdom, including annual, triennial, and combination strategies for different age groups.[180] For all invasive + DCIS cases diagnosed from age 40 to 85 years, overdiagnosis estimates ranged from 4.3 percent for triennial screening for women age 50 to 70 years, to 8.9 percent for annual screening from age 40 to 73 years. For screen-detected invasive + DCIS cases, overdiagnosis estimates ranged from 11.8 percent for triennial screening for women age 50 to 70 years, to 13.5 percent for annual screening from age 40 to 46 years followed by triennial screening from age 47 to 73 years.

A French study utilized a stochastic process for modeling all-cause mortality, lifetime probability of breast cancer, the natural course of breast cancer, and the detection of breast cancer clinically or by screening mammography.[177] Overdiagnosis estimates included 1.5 percent of all diagnosed and 3.3 percent of screen-detected invasive cancer cases, and 28 percent of all diagnosed and 31.9 percent of screen-detected DCIS cases. In a Spanish population, a Poisson regression model was used to estimate expected incidence, accounting for age at diagnosis, reproductive factors, use of mammography, and year of birth.[173] Estimates of overdiagnosis of invasive cancer varied from 0.4 percent in the oldest to 46.6 percent for the youngest cohort.

An Australian study estimated incidence in unscreened age groups (≤40 or ≥80 years) and in all age groups prior to implementation of screening adjusting for risk factors and lead time.[174] Assuming a 2-year lead time, estimates from the first approach ranged from 27 to 66 percent, while estimates from the second approach were 36 to 47 percent. In general, rates were higher among women age 50 to 59 than 60 to 69.

Anxiety, Distress, and Other Psychological Responses

Previous Reports

A systematic review of 54 studies evaluated the adverse psychological effects of mammography screening programs.[183] Most were cohort studies, and 24 used validated psychological measurement scales to assess the effects of screening. Studies indicated that women who received clear communication of their negative mammography results had minimal anxiety.[183] Results were mixed in studies of women who were recalled for further testing as a result of screening. In several studies, women had persistent anxiety, despite eventual negative results, whereas some showed only transient anxiety.[183] Some studies showed no differences between anxiety levels of women who had initial negative screening mammography results and those who had false-positive results.[183]

A second systematic review of 23 studies (in 27 publications, of which 15 were included in the systematic review described above) specifically examined the effects of false-positive screening

mammography results on women age 40 years or older.[184] Twenty studies were included that measured psychological distress, anxiety, and worry. False-positive mammography results had no consistent effect on most women's general anxiety and depression but increased breast cancer-specific distress, anxiety, apprehension, and perceived breast cancer risk for some.[184]

New Studies

A good-quality review of seven studies examined the effects of false-positive screening mammography results on women (**Table 22**).[185] Three studies that evaluated breast cancer specific worry or distress reported significantly more distress among women with false-positive results, even after 35 months (1 study), than women with normal screening results. The most distress was observed among women who had biopsies (RR 2.07; 95% CI, 1.22 to 3.52), FNA (RR 1.80; 95% CI, 1.17 to 2.77), and early recall (RR 1.82; 95% CI, 1.22 to 2.72).[183,186,187] Two studies that evaluated general anxiety and depression found no differences between women with true versus false-positive results.[188,189]Among six studies that evaluated re-attendance rates after receiving a false-positive result, two studies reported that women with false-positive results were less likely to return for their next mammogram (RR 0.97; 95% CI, 0.96 to 0.98 and RR 0.92; 95% CI, 0.86 to 0.98);[186,190] while two studies reported no differences.[191,192] One study reported an increase in re-attendance when women were given letters tailored to their last screening result (RR 1.10; 95% CI, 1.00 to 1.21).[193]

Another review rated fair-quality evaluated 17 studies of women age 40 to 74 years and reported that those with false-positive results had more anxiety, psychological distress, and breast cancer specific worry after screening (15 studies) compared with those with normal screening results.[194] In two studies anxiety increased when women were recalled for biopsies,[195,196] and in one study, anxiety persisted for 2 years after screening.[197] The findings in these reviews are consistent with those from the previous report.[183,184]

In addition to the reviews, 10 observational studies published after the reviews met inclusion criteria (**Table 23**). These include two fair-quality prospective cohort studies[198,199] and three fair-quality retrospective cohort studies (**Appendix B2-4**);[200-202] two good-quality[203,204] and one fair-quality[205] nested case-control studies; one fair-quality case-control study;[206] and one before-after study[207] that was not quality rated because rating criteria are not available for this study design.

Five studies compared women receiving false-positive results with those receiving normal screening results,[198,203-206] and reported similar findings as the reviews. Women with false-positive versus normal screening results experienced more breast cancer worry (49% vs. 10%, $p<0.0001$) and had more worries that affected mood or daily activities (31% vs. 2%, $p<0.0001$).[206] These women also had lower mental functioning and vitality measured by the Short Form 36 Health Survey (SF-36) at 6 months (mean mental functioning score: 80.6 vs. 85.0; $p=0.03$; mean vitality score: 70.3 vs. 77.0; $p=0.02$).[205] A study of 323 participants reported higher depression scores on the Hospital Anxiety and Depression Scale (HADS) – Depression Subscale (HADS-D) for women with false-positive versus normal screening results (6-months mean: 3.2 vs. 2.4, $p=0.045$), however neither group reached clinical thresholds.[205] Other studies of general anxiety and depression measured with the HADS or State-Trait Anxiety Inventory (STAI) reported no significant differences between groups.[198,204,206] However, in a study of

13,491 women, analysis of racial sub-groups indicated increased depression among non-white women (6%; n=847) with false-positive results (OR 3.23; 95% CI, 1.32 to 7.91).[198]

Psychological outcomes of women with false-positive, normal screen, and true-positive results (breast cancer diagnosis) were compared in a good-quality nested case-control study using the Consequences of Screening in Breast Cancer questionnaire.[203] Immediately after screening, women with normal screening results had better scores on all subscales compared with women with either false-positive or true-positive results ($p<0.001$ for all outcomes), but there were no differences between women with false-positive and true positive results. By 3 years after screening, women with normal screening results continued to have better scores on all subscales compared with women with true-positive results ($p<0.002$ for all outcomes). However, women with normal screening results also had better scores than those with false-positive results on subscales for sense of dejection, anxiety, negative impact on behavior or sleep, social network, existential values, and on single items of feeling less attractive and keeping mind off things ($p<0.03$ for all outcomes). Women with false-positive results had better scores than women with true-positive results on all but the breast examination and worried about breast cancer subscales ($p<0.03$ for all outcomes).

Anxiety and depression were evaluated in a before-after study of women with false-positive and true-positive results at the time of mammography recall and 4 weeks after.[207] The proportion meeting the HADS threshold for anxiety (score >11) decreased from recall to 4 weeks for women with false-positive (15% to 5.5%) and true positive results (19% to 17%). The proportion meeting the HADS threshold for depression (score >11) also decreased from recall to 4 weeks (1.4% to 1.3%) for women with false-positive results, but increased for women with true positive results (1.3% vs. 6.9%). In multivariate models, factors predicting anxiety or depression at followup included low general life expectations, previous history of anxiety and/or depression, and anxiety at baseline. Satisfaction with information also predicted depression. Anxiety and depression were also evaluated in a fair-quality prospective cohort study of 482 women that compared women recalled after their first screening mammography with those recalled after a repeat screening mammography.[199] Both groups had similar anxiety and depression scores initially that significantly declined over the following 6 months.

Three studies compared re-attendance rates of women with false-positive screening mammography results with women with normal screening results. [200-202] As with the systematic review of studies on re-attendance, the results of these studies were also inconsistent. One study reported higher re-attendance rates for women with normal results (93.2% vs. 52.1% for false-positive result), and the lowest rates for women recalled to screening more than once for different lesions (44.3%).[202] The other two studies reported higher rates of re-attendance for women with false-positive compared with normal screening results (90.7% vs. 89.0%, $p<0.001$[200] and 87.7% vs. 86.0%, difference of 1.61%, 95% CI, 0.54% to 2.62%).[201]
The OR for re-attendance was higher for women who did not receive tissue sampling after false-positive versus normal mammography screening (OR 1.20, 95% CI, 1.10 to 1.30).[201] Older women had lower odds of re-attendance at both prevalent (OR 0.89, 95% CI 0.86 to 0.93) and incident screening rounds (OR 0.99, 95% CI 0.98 to 0.99).

In a study of women with false-positive results, ORs for re-attendance were lower for women

receiving open biopsies (adjusted OR [AOR] 0.4, 95% CI, 0.3 to 0.6) but not core needle biopsies compared with women receiving no tissue sampling.[200] This study also found that older women had reduced odds of re-attendance (AOR 0.8, 95% CI, 0.7 to 0.9 for women aged 55 to 59 years and 0.8, 95% CI, 0.6 to 0.9 for women aged 60 to 62 years compared with women aged 50 to 54 years).

Radiation Exposure

Previous Reports

In the previous report, estimates of radiation exposure were provided by a systematic review that included various types of studies of radiation exposure as a basis for predicting risk for inducing breast cancer.[14] However, these estimates were not specific for radiation induced risk or mortality attributable to mammography or breast imaging.

New Studies

No studies directly measured the association between radiation exposure from mammography screening and the incidence of breast cancer and death for film, digital, or tomosynthesis. The general concern about the harms of radiation exposure stems from the assumption that higher doses of radiation induce cancers. Two-view digital mammography and screen-film mammography involve an average mean glandular radiation dose (MGD) of 3.7 and 4.7 mGy, respectively, and are considered low dose, low energy radiation. Radiation exposure for tomosynthesis is generally considered to be up to twice the dose of digital mammography.

Two modeling studies provided estimates of radiation exposure, breast cancer incidence, and death (**Table 24**).[208,209] In a study based on theoretical estimates, the average estimated MGD and the lifetime attributable risk (LAR) of radiation induced breast cancer incidence and mortality were calculated based on age-specific estimates in the United States screening population.[208] Results indicated that a 40 year old woman undergoing a single, bilateral, two-view screening mammogram has an LAR of breast cancer incidence of 5 to 7 cases per 100,000, and an LAR of breast cancer mortality of 1.3 to 1.7 deaths per 100,000. There was little effect on estimated risk when screening ended at age 80 years or later. Risks were similar for digital breast tomosynthesis (LAR 1.3 to 2.6 deaths).

A modeling study based on assumptions from the first study[208] created an excess absolute risk model to predict the number of radiation induced breast cancers attributable to the radiation dose received for a single typical digital mammogram.[209] Results indicated that the estimated number of deaths due to radiation induced cancer was between 2 per 100,000 in women age 50 to 59 years screened biennially, and up to 11 per 100,000 in women screened annually between ages 40 to 59 years. Women age 40 to 49 years undergoing annual mammographic screening would have an absolute risk of radiation induced mortality of 7.6 per 100,000. The calculations in this study are based on radiation doses from digital mammography, whereas previous estimates based on film mammography used higher doses per examination (3.7 mGy vs. 4.5 mGy, respectively).

Pain During Procedures

Previous Reports

A systematic review of 22 studies of pain and discomfort associated with mammography indicated that many women experience pain during the procedure (range, 1% to 77%), but few would consider this a deterrent from future screening.[14] In these studies, pain was associated with the stage of the menstrual cycle, anxiety, and the anticipation of pain.[14]

A good-quality systematic review of seven intervention trials to reduce pain with screening mammography[210] indicated that discomfort was reduced when written or verbal information was provided to women, and when a breast cushion was used. Use of different breast compression strategies or premedication with acetaminophen had no significant effects in reducing discomfort.

New Studies

Breast compression is used during mammography to create uniform density, reduce breast thickness, and flatten overlying skin and tissues, which contributes to sharper images and reduces the radiation dose. However, compression may add to the discomfort of mammography for some women.

A good-quality recent review of 20 observational studies, most cross-sectional, examined pain or discomfort after screening mammography and its effect on re-attendance for future screening mammography (**Table 25**).[211] Seven studies reported the proportion of women who experienced pain with previous mammography who directly stated this as their reason for non-re-attendance. In these studies, actual non-re-attendance indicating pain as the reason ranged from 11 to 46 percent (5 studies), and intended future non-re-attendance because of pain ranged from 3 to 18 percent (2 studies).

Fifteen studies reported the proportion of women who experienced pain with previous mammography and the proportion of women who re-attended as an outcome, but did not directly ask non-re-attenders for their reasons. There was no difference in actual re-attendance between women who experienced pain and those who did not (RR 1.38; 95% CI, 0.94 to 2.02; 5 studies).[211] However, non-re-attenders had significantly higher pain scores compared with re-attenders in two of three studies. Two studies reported less intent to re-attend for women with pain, with OR 0.61 (95% CI, 0.38 to 0.98) in one study; while three others reported no differences in intended re-attendance and pain. This review is consistent with findings from the previous report.

Key Question 6. How Do the Harms of Routine Breast Cancer Screening Vary by Different Screening Modality?

Summary

- Four of five observational studies demonstrated statistically significantly lower rates of recall for tomosynthesis and mammography compared with mammography alone.
- A U.S. study comparing tomosynthesis and mammography with mammography alone reported a reduction of 16 recalls per 1,000 women and an increase in cancer detection of 1.2 cases per 1,000 women, but also an increase of 1.3 biopsies per 1,000 women. Another U.S. study reported a 38 percent reduction in recall rates when tomosynthesis was added to digital mammography versus mammography alone.
- Women receiving mammography and CBE compared with mammography alone had higher recalls in a study from Canada (55 per 10,000 additional recalls with CBE).
- No studies evaluated screening with ultrasound or MRI in women who are not at high risk for breast cancer.

Evidence

Previous Reports

Previous evidence reviews for the USPSTF did not address this question.

New Studies

There are no RCTs of screening using tomosynthesis, ultrasound, or MRI in women who are not at high risk for breast cancer. Six observational studies compared false-positive recall rates of screening for breast cancer using mammography and tomosynthesis,[146,147,212-214] or CBE[215] compared with mammography alone (**Table 26**). No studies evaluated MRI screening in women who are not at high-risk for breast cancer. Use of supplemental imaging for women with dense breasts is included in a separate report.

Four of five studies demonstrated statistically significantly lower rates of recall for tomosynthesis and mammography compared with mammography alone.[146,147,212-214] One of the U.S. studies reported a reduction of 16 recalls per 1,000 women (95% CI, -18 to -14, $p<0.001$), increase of 1.3 biopsies per 1,000 women (95% CI, 0.4 to 2.1; $p=0.004$), increase in cancer detection of 1.2 per 1,000 women (95% CI, 0.8 to 1.6; $p<0.001$), and increase in invasive cancer detection of 1.2 per 1,000 women (95% CI, 0.8 to 1.6; $p<0.001$).[212]

Recall reductions were not statistically significant in another smaller U.S. study.[146] Importantly, there was an overall reduction in false positives and an increase in biopsies, accompanied by an increase in cancer detection involving only invasive cancers, regardless of breast density or age. [212] Another smaller, U.S. observational study demonstrated reduced recall rates with tomosynthesis after controlling for age, breast density, and breast cancer risk (AOR 0.62, 95%

CI, 0.55 to 0.70; p<0.0001) versus mammography alone.[214] Two European studies also found significantly lower rates of recalls for women screened with tomosynthesis and mammography (1% vs. 2%, p<0.0001;[213] and 53/1,000 vs. 61/1,000; p=0.001).[147]

Women receiving mammography and CBE compared with mammography alone had higher recalls in a study from Canada (8.7% vs. 6.5%; 55/10,000 additional recalls with CBE).[215]

Contextual Question 1. What Are the Rates of Specific Adverse Effects of Current Treatment Regimens for Invasive Breast Cancer and DCIS in the United States?

Rates of specific adverse effects of breast cancer treatment regimens are not provided in centralized sources, but rather the available information is found in publications of surgical case series, clinical trials, and information from drug package inserts. Examples of rates of several recommended and commonly used treatments in the U.S. are summarized in **Table 27**.

Most patients with DCIS and Stage I to III invasive cancer receive surgery, including lumpectomy or mastectomy with sentinel lymph node biopsy and, with more extensive disease, axillary lymph node dissection. Many will also undergo reconstruction surgery. The most common adverse effects include wound infection, skin flap necrosis, and chronic chest wall pain.[216] Approximately 5 percent of patients with sentinel lymph node biopsy and 16 to 18 percent with axillary lymph node dissection develop clinical lymphedema. Some patients experience phantom breast syndrome, pneumothorax, and brachial plexopathy.

Radiation therapy is provided to women with DCIS and Stage I to III disease, and with increasing frequency as the stage of disease progresses. Adverse effects to radiation therapy vary by dose and regimen. For example, among women with breast conserving surgery, a dose of 50 Gy (unit of radiation) in 25 fractions over 5 weeks may cause breast shrinkage in 25 percent, breast induration 18 percent, telangiectasia 5 percent, and breast edema 10 percent. Symptomatic rib fracture, lung fibrosis, ischemic heart disease and brachial plexopathy occur in less than 5 percent.[217]

Endocrine therapy for 5 to 10 years, depending on the drug, is indicated for patients with ER positive DCIS and Stage I to III disease. For some women, tamoxifen causes hot flashes, vaginal discharge, and irregular menses. Less common adverse effects are thromboembolism, endometrial cancer, and cataracts.[218] Anastrozole or other aromatase inhibitors are alternatives to tamoxifen that may cause hot flashes and joint pain. Less common adverse effects are vaginal bleeding, vaginal discharge, thromboembolic events, cataracts, and carpal tunnel syndrome.[219]

Several neoadjuvant/adjuvant chemotherapy regimens are available to treat patients with Stage I to III disease, and selection is based on ER, PR, and HER2 status. Adverse effects include short-term (hair loss, nausea, vomiting, fatigue, neuropathy, neutropenia) and long-term (persistent neuropathy, heart failure) adverse effects that depend on regimen, duration, and age (examples in **Table 27**). Chemotherapy regimens for Stage IV disease are usually provided over extended periods of time because Stage IV disease is not curable. While extended treatment regimens can

control the disease for variable amounts of time depending on disease biology, they may have many adverse effects. These include neutropenia, fatigue, anemia, neuropathy, hair loss, nausea, and stomatitis, among others.

Contextual Question 2. What Are the Absolute Incidence Rates of DCIS and Localized and Advanced Invasive Breast Cancer in Screened and Nonscreened Populations in the United States?

Absolute incidence rates for DCIS and localized and advanced invasive breast cancer are not provided according to screened and nonscreened populations in the United States. The majority of cases of DCIS are identified by mammography screening and the increased incidence of DCIS corresponds to the advent of widespread screening.[32] The most recent rates from SEER for invasive cancer include 129.6 per 100,000 for all age groups; 45.2 per 100,000 for age less than 50 years; and 350.4 per 100,000 for age 50 years or greater.[220] Rates of DCIS include 35.5 pre 100,000 for all age groups; 14.4 per 100,000 for less than 50 years, and 100.0 per 100,000 for age 50 years or greater.[220]

Contextual Question 3. How Do Women Weight Harms and Benefits of Screening Mammography, and How Do They Use This Information in Their Decisions to Undergo Screening?

Research that describes how women weigh the benefits and harms of screening mammography and use this information for clinical decision making is limited. A Cochrane review of RCTs evaluating the effects of personalized risk communication on informed decision making found no association between provision of numerical information and uptake of mammography for women 40 years or older (OR 0.95; 95% CI, 0.78 to 1.15; 6 trials).[221] However, there was an association for greater uptake of mammography when categorical information was given compared with general risk information (OR 1.29; 95% CI, 1.11 to 1.51; 6 trials). The review found that 45 percent (592/1309) of those who received personalized risk information made informed choices, compared with only 20 percent (229/1135) of those who received generic risk information (OR 4.48; 95% CI, 3.62 to 5.53; 3 trials).

Four main themes describing factors that influence a woman's decision to attend breast cancer screening were identified in a review of 12 observational studies.[222] These included psychological and practical factors; issues related to ethnicity; influence of socioeconomic status; and issues related to the screening program. In these studies, cancer anxiety and worry was associated with both the promotion and avoidance of breast cancer screening.[223,224] Some women cited embarrassment as their reason for non-attendance,[224] particularly women of specific religious groups.[225] Most women expressed a preference for a female medical professional performing the screening mammography.[224] Black women were more likely to get information about mammography from their primary physician, while white women were more likely to have received their information from media sources.[226]

In these studies, rates of screening uptake were lower among low-income populations[161,224,227-230] and non-English speakers, and higher income households were twice as likely to attend mammography screening.[228] Lower uptake rates were also associated with lower levels of education, the lack of health insurance, and unemployment. Women from lower socioeconomic backgrounds did not consider themselves at risk for breast cancer and focused on perceived negative aspects of screening and the intrinsic costs (time, embarrassment, and discomfort).[231] In contrast, many women overestimated their risk and the mortality reduction from mammography screening resulting in higher uptake of screening.[232,233]

Chapter 4. Discussion

Summary of Review Findings

Table 28 summarizes the evidence reviewed for this update and **Table 29** provides a concise summary of benefits and harms. Trials of mammography screening indicated reduced breast cancer mortality with screening for women age 39 to 69 years, although results for ages 39 to 49 and 50 to 59 years were of borderline statistical significance and varied depending on how cases were accrued in trials. The absolute breast cancer mortality reduction per 10,000 women screened for 10 years varied from 4 for age 39 to 49 years; 5 to 8 for age 50 to 59 years; and 12 to 21 for age 60 to 69 years. Estimates for age 70 to 74 years were limited by low numbers of events in trials that had smaller numbers of women in this age group. The meta-analysis results reflect updated data from the Canadian (CNBSS-1 and CNBSS-2), Swedish Two-County Study, and Age trials that were not available for the previous review, as well as previously published results from the Stockholm, Gothenburg, Malmö (MMST I and MMST II), and HIP trials. The meta-analyses used long and short case accrual methods in order to explore the methodological differences of the trials and interpret findings using both approaches.

Observational studies of population-based mammography screening reported a wide range of reductions in breast cancer mortality. Most studies were conducted in Europe or the United Kingdom and included women age 50 to 69 years. Meta-analyses of studies indicated a breast cancer mortality RR of 0.75 (95% CI, 0.69 to 0.81) based on seven incidence-based mortality studies; and an OR of 0.69 (95% CI, 0.57 to 0.83) based on seven case-control studies. The 25 to 31 percent mortality reduction from observational studies compares with a 19 to 22 percent reduction estimated from the meta-analysis of screening trials for women age 50 to 69 years. A large observational study of Swedish women in their 40s indicated 26 percent reduction in breast cancer mortality for women invited to screening, while a Canadian study indicated 44 percent reduction for screening participants. These mortality reductions compare with 12 to 16 percent mortality reductions in the trials, although the trial estimates were only of borderline statistical significance.

All-cause mortality did not differ between randomized groups in meta-analyses of trials, regardless of whether trials were analyzed in combined or separate age groups. Also, no trials evaluated mortality outcomes on the basis of risk factors besides age, and there are no head-to-head trials of the effectiveness of different screening intervals or modalities.

The screening trials also provided several measures of intermediate breast cancer outcomes. When thresholds for advanced disease were defined by the most severe categories available from the trials (Stage III + IV disease, size ≥50 mm), a meta-analysis indicated a significant reduction in advanced disease for women age 50 years and older randomized to screening versus nonscreening groups (RR 0.62; 95% CI, 0.46 to 0.83; 3 trials), but not for women age 39 to 49 years. This reduction in intermediate outcomes aligns with the reduction in mortality outcomes that were also statistically significant in the trials for the older age groups.

Although no trials evaluated the incidence of advanced breast cancer outcomes and treatment on

the basis of risk factors or screening intervals, an analysis of BCSC data indicated a lower proportion of Stage III + IV disease among women age 40 to 49 years screened annually versus biennially. Also, BCSC data indicated that women age 40 to 49 years with extremely dense breasts had increased risks for advanced stage cancer (IIB+) and large-size tumors (>20 mm) with biennial compared with annual screening. These results suggest that women in their 40s with increased risk may reduce their risk for higher stage tumors with screening, even though mortality outcomes were not significantly reduced in the trials. These findings are consistent with a modeling study based on BCSC data that indicated that women in their 40s with 2-fold increases in risk (such as with extremely dense breasts) would experience benefits and harms comparable with average-risk women in their 50s when using life-years as the benefit metric.[66]

A Cochrane review that included five screening trials indicated that women randomized to screening were significantly more likely to have surgical and radiation therapy, and less likely to have hormone therapy than controls, while use of chemotherapy was similar between groups. This finding would be expected because screening increases detection of DCIS and early stage disease that are currently aggressively treated. However, treatment outcomes in the RCTs represent outdated therapies that limit their applicability. Observational studies of the impact of screening on advanced cancer diagnosis and treatment generally provided comparisons between screen-detected and nonscreened-detected cases rather than rates between screening populations that more directly address this Key Question.

There were few studies meeting inclusion criteria that compared the effectiveness of screening across various modalities, despite the increasing use of them in clinical practice. Tumor size, stage, and node status did not differ between women screened with tomosynthesis and digital mammography compared with those receiving mammography alone in two case series studies.

Several potential harms were also addressed in this systematic review. Updated BCSC data on digital mammography indicated that false-positive rates and recommendations for additional imaging were highest among women aged 40 to 49 years and declined with age, while false-negative rates were low across all age groups. Rates of recommendations for biopsy did not differ between ages. Results did not differ by time since last mammography screening regardless of whether broad or narrow estimates of one versus two years were used.

Several risk factors were statistically significantly associated with higher rates of false-positive and false-negative results and recommendations for additional imaging and biopsy across most age groups. These included family history of breast cancer, high breast density, and previous benign breast biopsy. Premenopausal status, use of menopausal hormone therapy, and lower BMI were associated with some of the outcomes for specific age groups only. Comparisons based on race and ethnicity indicated the lowest rates of false-positive results and additional imaging among Asians. Comparisons based on different combinations of breast density categories indicated that rates for all outcomes were lowest for women with almost entirely fat breasts, and highest for women with heterogeneously dense breasts or for those in the combined category of heterogeneous and extreme density. Women with extremely dense breasts had the highest rates of false-negative results.

While some risk factors reflect high exposure to estrogen and related changes in breast tissue

(premenopause, menopausal hormone therapy), others may serve primarily as markers of increased breast cancer risk (family history, previous benign biopsy). The mechanisms of these risk factors and whether screening outcomes are influenced by how they affect the mammographic image, increase clinical suspicion, or other ways, are beyond the scope of this analysis.

Additional publications of BCSC data indicated that 10-year cumulative rates of false-positive mammography and biopsy results were higher for annual than biennial screening (mammography 61% vs. 41%; biopsy 7% vs. 5%); for women with heterogeneously dense or extremely dense breasts; women in their 40s; and those who used combination hormone therapy.

Studies of overdiagnosis were primarily based on screening trials, screening programs and registries, or modeled data. Studies differed by their characteristics, methods, and measures, and estimates of the magnitude of overdiagnosis varied depending on the analytic approach, particularly regarding the different denominators used in the estimates. These estimates are difficult to apply to individual women because it is not known which types of cancer will progress, how quickly cancer will advance, and expected lifetimes.

Estimates of overdiagnosis from three RCTs that did not provide screening of controls at the end of the trial (Malmö I, CNBSS-1, CNBSS-2) indicated overdiagnosis rates of 11 to 22 percent. Unadjusted estimates from 13 observational studies indicated rates ranging from 0 to 54 percent; while six studies that adjusted for breast cancer risk and lead time indicated rates ranging from 1 to 10 percent.

Women with false-positive results were more distressed than women with negative results. Anxiety improved over time for most women, but persisted for over 2 years for some. Some women with false-positive results were less likely to return for their next mammogram, although studies were inconsistent. Although many women experienced pain during mammography (1% to 77%), the proportion of those experiencing pain who did not attend future screening varied (11% to 46%). Trials of interventions indicated that discomfort was reduced by providing written or verbal information or using breast cushions.

A U.S. study comparing tomosynthesis and mammography with mammography alone reported a significant reduction of 16 recalls per 1,000 women, but also an increase of 1.3 biopsies per 1,000 women. Mammography and CBE resulted in 55 per 10,000 additional recalls. Studies of screening with MRI or ultrasound focus on high-risk women. The number of deaths due to radiation induced cancer from screening with digital mammography was estimated through modeling as between 2 to 11 per 100,000 depending on age at onset and screening intervals. However, these models are based on assumptions that may not be accurate.

Limitations

Limitations of this review include using only English-language articles, which could result in language bias, although we did not identify non–English-language studies that otherwise met inclusion criteria in our searches. We only included studies that are applicable to current practice

in the United States in order to improve clinical relevance for the USPSTF, excluding much research in the field. This perspective may not be as relevant to other populations and settings. Despite using updated data, the RCTs of screening represent older technologies and cancer treatments that are not relevant today. Also, this update prioritized studies that addressed the Key Questions guiding the review. As with most areas of medicine, breast cancer screening does not exist in isolation, and applying inclusion criteria for studies places artificial boundaries around this complex topic. Many important issues could not be addressed because they were outside the scope of this review, including additional benefits (e.g., increasing breast awareness) and harms (e.g., economic hardship). Studies were lacking for some Key Questions, and the number, quality, and applicability of studies varied widely.

Emerging Issues and Next Steps

Breast cancer is a continuum of entities, not just one disease, that must be considered when choosing screening and treatment options and when balancing benefits and harms. None of the screening trials consider breast cancer in this manner. As diagnostic and treatment experiences become more individualized[234] and include patient preferences and decision making, it becomes even more difficult to characterize benefits and harms in a general way. Many patients would consider quality-of-life issues important outcomes, although these issues are more difficult to measure and report in research studies.

New technologies, such as tomosynthesis and MRI, are becoming more widely used in the United States without definitive studies of their effects on screening outcomes. Consumer expectations that new technology is better than old may obscure potential adverse effects, such as higher false-positive results, biopsies, and expense. No screening trials incorporating newer technologies have been published, and estimates of benefits and harms in this report are based predominantly on studies of film and digital mammography. No trials have evaluated the appropriate interval for mammography screening or the role of risk factors.

Relevance for Priority Populations

Women age 70 years and older are a rapidly growing population in the United States, yet research on breast cancer screening and prevention in this age group is limited. Observational studies suggest that older women may benefit from regular mammography screening.[235,236]

Most of the screening trials and studies of screening programs were based in Europe and the United Kingdom, and enrolled predominantly white women. Data on race and ethnicity from the BCSC suggest possible differences between groups, but inferences from these subgroups are generally inconclusive because of lower numbers of participants and missing data.

Very little research has been conducted on women who are not screened in the United States, whether by choice, access, or other issues. Individuals who do not participate in screening and prevention services differ from those who do, and particularly differ from women who enroll in research studies. More information about this population could lead to improvements that could

serve them better than currently available services.

Future Research

Additional research on benefits and harms of mammography screening with quality-of-life outcomes, as well as morbidity and mortality outcomes, would provide further understanding of the implications of routine screening. Data for specific groups of women, based on risk, racial and ethnic background, access to screening, or existence of co-morbidities, for example, could inform screening practice. Studies of older women are essential in order to improve the evidence on screening for them including when to discontinue screening. Studies on the role of additional imaging modalities in screening are required in order to appropriately incorporate this technology in the screening process. More information on DCIS is needed, including its implications and outcomes. Distinguishing aggressive from non-aggressive forms of DCIS could lead to more selective treatment and reduce the consequences of overdiagnosis, particularly uncertainties regarding the transition from DCIS to invasive cancer, and lead time issues. Improving the methodology and assumptions involved in estimates of overdiagnosis would provide more meaningful understanding of this potential harm.

Conclusions

Trials indicate that mammography screening prevents 4 deaths per 10,000 women age 40 to 49 years after 10 years; 5 to 8 for age 50 to 59 years; and 12 to 21 for age 60 to 69 years; while estimates for age 70 to 74 years are limited by low numbers. These results are generally supported by observational studies of screening programs of women age 50 to 69 years. Higher stage tumors are also reduced with screening for women over age 50 years and for younger women with dense breasts who have annual compared with biennial screening. False-positive results and additional imaging are common, particularly for younger women and those with risk factors, while biopsies occur less often. Rates of false-negative results are low. Estimates of overdiagnosis based on trials ranged from 11 to 22 percent, while estimates based on observational studies ranged from 1 to 10 percent. Although RCTs are lacking, observational studies of tomosynthesis and digital mammography indicate reduced recalls, but increased cancer detection and biopsy rates. Mammography screening at any age is a tradeoff of a continuum of benefits and harms that varies on population and individual levels.

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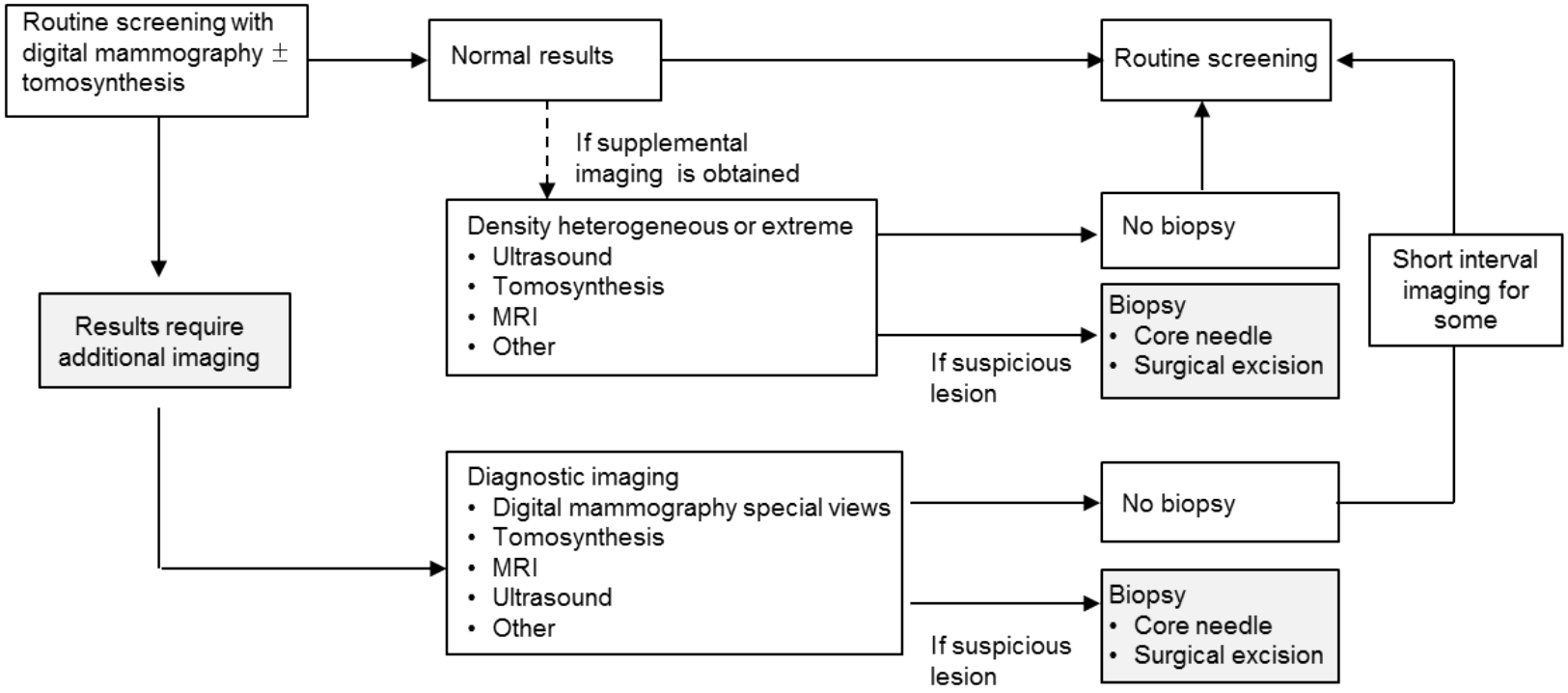
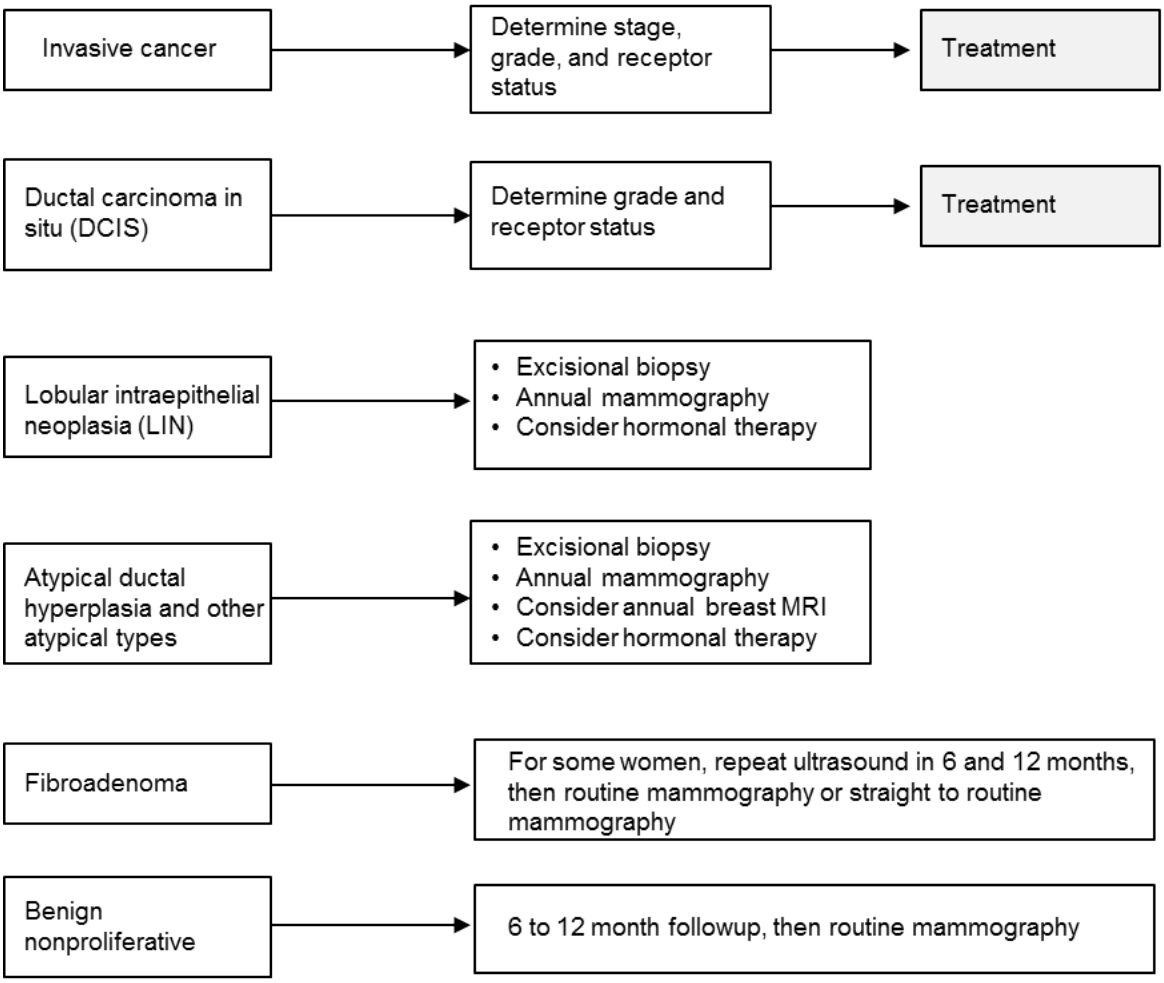
Figure 1. Breast Cancer Screening Clinical Pathway



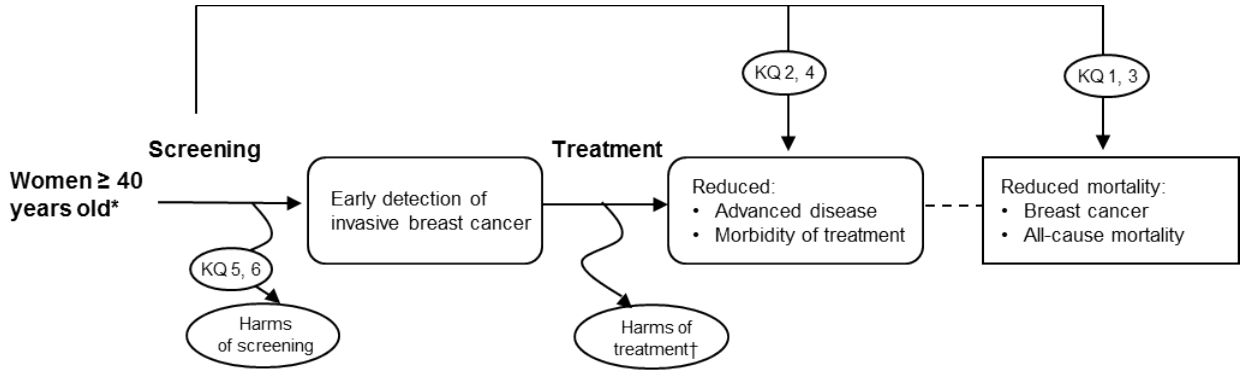
Abbreviation: MRI=magnetic resonance imaging.

Figure 2. Clinical Pathway After Biopsy



Abbreviation: MRI=magnetic resonance imaging.

Figure 3. Analytic Framework and Key Questions



Key Questions:

In the target population of women age 40 years and older*:

1. What is the effectiveness of routine mammography screening in reducing breast cancer–specific and all-cause mortality, and how does it differ by age, risk factor‡, and screening interval?
2. What is the effectiveness of routine mammography screening in reducing the incidence of advanced breast cancer and treatment-related morbidity§, and how does it differ by age, risk factor‡, and screening interval?
3. How does the effectiveness of routine breast cancer screening in reducing breast cancer–specific and all-cause mortality vary by different screening modality‖?
4. How does the effectiveness of routine breast cancer screening in reducing the incidence of advanced breast cancer and treatment-related morbidity§ vary by different screening modality‖?
5. What are the harms¶ of routine mammography screening, and how do they differ by age, risk factor‡, and screening interval?
6. How do the harms¶ of routine breast cancer screening vary by different screening modality‖?

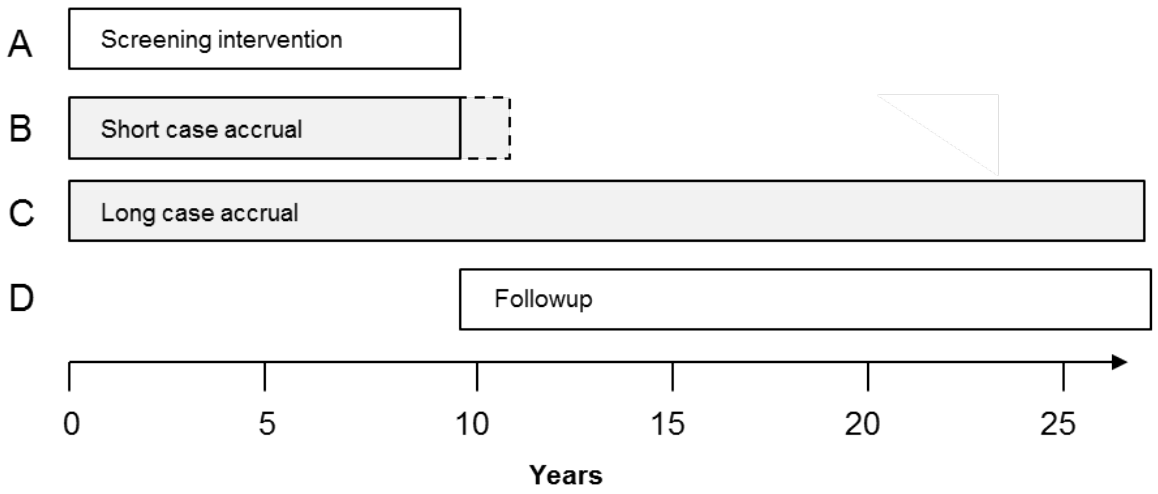
Contextual Questions:

1. What are the rates of specific adverse effects of current treatment regimens for invasive breast cancer and ductal carcinoma in situ (DCIS) in the United States?
2. What are the absolute incidence rates of DCIS and localized and advanced invasive breast cancer in screened and nonscreened populations in the United States?
3. How do women weigh the harms and benefits of screening mammography and how do they use this information in their decisions to undergo screening?

*Excludes women with pre-existing breast cancer; clinically significant BRCA mutations, Li-Fraumeni syndrome, Cowden syndrome, hereditary diffuse gastric cancer, or other familial breast cancer syndromes; high-risk lesions (DCIS, LCIS, ADH, ALH); or previous large doses of chest radiation (≥ 20 Gy) before age 30.
†Addresses contextual question 1.
‡Risk factors include: family history, breast density, race/ethnicity, menopausal status, current use of menopausal hormone therapy or oral contraceptives, prior benign breast biopsy, and, for women age >50 years, body mass index.
§Morbidity includes: physical adverse effects of treatment, quality of life measures, other measures of impairment.
‖Screening modalities include: mammography (digital, tomosynthesis), magnetic resonance imaging (MRI), ultrasound, and clinical breast examination (alone or in combination).
¶ Harms include: false positive findings, anxiety, false positive biopsies, false negative findings, false reassurance, overdiagnosis and resulting overtreatment, and radiation exposure.

Abbreviations: ADH=atypical ductal hyperplasia; ALH=atypical lobular hyperplasia; BRCA=breast cancer gene; DCIS=ductal carcinoma in situ; Gy=gray (unit of absorbed radiation); KQ=key question; LCIS=lobular carcinoma in situ; MRI=magnetic resonance imaging.

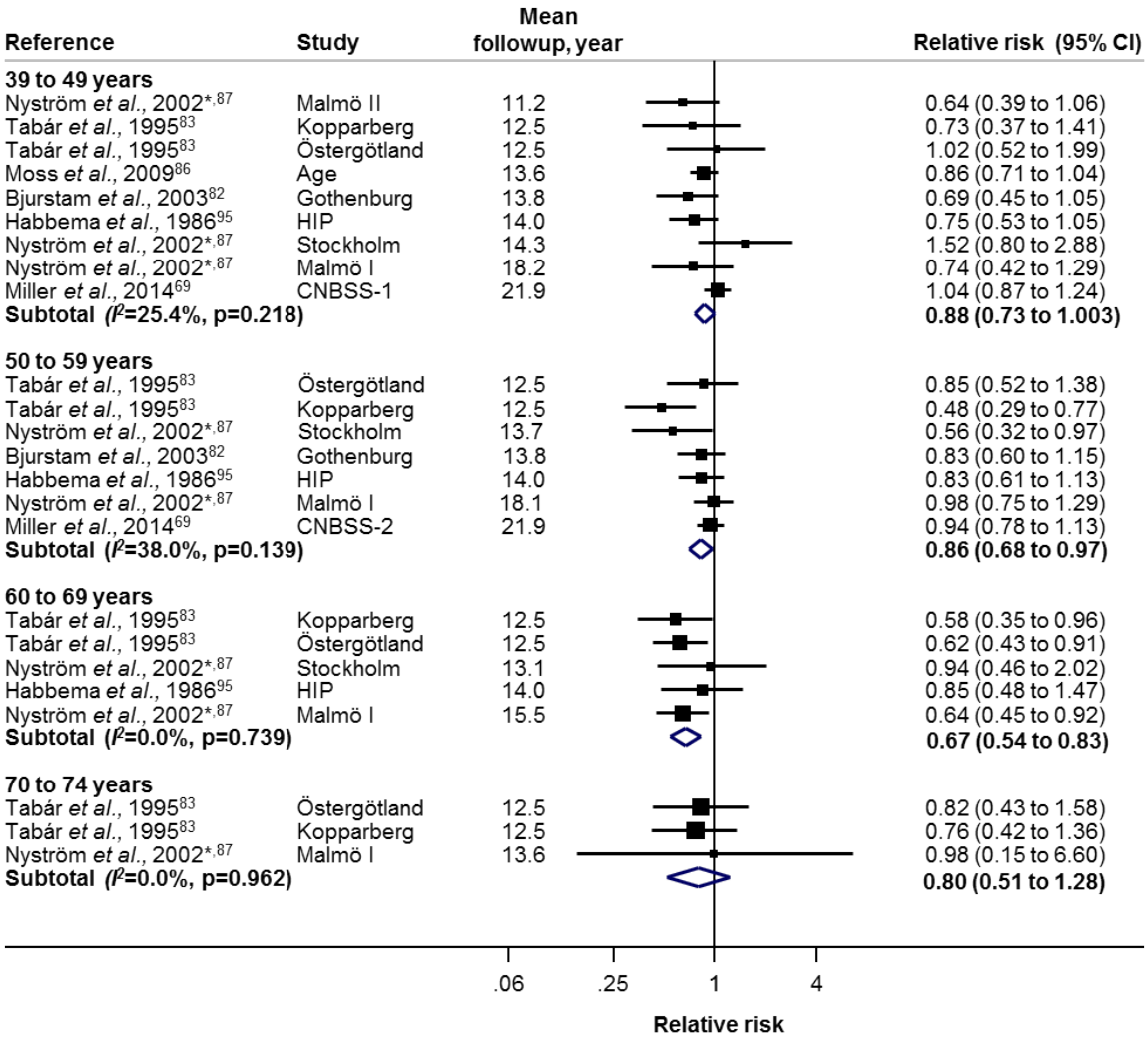
Figure 4. Methods of Case Accrual in Trials



Comparison of Accrual Methods

Short case accrual (B)	Includes deaths occurring among cases diagnosed during the screening intervention period (A), and in some trials, within an additional defined case accrual period.	• Includes fewer cases • Reduces contamination of control group if screened during followup • Can introduce bias in the absence of concurrent screening after the intervention
Long case accrual (C)	Includes deaths occurring among cases diagnosed during the screening intervention period plus the followup period (A+D).	• Includes more cases. • Potential to dilute a true benefit because participants from the control group may be screened after the study intervention period has ended.

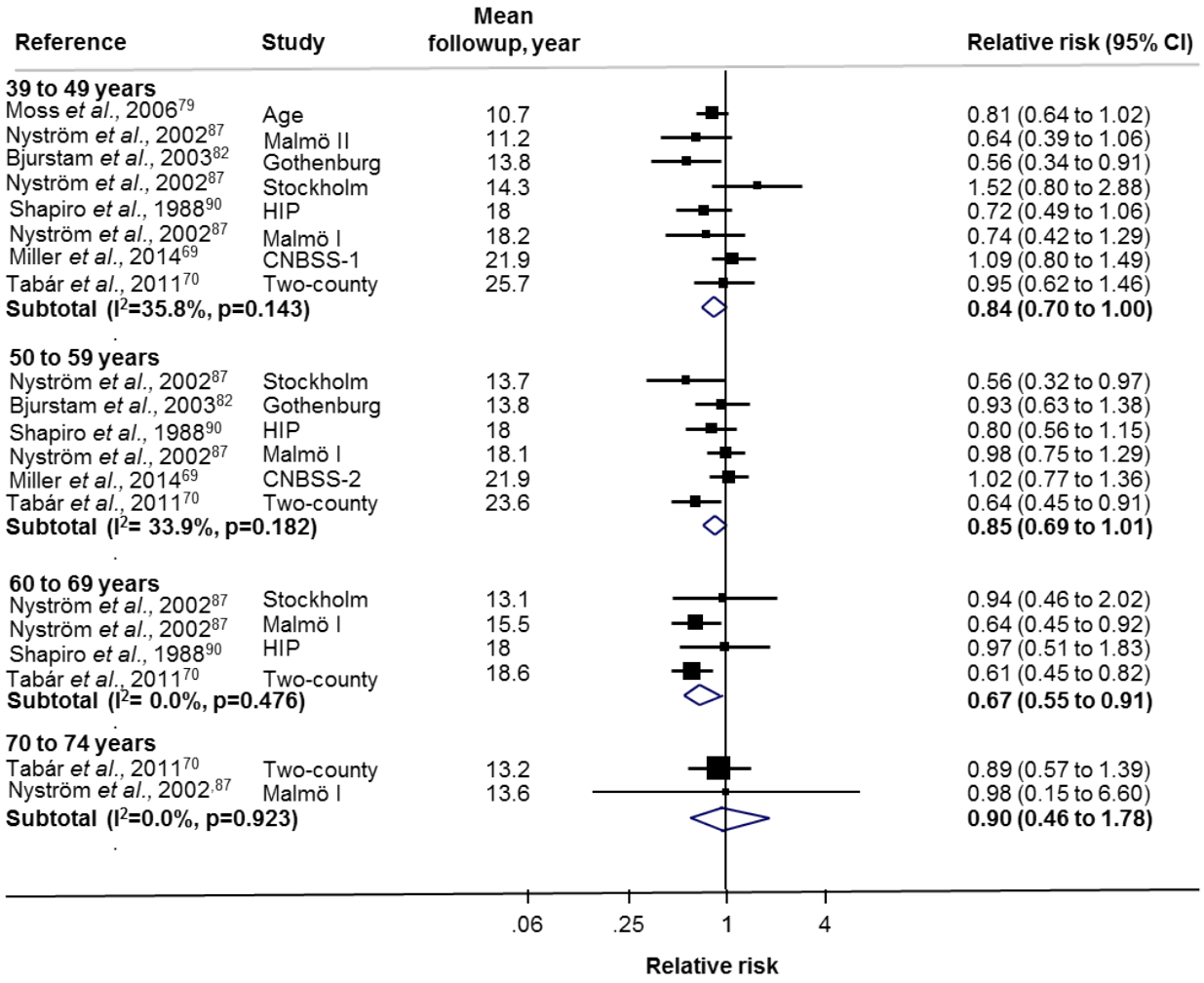
Figure 5. Meta-Analysis of Effects of Screening Trials on Breast Cancer Mortality With Longest Case Accrual Available



*Uses short case accrual, but these are the most inclusive results available.

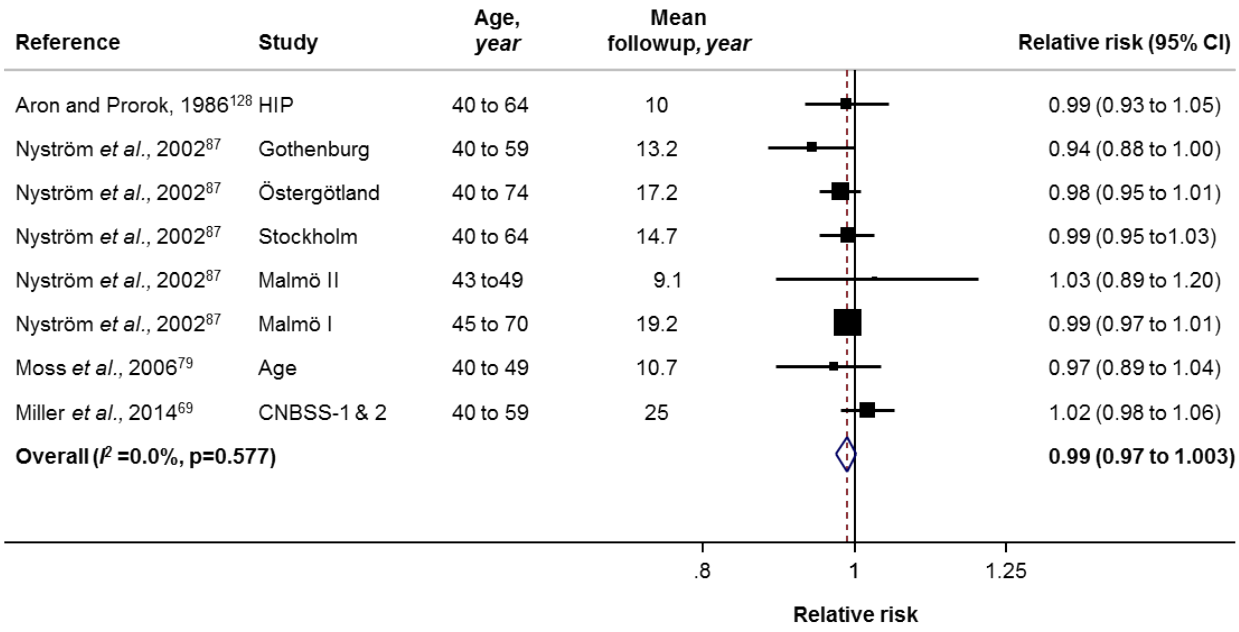
Abbreviations: CI=confidence interval; CNBSS=Canadian National Breast Screening Study; HIP=Health Insurance Plan of Greater New York.

Figure 6. Meta-Analysis of Effects of Screening Trials on Breast Cancer Mortality With Short Case Accrual



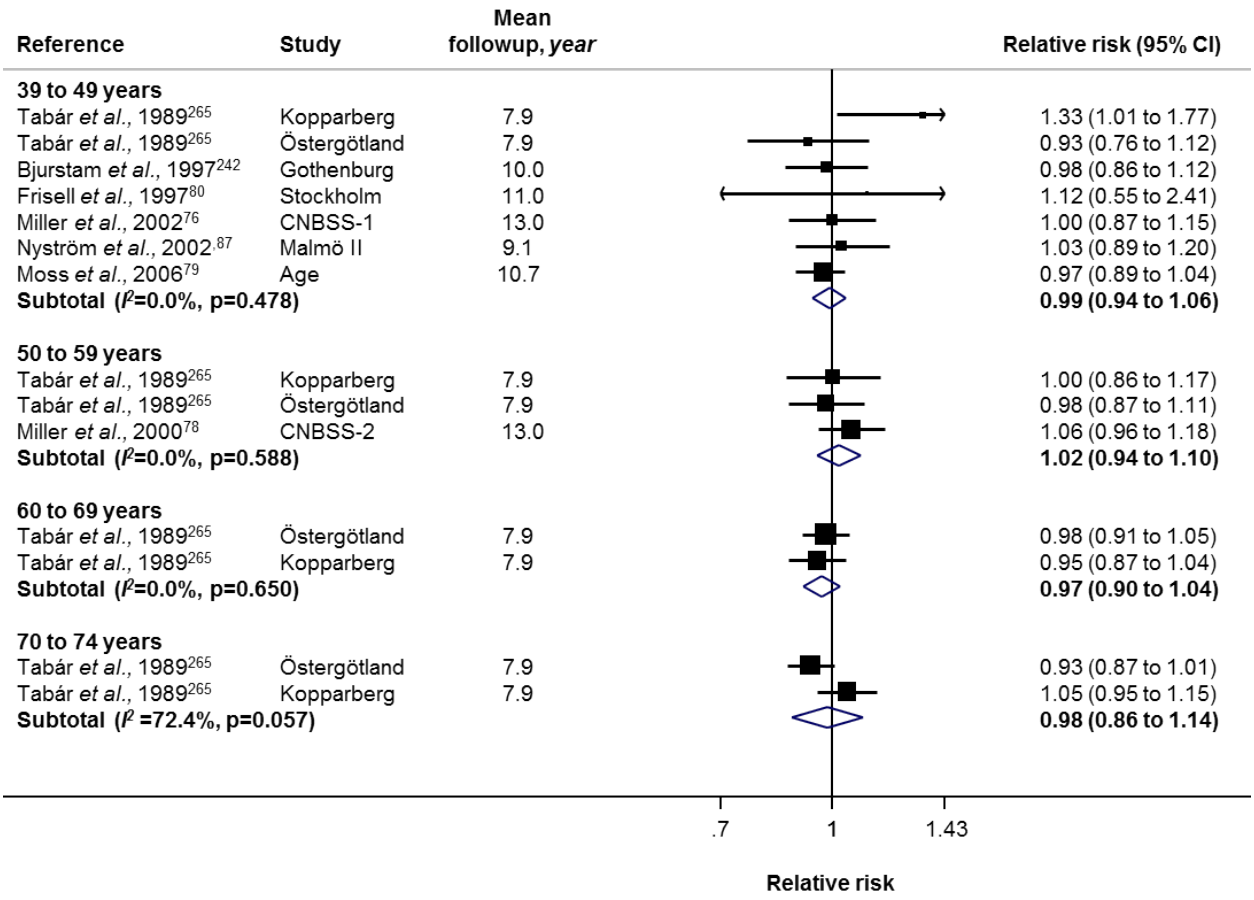
Abbreviations: CI=confidence interval; CNBSS=Canadian National Breast Screening Study; HIP=Health Insurance Plan of Greater New York.

Figure 7. Meta-Analysis of Effects of Screening Trials on All-Cause Mortality, With Combined Ages



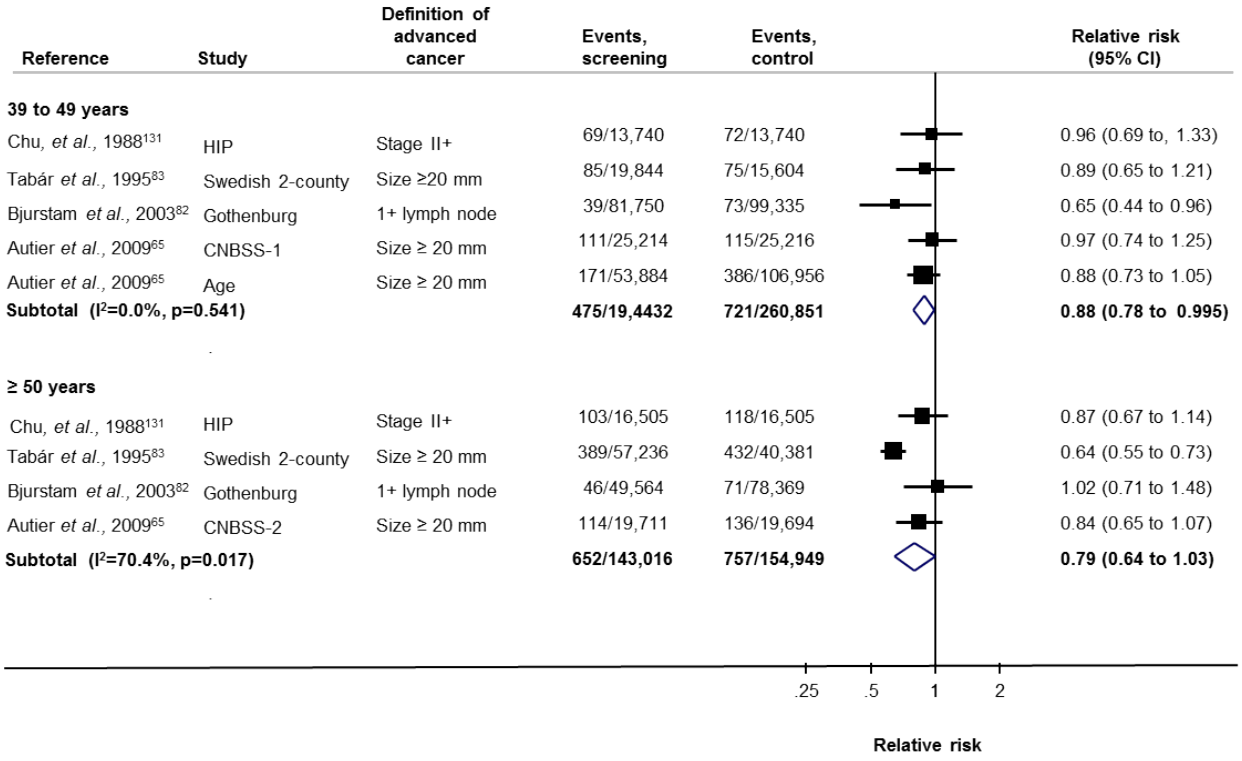
Abbreviations: CI=confidence interval; CNBSS=Canadian National Breast Screening Study; HIP=Health Insurance Plan of Greater New York.

Figure 8. Meta-Analysis of Effects of Screening Trials on All-Cause Mortality, Stratified by Age



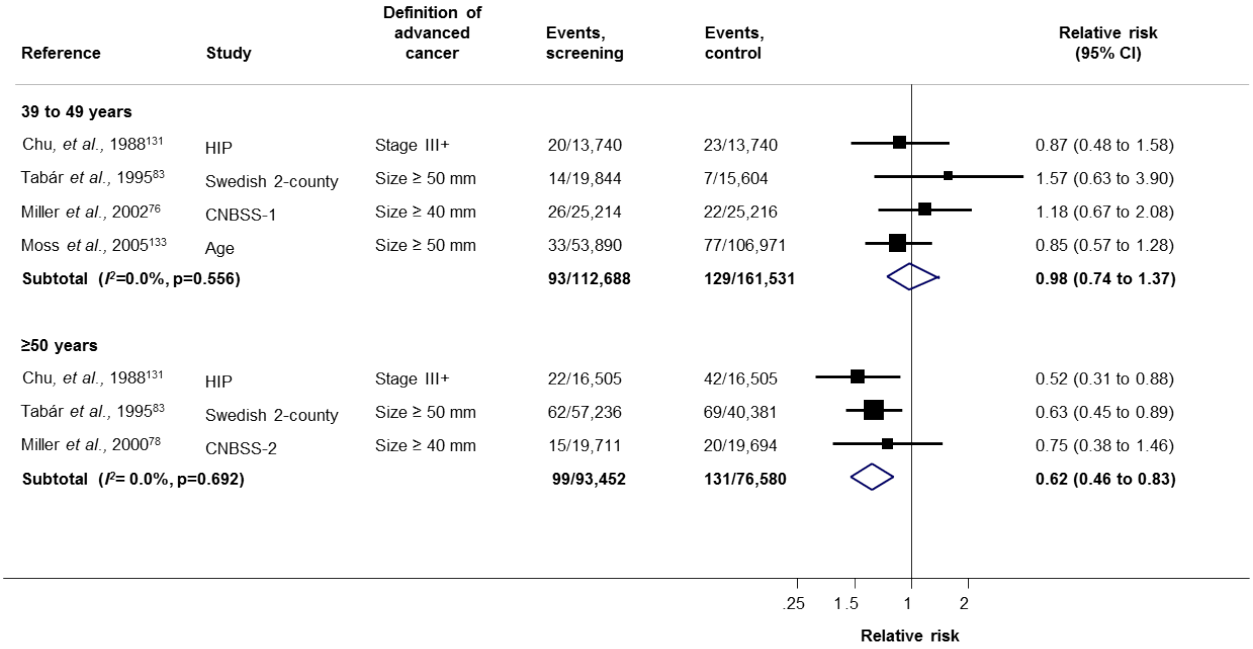
Abbreviations: CI=confidence interval; CNBSS=Canadian National Breast Screening Study; HIP=Health Insurance Plan of Greater New York.

Figure 9. Meta-Analysis of Effects of Screening Trials on Advanced Cancer Outcome Using a Low Threshold for Advanced Cancer



Abbreviations: CI=confidence interval; CNBSS=Canadian National Breast Screening Study; HIP=Health Insurance Plan of Greater New York; mm=millimeter.

Figure 10. Meta-Analysis of Effects of Screening Trials on Advanced Cancer Outcome Using a Higher Threshold for Advanced Cancer



Abbreviations: CI=confidence interval; CNBSS=Canadian National Breast Screening Study; HIP=Health Insurance Plan of Greater New York; mm=millimeter.

Table 1. Breast Cancer Staging System*

Description	
Primary tumor (T)	T1=tumor size ≤20 mm T2=>20 mm but ≤50 mm T3=>50 mm T4=tumor of any size with direct extension to the chest wall and/or skin
Regional lymph nodes (N)	N0=no regional lymph node metastases N1mi=micrometastases N1=metastases to moveable ipsilateral axillary lymph nodes N2=metastases in ipsilateral axillary lymph nodes that are clinically fixed N3=metastases that are more extensive
Distant metastasis (M)	M0=no evidence of distant metastases M1=distant detectable metastases as determined by clinical and radiographic means
Stage	
0	DCIS
I	IA=T1, N0, M0 IB=T0, N1mi, M0 or T1, N1mi, M0
II	IIA=T0, N1, M0 or T1, N1, M0 or T2, N0, M0 IIB=T2, N1, M0 or T3, N0, M0
III	Larger size tumors with various combinations of lymph node involvement that are more extensive than stage II, but no distant metastases
IV	Distant metastases (M1)

*Adapted from 2014 National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology.[36]

Abbreviations: DCIS=ductal carcinoma in situ; mm=millimeter.

Table 2. Treatment of DCIS and Invasive Breast Cancer by Stage*

Treatment	0 (DCIS)	I, IIA, IIB, or T3, N1, M0	III (locally advanced)	IV (metastatic)
Surgery	Total mastectomy ± sentinel node biopsy ± reconstruction; or lumpectomy without lymph node surgery.	Total mastectomy or lumpectomy + axillary staging ± breast reconstruction.	If response to pre-operative therapy, total mastectomy or lumpectomy + axillary dissection ± delayed breast reconstruction.	None
Radiation	Whole breast radiation may be added to lumpectomy.	Radiation to whole breast and lymph nodes if involved; follows chemotherapy if provided.	Radiation to chest wall and lymph nodes.	Selective radiation to bone or brain metastases.
Chemotherapy†	None	Systemic adjuvant therapy as indicated by ER, PR, and HER2 status and predictive tests for chemotherapy benefit.	• Pre-operative systemic therapy. • 1-year therapy with trastuzumab if HER2-positive.	• If bone disease present, denosumab, zoledronic acid, or pamidronate. • If ER and PR-negative; or ER and/or PR-positive and endocrine refractory; consider chemotherapy.‡
Endocrine treatment§	If ER-positive, consider tamoxifen for 5 years for prevention.	If ER-positive, tamoxifen for 10 years or aromatase inhibitor for 5 years (if post-menopausal only) or switching strategy of tamoxifen/aromatase inhibitor.	If ER-positive, tamoxifen for 10 years or aromatase inhibitor for 5 years (if post-menopausal only) or switching strategy of tamoxifen/aromatase inhibitor.	• Treatment regimen based on receptor status. • If ER positive, consider ovarian ablation/ suppression for premenopausal women

*Adapted from 2014 National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology.[35]
†Neoadjuvant/adjuvant chemotherapy: HER2-negative disease=AC (doxorubicin/cyclophosphamide) followed by paclitaxel, or TC (docetaxel and cyclophosphamide); HER2-positive disease=doxorubicin/cyclophosphamide followed by paclitaxel plus trastuzumab ±pertuzumab, or TCH (docetaxel/carboplatin/trastuzumab) ± pertuzumab.
‡Chemotherapy regimens for stage IV (metastatic cancer): preferred single agents=anthracyclines (doxorubicin, pegylated liposomal doxorubin), taxanes (paclitaxel, docetaxel, nab-paclitaxel), anti-metabolites (capecitabine, gemcitabine), other microtubule inhibitors (vinorelbine, eribulin); chemotherapy combinations=CAF/FAC (cyclophosphamide/doxorubicin/fluorouracil), FEC (fluorouracil/epirubicin/cyclophosphamide), AC (doxorubicin/cyclophosphamide), EC (epirubicin/cyclophosphamide), CMF (cyclophosphamide/methotrexate/fluorouracil), docetaxel/capecitabine, GT (gemcitabine/paclitaxel), gemcitabine/carboplatin, paclitaxel/bevacizumab.
§Endocrine therapy for systemic disease: stage I-III=non-steroidal aromatase inhibitor (anastrozole, letrozole); steroidal aromatase inactivator (exemestane); tamoxifen; stage IV=non-steroidal aromatase inhibitor (anastrozole, letrozole); steroidal aromatase inactivator including exemestane, exemestane + everolimus, fulvestrant, tamoxifen or toremifene, megestrol acetate, fluoxymesterone, ethinyl estradiol.

Abbreviations: DCIS=ductal carcinoma in situ; ER=estrogen receptor; HER2=human epidermal growth factor receptor 2; PR=progesterone receptor.

Table 3. Imaging Modalities for Breast Cancer Screening of Average-Risk Women*

Imaging modality†	Description; indication for use; average radiation dose (MQSA)[237]	Limitations	Summary of performance‡
Mammography	• A screening mammogram is performed in a woman with no clinical symptoms or complaints to detect early stage or clinically occult breast cancer. • Two views (craniocaudal and mediolateral oblique) of each breast are obtained for routine evaluation.	Limitations vary by type of mammography	Variable performance by type of mammography
Film mammography	• Uses x-rays transmitted through the breast tissue to create an image that is processed and displayed as a grayscale image directly on a film. • Adequate breast compression is required. • Women with larger breasts may require more than two views of each breast to ensure imaging of all breast tissues. • Average radiation dose is 4.7 mGy.	• Limited sensitivity in women with radiographically dense breasts. • Subject to artifacts from processing and storage. • Inability to manipulate the image following exposure.	All women: • Sensitivity 0.41 ±0.03 • Specificity 0.98 ±0.001 • PPV 0.13 ±0.01 Women <50: • Sensitivity 0.35 ±0.06 • Specificity 0.98 ±0.001 • PPV 0.07 ±0.01
Digital mammography (DM)	• Digital detectors convert the x-ray photons to an electronic signal that is changed to a digital image and is processed and displayed as a gray scale image to be stored or sent electronically. Software can be used to help interpret digital images. • Available in >90% of imaging centers in the United States as of 2013 .[238] • May be more effective than film in women <50; woman with heterogeneously or extremely dense breast tissue; or pre- or perimenopausal women. • Average radiation dose is 3.7 mGy.	• Less spatial resolution compared with film. • More expensive (1.5 to 4 times cost of film).[239]	All women: • Sensitivity 0.41 ±0.03 • Specificity 0.98 ±0.001 • PPV 0.12 ±0.01 Women <50: • Sensitivity 0.49 ±0.06 • Specificity 0.97 ±0.001 • PPV 0.08 ±0.01
Tomosynthesis	• A modification of DM that acquires images of a stationary, compressed breast at multiple angles during a short scan. • Individual images are reconstructed to generate a series of thin sections of images that can be displayed individually or in a loop. • Used in combination with standard DM for screening. Average radiation dose 1 to 2 times DM.	When performed in the screening setting, the patient is exposed to approximately twice the usual radiation dose, which can be even greater if the patient has dense or thick breasts.	Compared to digital mammography: PPV for recall 6.4% (±2.1%; 95% CI,1.7% to 2.5%, p<0.001)[212]

Table 3. Imaging Modalities for Breast Cancer Screening of Average-Risk Women*

Imaging modality†	Description; indication for use; average radiation dose (MQSA)[237]	Limitations	Summary of performance‡
Ultrasound	• Sound waves used to create images of the breast using a non-invasive, hand held device. Images obtained by radiologist or technologist and are operator dependent. Whole breast ultrasound recently approved by the FDA for screening of patients with dense breasts. • Not currently indicated for routine screening. • There are no RCTs showing survival benefit of screening women with dense breasts with supplemental whole breast ultrasound screening (whole breast ultrasound) in addition to mammography. • Several states have now implemented standard reporting on breast density, which includes the recommendation for ultrasound for dense breasts. • No radiation.	• Not an appropriate initial screening modality for breast cancer, but has been approved as an adjunct to mammography for screening in women with increased breast density.[240] • Ultrasound alone is not a good breast cancer screening tool and has many false-positive and false-negative results. • No uniform standards for performance. • Variable image quality depending on the skill and experience of the examiner. • Highly operator dependent and there can be significant intra- and inter-observer variability. • Limited ability to detect DCIS.	No data for average risk women; available performance measures are based on studies of women with increased risk and dense breasts.[46]
MRI with and without contrast	• Magnetic fields are used to create an image of the breast. Intravenous contrast agent given for the procedure. • Not indicated for screening in average-risk populations; diagnostic modality in specific subpopulations. • No radiation.	Not an appropriate initial screening modality for breast cancer, but has been promoted as a screening test among women at elevated risk, including *BRCA1/2* mutation carrier, strong family history of breast cancer, or several genetic syndromes.	No data for average risk women; available performance measures are based on studies of high-risk women. [46]

Adapted from 2013 ACR BIRADS Atlas 5th Edition.[29]
*Average-risk women: women with <15% lifetime risk of breast cancer. Performance measures may vary based on risk, including breast density.
†Does not include other technologies *not* approved for screening: Positron emission mammography (PEM) and breast specific gamma imaging (BSGI).
‡Performance based on DMIST: Pisano, ED. Diagnostic performance of digital versus film mammography for breast-cancer screening. *N Engl J Med*. 2005;353(17):1773-83.

Abbreviations: BRCA=breast cancer susceptibility gene; CI=confidence interval; DCIS=ductal carcinoma in situ; DM=digital mammography; FDA=U.S. Food and Drug Administration; mGy=milligray; MQSA=Mammography Quality Standards Act; MRI=magnetic resonance imaging; PPV=positive predictive value; RCT=randomized controlled trial.

Table 4. Mammography Screening Trials

Trial (references)	Year trial began	Setting/population (screening, *n*; control, *n*)*	Method of randomization	Comparison groups	Interval, *months*	Rounds, *n*	Views, *n*	Adherence, *%*	Duration, *years*	Longest followup, *years*	USPSTF quality rating; limitations
HIP[90,95,128,131]	1963	New York health plan members age 40-64 (30,239; 30,765)	Age and family size stratified pairs of women were individually randomized by drawing from a list	M + CBE vs. UC	12	4	2	46	4	18	Fair†‡§
CNBSS-1; CNBSS-2‖[69,76,78]	1980	Self-selected participants from 15 centers in Canada age 40-49 (CNBSS-1; 25,214; 25,216) and 50-59 (CNBSS-2; 19,711; 19,694)	Individual within blocks stratified by center and 5-year age group after CBE	M + CBE vs. UC (all women prescreened with CBE and instructed in BSE); women 50-59 UC involved annual CBE; all age ≥50 offered screening after trial completed	12	4-5	2	85	4.5	25	Fair†
Gothenburg[82,241,242]	1982	All women age 39-59 born between 1923 to 1944 living in Gothenburg, Sweden (21,650; 29,961)	Cluster, based on day of birth for 1923 to 1935 cohort (18%), by individual for 1936 to 1944 cohort (82%)	M vs. UC; controls offered screening after 5 years, trial completed after approximately 7 years	18	5	1-2	75	9	12	Fair†‡¶
Stockholm[80,243]	1981	Residents age 40-64 from southeast greater Stockholm, Sweden (40,318; 19,943)	Individual, by day of month; ratio of screening to control group 2:1	M vs. UC; controls screened after 5 years	24-28	2	1	81	4.8	11.4	Fair†
Malmö I & II[81, 244,245]	1976-1978	All women age 43-69 born between 1908 to 1945 living in Malmo, Sweden (MMST I=21,088; 21,195, MMST II=9,581; 8,212)	Individual, within birth year	M vs. UC; controls offered screening after year 14	18-24	9	1-2	70	10+	11-13; 15.5	Fair†‡¶
Swedish Two-County[83,246, 247]	1977	Women age 40-70 from Ostergotland and Kopparberg counties in Sweden (77,080; 55,985)	Clusters, based on geographic units; blocks designed to be demographically homogeneous	M vs. UC; controls offered screening after year 7	24-33	3	1	84	7	20; 15.5	Fair†

Table 4. Mammography Screening Trials

Trial (references)	Year trial began	Setting/population (screening, *n*; control, *n*)*	Method of randomization	Comparison groups	Interval, *months*	Rounds, *n*	Views, *n*	Adherence, *%*	Duration, *years*	Longest followup, *years*	USPSTF quality rating; limitations
Age‖[79,86]	1991	Women age 39-41 from 23 National Health Service breast screening units in England, Scotland, and Wales (53,884; 106,956)	Individual stratified by general practitioner group with random number generation 1991 to 1992; 1992 onwards randomization via Health Authority computer system	M vs. UC; all women offered screening at ages 50-52	12	4-6, varied by center	2	57	9	13	Fair†¶

*Numbers of participants in screening and control groups vary by publication.
† Generally effective randomization and comparable groups are assembled initially, but some question remains whether some, although not major, differences occurred in followup.
‡ Important differential loss to followup or overall high loss to followup; adherence <80%.
§ Numbers of participants in screening and control groups vary by publication.
‖ New data since prior recommendation.
¶ Maintenance of comparable groups (includes attrition, crossovers, adherence, contamination).

Abbreviations: BSE=breast self-examination; CBE=clinical breast examination; CNBSS=Canadian National Breast Screening Studies; HIP=Health Insurance Plan of New York; M=mammography; MMST=Malmö Mammographic Screening Trial; n=number; UC=usual care; USPSTF=U.S. Preventive Services Task Force; vs.=versus.

Table 5. Age-Specific Rates of Breast Cancer Mortality Reduction With Screening

Number of deaths prevented if 10,000 women were followed for 10 years

Age, *years*	Mortality rate in the control group per 100,000 person-years (95% CI)*	Breast cancer mortality reduction RR (95% CI)†	Deaths prevented with screening over 10 years (95% CI)
Long case accrual			
39-49	34 (26 to 44)	0.88 (0.73 to 1.003)	4.1 (-0.1 to 9.3)
50-59	54 (50 to 58)	0.86 (0.68 to 0.97)	7.7 (1.6 to 17.2)
60-69	65 (52 to 81)	0.67 (0.54 to 0.83)	21.3 (10.7 to 31.7)
70-74	62 (48 to 80)	0.80 (0.51 to 1.28)	12.5 (-17.2 to 32.1)
50-69	58 (55 to 62)	0.78 (0.68 to 0.90)	12.5 (5.9 to 19.5)
Short case accrual			
39-49	23 (16 to 32)	0.84 (0.70 to 1.002)	3.5 (-0.1 to 7.4)
50-59	31 (24 to 39)	0.86 (0.69 to 1.007)	4.5 (-0.2 to 9.8)
60-69	40 (28 to 56)	0.67 (0.55 to 0.91)	12.1 (3.4 to 20.7)
70-74	49 (36 to 64)	0.90 (0.46 to 1.78)	12.2 (-37.7 to 26.9)
50-69	32 (24 to 41)	0.81 (0.69 to 0.95)	6.1 (1.2 to 10.9)

*Based on trials of screening included in the meta-analysis.
†From meta-analysis of screening trials using two different methods of case accrual.

Abbreviations: CI=confidence interval; RR=relative risk.

Table 6. Biases and Limitations of Observational Studies of Mammography Screening

Study design	Description	Limitations
Time-trend	Compares changes in breast cancer mortality among populations in relation to the introduction of screening (before/after or ecologic).	• Applicability to current populations and settings may be low. • Mortality rates may be affected by changes in diagnosis and treatment over time. • Analysis assumes constancy over time. • High risk for lead-time and length-time biases depending on the choice of comparison time periods. • Comparison groups based on age or location are not stable over time. • Opportunistic screening in the control group may dilute mortality estimates or screening effects.
Incidence-based mortality	Compares mortality rates of women screened or invited to screen with women not screened or invited. To reflect the incidence of breast cancer, rather than prevalence, these studies include only breast cancer cases diagnosed during a specific time period that follows the initial screen.	• High risk for lead-time and length-time biases. • Short case accrual or followup periods inadequately determine mortality effect. • Opportunistic screening in the control group may dilute mortality estimates or screening effects. • Self-selection bias results in important differences between women attending screening and those who do not; including social, demographic, and health factors that independently influence outcomes. • Dependent on correct choices of comparison groups.
Case-control	Compares histories of screening between women dying of breast cancer with women not dying of breast cancer.	• Self-selection bias. • Women who had access to screening likely had access to effective treatment. • Retrospective data analysis is subject to recall bias and missing data. • Lower power to detect mortality differences between groups.

Table 7. Observational Studies of Screening and Mortality Not Included in Systematic Reviews

Author, year	Study design	Population; age, year; participants, n	Study years; participation rate, %; comparison	Adjusted for previous breast cancer	Reduction in breast cancer mortality	Reduction in all-cause mortality	Quality rating; limitations
Coldman et al, 2008[129]	Time-trend	British Columbia, Canada, 4 cohorts based on date and age at first screening; 40-79; 658,151	1988-2005; 70%; change from annual to biennial in 1997 for age 50-79	NR	Breast cancer deaths (mortality ratio pre vs. post) • 40-49 years: 0.67 (95% CI, 0.33 to 1.37) • ≥50 years: 1.06 (95% CI, 0.76 to 1.46)	NR	NA
Coldman et al, 2014[124]	Incidence-based mortality	Canadian Screening Programs; 40-79; 2,796,472	1990-2009; 85% of Canadians; women participating in screening vs. not participating	NR	Breast cancer deaths (standardized mortality ratio) • 40-49 years: 0.56 (95% CI, 0.45 to 0.67) • 50-59 years: 0.60 (95% CI, 0.49 to 0.70) • 60-69 years: 0.58 (95% CI, 0.50 to 0.67) • 70-79 years: 0.65 (95% CI, 0.56 to 0.74)	NR	NA
Hellquist et al, 2011[123]	Prospective cohort (Poisson distribution)	Swedish counties in Mammography Screening of Young Women cohort; 40-49; 620,620	1986-2005; 80-90%; invited vs. not invited to screen	Yes	Breast cancer deaths (person-years), invited vs. not • Adjusted for invitation: 619 vs. 1,205; RR 0.74 (95% CI, 0.66 to 0.83) • Adjusted for attendance: 523 vs. 1,205; RR 0.71 (95% CI, 0.62 to 0.80) • NNS during a 10-year period to save 1 life: 1,252 (95% CI, 958 to 1,915)	NR	Fair
Hofvind et al, 2012[125]	Time-trend	Norwegian Breast Cancer Screening Program; 55-74; N=10,478 cancer cases	Pre-screening (1984-1995) vs. biennial screening (1996-2007)	Unclear	Age standardized breast cancer mortality rate • Pre: 20/100,000 • Post: 14/100,000	Age standardized mortality rate • Pre: 68/100,000 to 80/100,000 • Post: 51/100,000	NA
Hofvind et al, 2013[126]	Prospective cohort	Norwegian Breast Cancer Screening Program; 50-69; 699,628	1996-2010; 84%; screened vs. non-screened	Unclear	Breast cancer deaths (women years), nonscreened vs. screened • Number of deaths: 392/2,055 vs. 998/13,162 • Adjusted breast cancer mortality: 1.00 vs. 0.39 (95% CI, 0.35 to 0.44) • Adjusted for self-selection bias: 1.00 vs. 0.57 (95% CI, 0.51 to 0.64)	NR	Fair*

Table 7. Observational Studies of Screening and Mortality Not Included in Systematic Reviews

Author, year	Study design	Population; age, year; participants, n	Study years; participation rate, %; comparison	Adjusted for previous breast cancer	Reduction in breast cancer mortality	Reduction in all-cause mortality	Quality rating; limitations
Mook et al, 2011[127]	Retrospective cohort	Netherlands; 50-69; 2,592	1990-2000; 70-80%; screened vs. non-screened	Yes	Breast cancer mortality, screen-detected vs. not • Univariate HR: 0.43 (95% CI, 0.34 to 0.53, p<0.001) • Multivariate HR: 0.66 (95% CI, 0.50 to 0.86, p=0.002) • Absolute reduction in breast cancer mortality at 10 years of followup: 7%	All-cause mortality • Univariate HR: 0.60 (95% CI, 0.51 to 0.69, p<0.001) • Multivariate HR: 0.77 (95% CI, 0.64 to 0.92, p=0.005)	Poor*
Parvinen et al, 2011[130]	Retrospective cohort	Finland, national screening program registry data; 40-49; 14,765	1987-2003; 85%; annual vs. triennial screening	No	Breast cancer mortality (per 100,000 person-years) • Triennial: 17.9; RR (reference) • Annual: 20.3; RR 1.14 (95% CI, 0.59 to 1.27)	All-cause mortality (per 100,000 person-years) • Triennial: 192.6; RR (reference) • Annual: 230.9; RR 1.20 (95% CI, 0.99 to 1.46)	Fair*†
Schonberg et al, 2009[91]	Retrospective cohort	U.S., medical record review at community health centers; >80; 2,011	1994-2004; screened vs. non-screened	Yes	Breast cancer deaths: 1 vs. 2	All-cause deaths: 12 vs. 12	Fair†

*Did not maintain comparable groups (includes attrition, crossovers, adherence, contamination).
†Statistical limitations including low power to detect differences.

Abbreviations: CI=confidence interval; HR=hazard ratio; MR=mortality ratio; n=number; NA=not applicable (quality rating criteria not available for this study design); NNS=number needed to screen; NR=not reported; RR=relative risk; U.S.=United States; vs.=versus.

Table 8. Advanced Breast Cancer Outcomes Reported in Screening Trials

Trial (reference)	Stage	+Lymph nodes, n*	Size, mm†	Definition of advanced cancer‡	RR for advanced cancer (95% CI)§	Definition of advanced cancer‖	RR for advanced cancer (95% CI)§
HIP[131]	I, II, III, IV	NR	NR	Stage II+	40-64 years: 0.85 (0.69 to 1.05)‡ 40-49 years: 0.96 (0.69 to 1.33) 50-64 years: 0.87 (0.67 to 1.14)	Stage III-IV	40-49 years: 0.87 (0.48 to 1.58) 50-64 years: 0.52 (0.31 to 0.88)
CNBSS-1[75,76]	NR	0, 1-3, 4+	1-9, 10-14, 15-19, 20-39, ≥40	Size ≥20 mm 1+ lymph node	40-49 years: 0.97 (0.74 to 1.25)‡ 40-49 years: 1.55 (1.13 to 2.11)	Size ≥40 mm 4+ lymph nodes	40-49 years: 1.18 (0.67 to 2.03) 40-49 years: 2.00 (1.20 to 3.34)
CNBSS-2[77,78]	NR	0, 1-3, 4+	1-9, 10-14, 15-19, 20-39, ≥40	Size ≥20 mm 1+ lymph node	50-59 years: 0.84 (0.65 to 1.07)‡ 50-59 years: 1.09 (0.82 to 1.15)	Size ≥40 mm 4+ lymph nodes	50-59 years: 0.75 (0.38 to 1.46) 50-59 years: 0.91 (0.55 to 1.49)
Gothenburg[82]	NR	0, 1+	NR	1+ lymph node	39-59 years: 0.80 (0.61 to 1.05)‡ 39-49 years: 0.65 (0.44 to 0.96) 50-59 years: 1.02 (0.70 to 1.48)	NR	
Stockholm[80]	0, I, II, III-IV	NR	NR	Stage II+	40-64 years: 0.88 (0.68 to 1.12)‡	Stage III+	40-64 years: 1.15 (0.59 to 2.07)
Malmö[81]	0, I, II, III-IV, II-IV	NR	NR	Stage II+	45-70 years: 0.83 (0.68 to 1.00)‡	Stage III+	45-70 years: 0.82 (0.56 to 1.20)
Swedish Two-County[83,132]	I, II, III-IV	0, 1+	1-9, 10-14, 15-19, 20-29, 30-49, ≥50	Stage II+	40-74 years: 0.69 (0.61 to 0.78)‡	NR	
				Size ≥20 mm	40-49 years: 0.89 (0.65 to 1.21) 50-74 years: 0.64 (0.55 to 0.73)	Size ≥50 mm	40-49 years: 1.57 (0.63 to 3.94) 50-74 years: 0.63 (0.45 to 0.82)
				1+ lymph node	40-49 years: 0.85 (0.60 to 1.19) 50-74 years: 0.70 (0.60 to 0.82)	NR	
Age[248]	NR	0, 1-3, 4+	1-9, 10-14, 15-19, 20-29, 30-49, ≥50	Size ≥20 mm 1+ lymph node	39-49 years: 0.88 (0.73 to 1.05)‡ 39-49 years: 0.89 (0.72 to 1.10)	Size ≥50 mm 4+ lymph nodes	39-49 years: 0.85 (0.57 to 1.23) 39-49 years: 0.77 (0.53 to 1.13)

*Lymph nodes with micrometastases are classified as Stage IB, otherwise ≥1 positive lymph node is classified as Stage IIA or higher.
†Size ≥20 mm is classified as Stage IIA or higher; size ≥50 mm is classified as Stage IIB or higher.
‡Autier, 2009[65].
§Screening vs. control.
‖Represents the highest category of disease reported by the trials.

Abbreviations: CI=confidence interval; CNBSS=Canadian National Breast Screening Studies; HIP=Health Insurance Plan of Greater New York; mm=millimeter; n=number; NR=not reported; RR=relative risk; vs.=versus.

Table 9. Observational Studies of Advanced Cancer Outcomes With Mammography Screening

Author, year	Study design	Population; age, years; participants, n	Study years; comparison	Outcome measures	Results
Breast Screening Frequency Trial Group, 2002[134]	RCT	U.K., 5 screening units in NHS Breast Screening Programme; 50-62 years; 76,022	1989 to 1996; annual screening vs. no screening during study period	Size >20 mm; ≥1 positive node	Invasive: 235 vs. 208 Tumor size >20 mm: 27% (63/233) vs. 34% (69/203), p<0.05 ≥1 node positive: 34% (63/185) vs. 37% (61/166), p=0.50
Buseman et al, 2003[135]	Case series	U.S., Kaiser Permanente; 42-49 years; 247	1994 to 2000; screened vs. unscreened	Stage II-IV; III-IV	• Stage II-IV: 39% (41/105) vs. 52% (74/142), p=0.06 • Stage III or IV: 4% (n=NR) vs. 9% (n=NR), p=NR
Dittus et al, 2013[141]	Case series	U.S., BCSC data, multisite; 40-74 years; 4,432	1996 to 2008; 1-year vs. 2-year screening intervals	Stage; size >20 mm; node positive	OR (95% CI) for 2-year vs. 1-year interval: No statistically significant differences for stage, size, lymph node positive by weight status.
Fernández et al, 2013[136]	Case series	Spain, breast cancer program and regular public health system; 50-69 years; 904	2002 to 2012; screened vs. non-screened	Node positive; ≥3 nodes positive; size >20 mm	• Cancer detection rate: 3.8/1,000 (475/123,445) vs. 9.4/1,000 (382/40,797) • Invasive: 80% (419/523) vs. 92% (373/403), p<0.001 • Lymph node positive: 75% (312/419) vs. 57% (204/373), p<0.001 • ≥3 nodes positive: 28% (28//103) vs. 42% (66.156), p<0.001 • Tumor size >20 mm: 16.5% (69/419) vs. 48.5% (181/373), p<0.001
Goel et al, 2007[142]	Case series	U.S., Vermont Breast Cancer Surveillance System; >40 years; 1,944	1994 to 2002; 1-year vs. 2-year screening intervals	Advanced either Stage IIB+; size >20mm; >1 positive node	• Advanced: 21% vs. 24%, p=0.262 • No statistically significant differences by age
Hubbard et al, 2011[143]	Case series	U.S., BCSC data, multisite; 40-59 years; 4,492	1996 to 2006; 1-year vs. 2-year screening intervals	Stage IIB+	Adjusted proportion (95% CI) of cancer stage for 2-year vs 1-year intervals: • Stage III or IV for 40-49 years: 4.8 (1.3 to 8.4) • No statistically significant differences for other stages
Jensen et al, 2003[137]	Case series	Denmark and Sweden; 50-69 years; 2,104	1996 to 1997; regions with mammography screening vs. regions without	Stage III-IV; median size	• Stage III or IV: 8.8% (81/917) vs. 13.6% (162/1,187), p<0.001 • Median tumor size (mm): 18 (Malmo) and 17 (Funen) vs. 20 (Aarhus and Northern Jutland), p<0.001
Kerlikowske et al, 2013[144]	Case series	U.S., BCSC data, multisite; 40-74 years; 11,474	1996 to 2008; 1-year vs. 2-year vs. 3-year screening intervals	Stage IIB-IV	Adjusted OR (95% CI) for 2-year vs. 1-year intervals: • Stages IIB-IV in age 40-49 + extreme breast density: 1.89 (1.06 to 3.39) • Tumor size >20 mm in age 40-49 + extreme breast density: 2.39 (1.37 to 4.18) • No statistically significant differences for 50-74 years, 40-49 years without extreme density, or for any comparisons between 3-year vs. 2-year intervals

Table 9. Observational Studies of Advanced Cancer Outcomes With Mammography Screening

Author, year	Study design	Population; age, years; participants, n	Study years; comparison	Outcome measures	Results
Olivotto et al, 1999[138]	Case series	Canada, Screening Mammography Program of British Columbia; 40-89 years; 13,636	1989 to 1996; screening attenders vs. non-attenders	Stage III-IV; size >20 mm	• Invasive: 88% (1,712/1,946) vs. 92.3% (7,523/8,149), p<0.001 • Stage III or IV: 4.3% (84/1,946) vs. 11.9% (969/8,149), p<0.001 • Tumor size >20 mm: 24.1% (3413/1,946) vs. 38.3% (2,885/8,149), p<0.001
Olsson et al, 2009[139]	Case series	Sweden, MMST; 45-69 years; 2478	1961 to 1991; invited to screen vs. not invited	Size >20 mm; node positive	• Tumor size >20 mm: 23% vs. 36%, p<0.05 • Lymph node positive: 28% vs. 36%, p<0.05
White et al, 2004[145]	Case series	U.S., BCSC data, multisite; 40-89 years; 7,840	1996 to 2001; 1-year vs. 2-year screening intervals	Stage III-IV; size >20 mm	• Stage III or IV: 3% vs. 4% • Tumor size >20 mm: 22% vs. 24% OR (95% CI) for 2-year interval vs. 1-year interval: • Late stage for invasive cancers only: 0.97 (0.84 to 1.13) • Tumor size >20 mm for invasive: 1.07 (0.92 to 1.24)

Abbreviations: BCSC=Breast Cancer Surveillance Consortium; BMI=body mass index; CI=confidence interval; DCIS=ductal carcinoma in situ; kq=kilogram; m=meter; MMST=Malmö Mammographic Screening Trial; N=number; NHS=National Health Service; NR=not reported; NS=not statistically significant; U.S.=United States; U.K.=United Kingdom; vs.=versus.

Table 10. Studies of Breast Cancer Treatment for Screened and Nonscreened Women

Author, year	Study design	Population; age, years; participants, n	Study years; comparison	Results
Buseman et al, 2003[135]	Case series	U.S., Kaiser Permanente; 42-49 years; 247	1994 to 2000; screened vs. nonscreened	• Lumpectomy + radiation treatment: 61% (64/105) vs. 57% (81/142), NS • Chemotherapy: 55% (58/105) vs. 61% (86/142), NS
Fernádez et al, 2013[136]	Case series	Spain, breast cancer program and regular public health system; 50-69 years; 904	2002 to 2012; screened vs. nonscreened	Primary treatment: • Conservative surgery: 83% (433/523) vs. 57% (230/403), p<0.001 • Radical surgery: 16% (84/523) vs. 41% (163/403), p<0.001 • Chemotherapy: 0.4% (2/510) vs. 0.8% (3/394), p<0.001 • Sentinel node biopsy: 73% (384/523) vs. 50% (200/403), p<0.001 Adjuvant treatment: • Chemotherapy: 41% (211/510) vs. 72% (284/394), p<0.001 • Hormone therapy: 86% (439/510) vs. 80% (317/394), p<0.001 • Radiotherapy: 87% (444/510) vs. 75% (296/393), p<0.001
Jensen et al, 2003[137]	Case series	Denmark and Sweden; 50-69 years; 2,104	1996 to 1997; regions with mammography screening vs. regions without	• Mastectomy: 61% (556/917) vs. 85% (893/1,051), p<0.001 • Lumpectomy: 32% (295/917) vs. 6.8% (72/1,051), p<0.001 • Biopsy only: 6.4% (59/917) vs. 8% (84/1,051), p<0.001
Olivotto et al, 1999[138]	Case series	Canada, Screening Mammography Program of British Columbia; 40-89 years; 13,636	1989 to 1996; attenders vs. non-attenders	Definitive breast surgery: • Total mastectomy: 35% (603/1,712) vs. 46% (3,452/7,523), p<0.001 • Breast conservation: 65% (1,109/1,712) vs. 54% (4,071/7,523), p<0.001 Adjuvant systemic therapy: • Tamoxifen alone: 29% (493/1,712) vs. 36% (2,694/7,523), p<0.001 • Chemotherapy: 23% (392/1,712) vs. 27% (2,060/7,523), p<0.001

Abbreviations: CI=confidence interval; MMST=Malmö Mammographic Screening Trial; N=number; NR=not reported; NS=not statistically significant; OR=odds ratio; U.S.=United States; U.K.=United Kingdom; vs.=versus.

Table 11. Studies of Advanced Cancer Outcomes With Mammography Plus Tomosynthesis

Author, year	Study design	Population; age, years; participants, n	Study years; comparison	Outcome measures/ definitions	Results
Rose et al, 2013[146]	Case series	U.S., multisite community-based breast center; >18 years; 18,202 DM and 10,878 DM + T	2011 to 2012; DM vs. DM+T	Cancer detection rate; positive nodes	• Cancer detection rate: 4.0 vs 5.4/1000, NS • Positive nodes: 4 vs. 6; p=0.84
Skaane et al, 2013[147]	Post-intervention series	Norway, Oslo screening program; 50-69; 12,631	2010 to 2011; DM vs. DM+T (biennial screening)	Cancer detection rate; positive nodes; size ≥20 mm	• Cancer detection rate: 6.1/1,000 vs. 8.0/1,000, (p=0.001) • Positive nodes: 9 vs. 13, NS • Size ≥20 mm: 12 vs. 15, NS

Abbreviations: DM=digital mammography; mm= millimeter; NS=not statistically significant; T=tomosynthesis; U.S.=United States; vs.=versus.

Table 12. Age-Specific Rates of False-Positive and False-Negative Digital Mammography Results and Recommendations for Additional Imaging and Biopsies From a Single Screening Round in the BCSC

	Age, *y*					Difference (*P*-value)*
	40-49	**50-59**	**60-69**	**70-79**	**80-89**	
Women screened, *n*	113,770	127,958	94,507	50,204	18,752	
Invasive breast cancer cases, *n*	349	574	651	427	154	
DCIS cases, *n*	191	246	208	120	43	
Outcomes, *n per 1,000 women screened (95% CI)*						
False-positive mammography result	121.2 (105.6, 138.7)	93.2 (82.8, 104.7)	80.8 (72.9, 89.4)	69.6 (62.6, 77.3)	65.2 (58.8, 72.2)	<0.001
False-negative mammography result	1.0 (0.9, 1.2)	1.1 (0.9, 1.3)	1.2 (0.9, 1.5)	1.5 (1.1, 1.9)	1.3 (0.9, 1.9)	0.32
Additional imaging recommended†	124.9 (109.3, 142.3)	98.5 (88.0, 110.1)	88.7 (80.6, 97.4)	79.0 (71.9, 86.9)	74.4 (67.4, 82.2)	<0.001
Biopsy recommended†	16.4 (13.2, 20.3)	15.9 (12.7, 19.7)	16.5 (14.3, 19.1)	17.5 (15.2, 20.2)	15.6 (13.4, 18.2)	0.12
Screen-detected invasive cancer	2.2 (1.8, 2.6)	3.5 (3.1, 4.0)	5.8 (5.3, 6.4)	7.2 (6.4, 8.1)	7.1 (5.9, 8.5)	<0.001
Screen-detected DCIS	1.6 (1.3, 1.9)	1.8 (1.5, 2.2)	2.1 (1.7, 2.5)	2.3 (1.7, 3.0)	2.1 (1.5, 3.0)	0.05

*2-sided P-values and 95% confidence intervals from a logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.
†After positive mammography result.

Abbreviations: CI=confidence interval; DCIS=ductal carcinoma in situ.

Table 13. Rates of False-Positive and False-Negative Digital Mammography Results and Recommendations for Additional Imaging and Biopsies Based on Time Since Last Mammography Examination*

Outcome	Time since last exam, *mo*	Age, *y* 40-49		50-59		60-69		70-79		80-89	
Comparing 9-18 vs. 19-30 months											
Women screened, *n*	9-18	79,637		91,864		71,324		39,474		14,865	
	19-30	34,133		36,094		23,183		10,730		3,887	
Invasive breast cancer cases, *n*	9-18	240		391		474		322		119	
	19-30	109		183		177		105		35	
DCIS cases, *n*	9-18	126		185		156		94		32	
	19-30	65		61		52		26		11	
Outcomes, *n per 1,000 women screened (95% CI)*											
False-positive mammography result	9-18	122.1 (105.4, 141.0)	0.65	94.2 (83.3, 106.5)	0.37	80.6 (72.8, 89.2)	0.89	69.1 (61.9, 77.0)	0.55	66.5 (60.8, 72.8)	0.22
	19-30	119.0 (103.0, 137.1)		90.5 (80.4, 101.8)		81.1 (71.4, 92.1)		71.6 (62.2, 82.2)		60.2 (49.3, 73.3)	
False-negative mammography result	9-18	1.1 (0.9, 1.3)	0.14	1.2 (1.0, 1.4)	0.06	1.3 (1.0, 1.6)	0.26	1.6 (1.2, 2.1)	0.17	1.4 (0.9, 2.2)	0.27
	19-30	0.8 (0.6, 1.1)		0.9 (0.6, 1.2)		0.9 (0.6, 1.5)		1.0 (0.5, 2.0)		0.8 (0.3, 2.3)	
Additional imaging recommended†	9-18	125.6 (109.0, 144.3)	0.74	99.3 (88.2, 111.7)	0.47	88.2 (80.2, 96.9)	0.59	78.0 (70.7, 86.1)	0.30	75.3 (68.6, 82.6)	0.46
	19-30	123.3 (107.0, 141.7)		96.4 (85.9, 108.0)		90.1 (80.1, 101.2)		82.8 (72.5, 94.3)		71.3 (59.8, 84.8)	
Biopsy recommended†	9-18	15.6 (12.8, 19.0)	0.11	15.7 (12.7, 19.3)	0.50	15.9 (14.0, 18.2)	0.10	17.3 (15.2, 19.6)	0.44	14.9 (12.4, 17.9)	0.25
	19-30	18.2 (13.7, 24.1)		16.4 (12.5, 21.4)		18.4 (14.7, 23.0)		18.5 (14.6, 23.5)		18.3 (13.9, 24.0)	
Screen-detected invasive cancer	9-18	2.0 (1.6, 2.5)	0.12	3.2 (2.7, 3.7)	0.009	5.5 (4.9, 6.2)	0.07	6.7 (5.8, 7.7)	0.04	6.8 (5.4, 8.5)	0.39
	19-30	2.5 (2.1, 3.0)		4.3 (3.7, 5.1)		6.8 (5.7, 8.1)		8.9 (7.4, 10.8)		8.2 (5.8, 11.6)	
Screen-detected DCIS	9-18	1.5 (1.2, 1.8)	0.18	1.9 (1.5, 2.4)	0.13	2.0 (1.8, 2.4)	0.79	2.3 (1.7, 3.0)	0.97	2.0 (1.2, 3.1)	0.42
	19-30	1.8 (1.4, 2.3)		1.6 (1.2, 2.0)		2.2 (1.4, 3.3)		2.2 (1.4, 3.6)		2.8 (1.5, 5.3)	
Comparing 11-14 vs. 23-26 months											
Women screened, *n*	11-14	55,278		65,219		53,419		30,497		11,299	
	23-26	13,584		14,407		9,907		4,291		1,504	
Invasive breast cancer cases, *n*	11-14	163		274		348		247		78	
	23-26	42		70		76		41		15	
DCIS cases, *n*	11-14	83		127		111		71		20	
	23-26	26		22		23		12		3	
Outcomes, *n per 1,000 women screened (95% CI)*											
False-positive mammography result	11-14	119.1 (103.5, 136.8)	0.69	93.3 (82.8, 105.0)	0.46	79.2 (72.2, 86.8)	0.91	67.6 (60.7, 75.2)	0.70	63.8 (58.2, 69.9)	0.71
	23-26	115.8 (98.7, 135.4)		89.9 (78.8, 102.4)		79.6 (70.3, 90.2)		65.7 (56.7, 76.0)		61.2 (47.3, 78.7)	
False-negative mammography result	11-14	1.2 (1.0, 1.5)	0.20	1.2 (1.0, 1.5)	0.11	1.2 (0.9, 1.6)	0.32	1.4 (1.1, 2.0)	0.95	1.2 (0.7, 1.8)	0.44
	23-26	0.9 (0.5, 1.5)		0.8 (0.4, 1.4)		0.8 (0.4, 1.8)		1.4 (0.6, 3.4)		2.0 (0.7, 6.0)	

Table 13. Rates of False-Positive and False-Negative Digital Mammography Results and Recommendations for Additional Imaging and Biopsies Based on Time Since Last Mammography Examination*

Outcome	Time since last exam, *mo*	Age, *y*									
		40-49		50-59		60-69		70-79		80-89	
Additional imaging recommended†	11-14	122.4 (106.7, 139.9)	0.77	98.3 (87.7, 109.9)	0.57	86.6 (79.5, 94.3)	0.55	76.6 (69.3, 84.5)	0.98	71.3 (65.4, 77.7)	0.98
	23-26	119.9 (102.6, 139.7)		95.5 (83.9, 108.5)		88.8 (79.2, 99.5)		76.7 (66.5, 88.2)		71.1 (57.1, 88.3)	
Biopsy recommended†	11-14	14.7 (12.2, 17.8)	0.31	15.1 (12.2, 18.6)	0.66	15.2 (13.5, 17.2)	0.03	16.6 (14.5, 18.9)	0.85	13.2 (10.8, 16.0)	0.33
	23-26	16.9 (11.9, 24.0)		15.8 (11.7, 21.3)		18.8 (15.2, 23.2)		17.0 (12.6, 23.0)		16.6 (11.2, 24.7)	
Screen-detected invasive cancer	11-14	1.8 (1.5, 2.3)	0.31	3.1 (2.6, 3.7)	0.05	5.5 (4.9, 6.2)	0.07	6.8 (5.8, 7.9)	0.35	5.9 (4.5, 7.8)	0.33
	23-26	2.3 (1.6, 3.2)		4.2 (3.3, 5.4)		7.0 (5.7, 8.5)		8.4 (5.7, 12.4)		8.0 (4.9, 13.1)	
Screen-detected DCIS	11-14	1.4 (1.1, 1.8)	0.20	1.9 (1.4, 2.4)	0.22	1.9 (1.6, 2.3)	0.59	2.2 (1.6, 3.0)	0.69	1.6 (0.9, 2.8)	0.75
	23-26	1.8 (1.3, 2.7)		1.4 (0.9, 2.1)		2.2 (1.3, 3.7)		2.6 (1.3, 5.1)		2.0 (0.6, 6.1)	

*2-sided P-values and 95% confidence intervals from a logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.
†After positive mammography result.

Abbreviations: CI=confidence interval; DCIS=ductal carcinoma in situ.

Table 14. Rates of False-Positive Results After Screening With Digital Mammography by Risk Factors*

Risk Factor		Age, *y* 40-49		50-59		60-69		70-79		80-89	
Women screened, *n*		113,770		127,958		94,507		50,204		18,752	
False-positive, *n*		13,784		11,923		7,633		3,494		1,223	
Number per 1,000 women screened per round (95% CI)											
First-degree relatives with breast cancer	None	118.7 (104.3, 134.7)	0.03	90.4 (81.1, 100.7)	0.005	79.4 (71.8, 87.7)	0.02	68.6 (61.1, 76.8)	0.11	63.3 (56.8, 70.5)	0.05
	One or more	139.8 (113.9, 170.5)		109.0 (92.3, 128.2)		87.2 (77.2, 98.4)		75.0 (67.6, 83.1)		73.1 (64.1, 83.3)	
Breast density†	Fat-Scattered	108.4 (95.5, 122.7)	<0.001	80.5 (71.1, 90.9)	<0.001	74.1 (66.4, 82.6)	<0.001	67.3 (60.4, 74.9)	0.003	60.3 (54.0, 67.4)	0.001
	Hetero-geneous	142.2 (120.2, 167.4)		115.8 (100.3, 133.2)		101.8 (91.0, 113.8)		88.7 (78.7, 99.9)		82.4 (72.6, 93.5)	
	Extreme	112.1 (94.4, 132.7)		92.7 (77.5, 110.5)		75.2 (64.7, 87.1)		57.7 (43.9, 75.5)		85.1 (61.7, 116.2)	
Benign breast biopsy	None	114.3 (99.8, 130.5)	0.001	85.9 (76.7, 96.0)	<0.001	74.6 (66.8, 83.1)	<0.001	63.4 (56.2, 71.3)	<0.001	63.0 (56.3, 70.6)	0.09
	Previous	167.3 (140.6, 197.9)		122.5 (106.2, 140.7)		98.6 (88.8, 109.3)		88.6 (79.1, 99.2)		71.6 (62.3, 82.3)	
Race/ethnicity	White	127.0 (115.5, 139.4)	0.001	97.6 (89.5, 106.4)	0.01	83.8 (77.4, 90.7)	0.006	73.5 (67.7, 79.8)	<0.001	68.9 (62.6, 75.7)	0.04
	Black	92.6 (82.0, 104.5)		78.9 (65.2, 95.3)		64.5 (53.6, 77.3)		58.9 (51.7, 67.0)		52.4 (43.6, 63.0)	
	Asian	85.2 (72.2, 100.4)		67.6 (56.5, 80.7)		58.0 (47.9, 70.2)		43.6 (36.9, 51.6)		35.8 (29.6, 43.4)	
	Hispanic	125.4 (106.8, 146.7)		80.9 (69.1, 94.6)		72.9 (60.3, 87.8)		60.7 (50.6, 72.8)		55.7 (31.3, 97.2)	
	Other	127.8 (105.8, 153.6)		102.3 (88.5, 117.8)		91.5 (76.2, 109.5)		72.6 (53.3, 98.2)		48.9 (29.3, 80.6)	
Menopausal hormone therapy	None	123.3 (107.4, 141.2)	0.69	91.8 (81.6, 103.2)	0.27	76.2 (69.2, 84.0)	0.22	67.6 (61.1, 74.8)	0.01	62.2 (55.5, 69.8)	
	Combination	122.0 (78.8, 184.1)		131.1 (99.5, 170.7)		122.5 (87.3, 169.2)		105.9 (81.8, 136.0)		94.0 (74.0, 118.8)	
	Estrogen	108.7 (84.4, 138.8)		101.3 (87.1, 117.6)		97.6 (77.3, 122.5)		114.0 (94.8, 136.5)		89.1 (68.5, 115.1)	
Oral contraceptives	No current	122.9 (107.2, 140.6)	0.05	93.6 (83.1, 105.4)	0.63	NA		NA		NA	
	Current use	106.2 (86.4, 130.0)		97.0 (81.3, 115.2)							

Table 14. Rates of False-Positive Results After Screening With Digital Mammography by Risk Factors*

Risk Factor		Age, *y*									
		40-49		**50-59**		**60-69**		**70-79**		**80-89**	
Body mass index, *kg/m²*	<25	129.0 (113.8, 145.9)	0.009	99.5 (89.3, 110.8)	0.04	85.8 (77.9, 94.4)	0.14	70.5 (62.0, 80.0)	0.78	73.9 (60.6, 89.8)	0.33
	25 to <30	124.8 (110.1, 141.2)		93.6 (85.0, 103.0)		78.6 (69.5, 88.9)		72.7 (64.8, 81.6)		62.2 (51.4, 75.1)	
	≥30	107.2 (96.0, 119.5)		86.1 (77.7, 95.2)		81.1 (74.1, 88.6)		74.2 (64.1, 85.7)		73.8 (59.1, 91.9)	

*2-sided P-values and 95% confidence intervals from a logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.
†Categories include: almost entirely fat=fat; scattered fibroglandular densities=scattered; heterogeneously dense=heterogeneous; and extremely dense=extreme.

Abbreviations: kg=kilogram; m=meter; NA=not applicable; peri=perimenopausal; pre=premenopausal; post=postmenopausal.

Table 15. Rates of False-Negative Results After Screening With Digital Mammography by Risk Factors*

Risk Factor		Age, *y* 40-49		50-59		60-69		70-79		80-89	
Women screened, *n*		113,770		127,958		94,507		50,204		18,752	
False-negative mammography result, *n*		115		139		112		73		24	
Number per 1,000 women screened per round (95% CI)											
First-degree relatives with breast cancer	None	0.9 (0.8, 1.1)	0.02	1.0 (0.8, 1.2)	0.09	1.1 (0.8, 1.4)	0.10	1.2 (0.9, 1.6)	0.01	1.2 (0.8, 1.9)	0.49
	One or more	1.8 (1.3, 2.5)		1.6 (1.1, 2.4)		1.7 (1.1, 2.7)		2.4 (1.6, 3.7)		1.6 (0.8, 3.1)	
Breast density	Fat-Scattered	0.4 (0.3, 0.6)	<0.001	0.6 (0.4, 0.8)	0.002	0.8 (0.5, 1.1)	0.006	1.0 (0.6, 1.5)	0.01	0.9 (0.5, 1.6)	0.25
	Heterogeneous	1.3 (1.0, 1.7)		1.4 (1.0, 2.0)		1.7 (1.3, 2.3)		2.3 (1.6, 3.4)		1.1 (0.5, 2.4)	
	Extreme	1.7 (1.2, 2.5)		1.6 (0.9, 2.8)		1.2 (0.6, 2.7)		5.6 (2.4, 12.9)		6.9 (2.5, 18.5)	
Benign breast biopsy†	None	0.9 (0.8, 1.1)	0.53	0.8 (0.7, 1.1)	0.002	0.8 (0.6, 1.1)	0.001	0.9 (0.6, 1.3)	0.004	0.9 (0.5, 1.6)	0.02
	Previous	1.1 (0.7, 1.7)		1.7 (1.3, 2.3)		2.1 (1.6, 2.8)		2.6 (1.8, 3.9)		2.6 (1.6, 4.2)	
Race/ethnicity	White	1.2 (1.0, 1.4)	0.31	1.2 (0.9, 1.4)	0.04	1.3 (1.0, 1.6)	0.36	1.7 (1.2, 2.4)	0.29	1.4 (0.9, 2.3)	0.77
	Black	0.7 (0.3, 1.4)		1.2 (0.6, 2.2)		1.5 (0.8, 2.9)		0.9 (0.3, 2.3)		1.0 (0.2, 6.4)	
	Asian	0.8 (0.5, 1.3)		1.1 (0.7, 1.7)		0.6 (0.3, 1.2)		0.8 (0.4, 1.6)		0‡	
	Hispanic	0.5 (0.2, 1.6)		0.2 (0.0, 1.1)		0.7 (0.2, 2.4)		0.8 (0.1, 4.6)		3.3 (0.4, 23.9)	
	Other	1.1 (0.4, 3.2)		1.6 (0.6, 4.1)		1.2 (0.2, 7.1)		1.5 (0.3, 8.5)		5.4 (1.0, 27.8)	
Menopausal status	Pre	1.2 (1.0, 1.4)	0.17	1.3 (0.9, 1.9)	0.53	NA		NA		NA	
	Peri	0.8 (0.2, 2.5)		1.0 (0.5, 2.1)							
	Post	0.7 (0.4, 1.3)		1.0 (0.8, 1.3)							
Menopausal hormone therapy	None	1.0 (0.9, 1.2)	0.76	1.0 (0.8, 1.2)	0.37	1.0 (0.8, 1.3)	0.33	1.3 (0.9, 1.8)	0.58	1.2 (0.8, 2.0)	0.62
	Combination	0‡		1.9 (0.9, 3.7)		2.3 (1.0, 5.6)		0‡		3.1 (1.5, 6.6)	
	Estrogen only	1.5 (0.2, 10.1)		0.4 (0.1, 2.6)		1.2 (0.4, 3.1)		0.8 (0.1, 5.6)		2.5 (0.4, 13.7)	
Oral contraceptives	No current	1.0 (0.8, 1.2)	0.77	1.1 (0.9, 1.3)	0.54	NA		NA		NA	
	Current use	1.1 (0.6, 2.1)		1.4 (0.6, 3.5)							
Body mass index, kg/m^2	<25	1.4 (1.2, 1.7)	0.06	1.3 (1.0, 1.6)	0.008	1.3 (0.9, 1.8)	0.66	2.4 (1.6, 3.6)	0.09	1.7 (0.7, 3.8)	0.96
	25 to <30	0.8 (0.6, 1.3)		1.0 (0.7, 1.6)		1.2 (0.7, 2.1)		1.0 (0.5, 1.8)		1.6 (0.7, 3.7)	
	≥30	0.7 (0.3, 1.4)		0.4 (0.2, 0.8)		1.0 (0.6, 1.8)		1.0 (0.4, 2.4)		0‡	

*2-sided P-value and 95% confidence intervals from logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.

†Categories include: almost entirely fat=fatty; scattered fibroglandular densities=scattered; heterogeneously dense=heterogeneous; and extremely dense=extreme.

‡No false-negative outcomes. Category omitted from model used to obtain CI and P-value.

Abbreviations: kg=kilogram; m=meter; NA=not applicable; peri=perimenopausal; pre=premenopausal; post=postmenopausal.

Table 16. Rates of Recommendations for Additional Imaging After Screening With Digital Mammography by Risk Factors*

Risk Factor		Age, *y* 40-49		50-59		60-69		70-79		80-89	
Women screened, *n*		113,770		127,958		94,507		50,204		18,752	
Additional imaging recommended, *n*		14,209		12,604		8,380		3,968		1,396	
Number per 1,000 women screened per round (95% CI)											
First-degree relatives with breast cancer	None	122.1 (107.7, 138.1)	0.02	95.2 (85.8, 105.6)	0.003	86.7 (79.0, 95.1)	0.002	77.5 (69.9, 85.7)	0.02	71.7 (64.6, 79.5)	0.01
	One or more	145.6 (119.6, 176.2)		117.1 (99.7, 137.0)		98.3 (87.9, 109.8)		86.9 (79.1, 95.4)		86.0 (75.5, 97.7)	
Breast density	Fat-Scattered	110.8 (97.9, 125.2)	0.001	84.4 (74.8, 95.1)	<0.001	81.0 (73.1, 89.6)	<0.001	75.6 (68.5, 83.4)	0.003	68.9 (61.7, 76.9)	0.002
	Heterogeneous	146.0 (123.9, 171.3)		121.6 (105.8, 139.3)		110.6 (99.7, 122.6)		99.0 (87.9, 111.4)		93.6 (82.4, 106.2)	
	Extreme	116.5 (98.4, 137.4)		98.4 (83.1, 116.2)		81.0 (70.3, 93.2)		63.3 (49.7, 80.1)		92.0 (66.6, 125.7)	
Benign breast biopsy	None	117.8 (103.4, 134.0)	0.001	90.9 (81.7, 101.0)	<0.001	81.9 (74.1, 90.6)	<0.001	72.2 (65.1, 79.9)	<0.001	72.1 (64.3, 80.7)	0.07
	Previous	172.5 (145.9, 202.8)		129.3 (112.8, 147.8)		108.2 (98.2, 118.9)		100.5 (90.0, 112.1)		82.7 (72.9, 93.7)	
Race/ethnicity	White	131.1 (119.4, 143.8)	0.001	103.2 (94.8, 112.3)	0.01	92.4 (85.7, 99.4)	0.005	83.3 (77.1, 90.1)	0.004	78.0 (71.1, 85.5)	0.11
	Black	95.9 (85.0, 108.0)		82.6 (68.4, 99.4)		70.8 (59.3, 84.3)		66.3 (59.1, 74.4)		60.3 (49.1, 74.0)	
	Asian	89.1 (76.0, 104.2)		73.5 (62.1, 86.8)		64.6 (54.0, 77.0)		52.6 (44.9, 61.4)		40.5 (33.4, 48.9)	
	Hispanic	127.8 (109.2, 149.0)		84.6 (71.9, 99.3)		76.9 (64.1, 92.0)		72.1 (61.6, 84.3)		62.3 (38.7, 98.9)	
	Other	131.6 (109.8, 157.1)		109.8 (97.1, 123.8)		98.8 (82.5, 117.8)		84.7 (64.0, 111.3)		65.2 (39.4, 106.2)	
Menopausal status	Pre	135.4 (117.4, 155.6)	0.01	124.6 (113.6, 136.4)	<0.001	NA		NA		NA	
	Peri	109.0 (92.8, 127.7)		101.4 (78.7, 129.8)							
	Post	114.2 (103.1, 126.4)		92.7 (84.0, 102.1)							
Menopausal hormone therapy	None	127.0 (111.2, 144.8)	0.63	97.0 (86.7, 108.5)	0.28	83.8 (76.5, 91.7)	0.18	76.5 (69.8, 83.9)	0.01	71.5 (64.2, 79.6)	0.20
	Combination	125.8 (83.6, 185.0)		137.4 (105.5, 177.1)		129.5 (96.3, 172.0)		120.7 (94.9, 152.4)		106.6 (79.4, 141.6)	
	Estrogen only	110.1 (85.6, 140.7)		105.4 (90.9, 121.8)		106.1 (86.0, 130.3)		125.1 (106.4, 146.6)		106.4 (82.6, 136.1)	

Table 16. Rates of Recommendations for Additional Imaging After Screening With Digital Mammography by Risk Factors*

Risk Factor		Age, *y*									
		40-49		50-59		60-69		70-79		80-89	
Oral contraceptives	No current	126.6 (110.9, 144.2)	0.05	99.0 (88.3, 110.7)	0.85	NA		NA		NA	
	Current use	110.4 (90.9, 133.6)		100.3 (84.4, 118.9)							
Body mass index, *kg/m²*	<25	133.9 (118.1, 151.3)	0.006	105.9 (95.6, 117.2)	0.05	93.4 (85.4, 102.1)	0.31	79.5 (70.5, 89.5)	0.28	83.4 (69.8, 99.5)	0.20
	25 to <30	129.2 (114.7, 145.2)		99.3 (90.4, 108.9)		88.7 (79.1, 99.4)		84.1 (75.5, 93.6)		69.5 (58.5, 82.3)	
	≥30	110.7 (99.4, 123.2)		93.1 (84.2, 102.8)		89.2 (82.1, 96.8)		89.3 (78.5, 101.5)		88.4 (71.5, 108.8)	

*2-sided P-values and 95% confidence intervals from a logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.
†Categories include: almost entirely fat=fat; scattered fibroglandular densities=scattered; heterogeneously dense=heterogeneous; and extremely dense=extreme.

Abbreviations: kg=kilogram; m=meter; NA=not applicable; peri=perimenopausal; pre=premenopausal; post=postmenopausal.

Table 17. Rates of Recommendations for Biopsy After Screening With Digital Mammography by Risk Factors*

Risk Factor		Age, *y* 40-49		50-59		60-69		70-79		80-89	
Women screened, *n*		113,770		127,958		94,507		50,204		18,752	
Biopsy recommended, *n*		1,863		2,030		1,562		880		293	
Number per 1,000 women screened per round (95% CI)											
First-degree relatives with breast cancer	None	15.7 (12.6, 19.4)	0.002	14.8 (11.8, 18.4)	<0.001	15.8 (13.7, 18.3)	0.002	17.0 (14.7, 19.6)	0.09	15.2 (12.8, 18.0)	0.24
	One or more	21.1 (16.9, 26.3)		21.9 (17.5, 27.3)		20.1 (17.0, 23.7)		20.3 (16.7, 24.6)		17.6 (14.1, 22.1)	
Breast density†	Fat-Scattered	12.2 (9.9, 15.0)	<0.001	11.8 (9.6, 14.5)	<0.001	15.6 (13.7, 17.7)	0.008	16.2 (14.2, 18.4)	0.007	14.2 (12.0, 16.8)	0.07
	Heterogeneous	18.9 (15.8, 22.5)		20.2 (17.3, 23.7)		19.3 (16.9, 22.2)		21.0 (18.0, 24.5)		19.0 (15.5, 23.2)	
	Extreme	20.2 (16.8, 24.3)		19.2 (14.3, 25.7)		13.8 (10.5, 18.2)		13.0 (7.2, 23.3)		16.1 (8.0, 32.1)	
Benign breast biopsy	None	14.8 (11.8, 18.7)	<0.001	13.9 (11.1, 17.3)	<0.002	15.0 (12.7, 17.8)	<0.001	15.3 (13.1, 17.7)	<0.001	15.8 (13.4, 18.7)	0.54
	Previous	27.8 (22.8, 33.7)		25.1 (20.1, 31.2)		21.8 (19.1, 24.9)		25.2 (21.4, 29.7)		17.1 (13.7, 21.5)	
Race/ethnicity	White	16.7 (13.7, 20.3)	0.21	16.6 (13.6, 20.2)	0.39	17.6 (15.6, 20.0)	0.05	18.7 (16.6, 21.2)	0.23	16.2 (13.5, 19.4)	0.12
	Black	13.6 (10.4, 17.8)		14.7 (10.4, 20.6)		13.9 (10.6, 18.0)		14.9 (11.4, 19.5)		8.9 (4.4, 18.0)	
	Asian	16.2 (10.6, 24.5)		14.8 (9.5, 22.9)		12.0 (6.9, 20.6)		11.8 (6.8, 20.3)		9.2 (5.6, 15.3)	
	Hispanic	16.3 (10.3, 25.6)		11.9 (8.1, 17.5)		14.2 (11.4, 17.6)		15.9 (10.1, 25.1)		16.4 (8.5, 31.5)	
	Other	19.8 (14.4, 27.3)		17.4 (10.5, 28.6)		16.4 (10.8, 24.8)		16.6 (10.0, 27.6)		5.4 (0.7, 39.2)	
Menopausal status	Pre	17.6 (14.0, 22.1)	0.49	19.8 (15.7, 24.9)	0.02	NA		NA		NA	
	Peri	17.8 (14.4, 22.0)		16.4 (10.6, 25.4)							
	Post	15.8 (12.5, 20.0)		15.4 (12.1, 19.4)							
Menopausal hormone therapy	None	16.3 (13.2, 20.2)	0.34	15.6 (12.6, 19.2)	0.50	15.9 (13.9, 18.3)	0.37	17.2 (15.1, 19.4)	0.14	15.2 (12.8, 17.9)	0.13
	Combination	15.2 (8.2, 28.2)		18.3 (12.7, 26.3)		16.9 (12.6, 22.6)		33.0 (23.7, 45.9)		21.9 (14.0, 34.2)	
	Estrogen only	26.4 (14.7, 47.2)		18.3 (12.3, 27.2)		21.0 (14.5, 30.2)		25.3 (17.7, 36.1)		32.2 (22.2, 46.4)	

Table 17. Rates of Recommendations for Biopsy After Screening With Digital Mammography by Risk Factors*

Risk Factor		Age, *y*									
		40-49		50-59		60-69		70-79		80-89	
Oral contraceptives	No current	16.7 (13.6, 20.6)	0.007	16.0 (13.1, 19.5)	0.32	NA		NA		NA	
	Current use	12.5 (9.5, 16.3)		13.0 (7.0, 24.3)							
Body mass index, *kg/m²*	<25	21.4 (17.0, 26.8)	0.02	19.3 (14.7, 25.1)	0.40	17.4 (14.4, 21.0)	0.12	16.5 (13.5, 20.1)	0.02	17.1 (13.8, 21.2)	0.26
	25 to <30	17.6 (13.7, 22.6)		18.0 (13.3, 24.4)		18.9 (15.3, 23.4)		21.9 (18.2, 26.3)		16.6 (12.5, 21.9)	
	≥30	15.3 (12.3, 19.2)		18.4 (14.5, 23.4)		22.2 (18.1, 27.2)		26.7 (21.9, 32.4)		26.6 (18.5, 38.1)	

*2-sided P-values and 95% confidence intervals from a logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.
†Categories include: almost entirely fat=fat; scattered fibroglandular densities=scattered; heterogeneously dense=heterogeneous; and extremely dense=extreme.

Abbreviations: kg=kilogram; m=meter; NA=not applicable; peri=perimenopausal; pre=premenopausal; post=postmenopausal.

Table 18. Rates of False-Positive and False-Negative Digital Mammography Results and Recommendations for Additional Imaging and Biopsies by Different Breast Density Categories*

		Age, *y*									
		40-49		50-59		60-69		70-79		80-89	
Women screened, *n*		113,770		127,958		94,507		50,204		18,752	
False-positive mammography results Number per 1,000 women screened per round (95% CI)											
A	Fat-Scattered	108.4 (95.5, 122.7)	<0.001	80.5 (71.1, 90.9)	<0.001	74.1 (66.4, 82.6)	<0.001	67.3 (60.4, 74.9)	0.003	60.3 (54.0, 67.4)	0.001
	Heterogeneous	142.2 (120.2, 167.4)		115.8 (100.3, 133.2)		101.8 (91.0, 113.8)		88.7 (78.7, 99.9)		82.4 (72.6, 93.5)	
	Extreme	112.1 (94.4, 132.7)		92.7 (77.5, 110.5)		75.2 (64.7, 87.1)		57.7 (43.9, 75.5)		85.1 (61.7, 116.2)	
B	Fat	63.0 (51.2, 77.4)	<0.001	52.1 (44.9, 60.3)	<0.001	48.5 (43.1, 54.4)	<0.001	45.4 (39.7, 51.9)	<0.001	39.5 (32.1, 48.5)	<0.001
	Scattered	116.8 (102.9, 132.3)		87.7 (77.1, 99.6)		81.6 (72.7, 91.4)		73.4 (65.4, 82.2)		65.8 (58.4, 73.9)	
	Heterogeneous-Extreme	135.3 (113.9, 160.0)		112.0 (96.9, 129.2)		98.9 (88.4, 110.4)		86.2 (76.4, 97.1)		82.7 (72.6, 93.9)	
C	Fat	63.0 (51.2, 77.4)	<0.001	52.1 (44.9, 60.3)	<0.001	48.5 (43.1, 54.4)	<0.001	45.4 (39.7, 51.9)	<0.001	39.5 (32.1, 48.5)	<0.001
	Scattered	116.8 (102.9, 132.3)		87.7 (77.1, 99.6)		81.6 (72.7, 91.4)		73.4 (65.4, 82.2)		65.8 (58.4, 73.9)	
	Heterogeneous	142.2 (120.2, 167.4)		115.8 (100.3, 133.2)		101.8 (91.0, 113.8)		88.7 (78.7, 99.9)		82.4 (72.6, 93.5)	
	Extreme	112.1 (94.4, 132.7)		92.7 (77.5, 110.5)		75.2 (64.7, 87.1)		57.7 (43.9, 75.5)		85.1 (61.7, 116.2)	
D	Fat-Scattered	108.4 (95.5, 122.7)	0.003	80.5 (71.1, 90.9)	<0.001	74.1 (66.4, 82.6)	<0.001	67.3 (60.4, 74.9)	<0.001	60.3 (54.0, 67.4)	<0.001
	Heterogeneous-Extreme	135.3 (113.9, 160.0)		112.0 (96.9, 129.2)		98.9 (88.4, 110.4)		86.2 (76.4, 97.1)		82.7 (72.6, 93.9)	
False-negative mammography results Number per 1,000 women screened per round (95% CI)											
A	Fat-Scattered	0.4 (0.3, 0.6)	<0.001	0.6 (0.4, 0.8)	0.002	0.8 (0.5, 1.1)	0.006	1.0 (0.6, 1.5)	0.01	0.9 (0.5, 1.6)	0.25
	Heterogeneous	1.3 (1.0, 1.7)		1.4 (1.0, 2.0)		1.7 (1.3, 2.3)		2.3 (1.6, 3.4)		1.1 (0.5, 2.4)	
	Extreme	1.7 (1.2, 2.5)		1.6 (0.9, 2.8)		1.2 (0.6, 2.7)		5.6 (2.4, 12.9)		6.9 (2.5, 18.5)	
B	Fat	0.2 (0.0, 0.9)	<0.001	0.3 (0.1, 0.7)	<0.001	0.6 (0.2, 1.5)	0.007	0.3 (0.1, 1.1)	0.001	0.4 (0.1, 3.1)	0.14
	Scattered	0.5 (0.3, 0.7)		0.7 (0.5, 0.9)		0.8 (0.6, 1.2)		1.2 (0.7, 1.9)		1.0 (0.6, 1.7)	
	Heterogeneous-Extreme	1.4 (1.2, 1.8)		1.5 (1.1, 1.9)		1.6 (1.2, 2.2)		2.6 (1.8, 3.7)		1.7 (0.8, 3.3)	
C	Fat	0.2 (0.0, 0.9)	<0.001	0.3 (0.1, 0.7)	<0.001	0.6 (0.2, 1.5)	0.02	0.3 (0.1, 1.1)	0.002	0.4 (0.1, 3.1)	0.17
	Scattered	0.5 (0.3, 0.7)		0.7 (0.5, 0.9)		0.8 (0.6, 1.2)		1.2 (0.7, 1.9)		1.0 (0.6, 1.7)	
	Heterogeneous	1.3 (1.0, 1.7)		1.4 (1.0, 2.0)		1.7 (1.3, 2.3)		2.3 (1.6, 3.4)		1.1 (0.5, 2.4)	
	Extreme	1.7 (1.2, 2.5)		1.6 (0.9, 2.8)		1.2 (0.6, 2.7)		5.6 (2.4, 12.9)		6.9 (2.5, 18.5)	
D	Fat-Scattered	0.4 (0.3, 0.6)	<0.001	0.6 (0.4, 0.8)	<0.001	0.8 (0.5, 1.1)	0.002	1.0 (0.6, 1.5)	0.003	0.9 (0.5, 1.6)	0.18
	Heterogeneous-Extreme	1.4 (1.2, 1.8)		1.5 (1.1, 1.9)		1.6 (1.2, 2.2)		2.6 (1.8, 3.7)		1.7 (0.8, 3.3)	

Table 18. Rates of False-Positive and False-Negative Digital Mammography Results and Recommendations for Additional Imaging and Biopsies by Different Breast Density Categories*

		Age, *y*									
		40-49		50-59		60-69		70-79		80-89	
Recommendations for additional imaging Number per 1,000 women screened per round (95% CI)											
A	Fat-Scattered	110.8 (97.9, 125.2)	0.001	84.4 (74.8, 95.1)	<0.001	81.0 (73.1, 89.6)	<0.001	75.6 (68.5, 83.4)	0.003	68.9 (61.7, 76.9)	0.002
	Heterogeneous	146.0 (123.9, 171.3)		121.6 (105.8, 139.3)		110.6 (99.7, 122.6)		99.0 (87.9, 111.4)		93.6 (82.4, 106.2)	
	Extreme	116.5 (98.4, 137.4)		98.4 (83.1, 116.2)		81.0 (70.3, 93.2)		63.3 (49.7, 80.1)		92.0 (66.6, 125.7)	
B	Fat	64.4 (52.3, 79.1)	<0.001	54.1 (46.5, 62.8)	<0.001	53.4 (47.9, 59.4)	<0.001	52.0 (46.5, 58.2)	<0.001	44.8 (36.6, 54.6)	<0.001
	Scattered	119.4 (105.5, 135.0)		92.1 (81.2, 104.3)		89.0 (79.9, 99.1)		82.1 (73.9, 91.2)		75.2 (66.5, 84.8)	
	Heterogeneous-Extreme	139.3 (117.7, 164.1)		117.8 (102.4, 135.3)		107.3 (96.7, 118.9)		96.1 (85.5, 107.9)		93.5 (82.1, 106.3)	
C	Fat	64.4 (52.3, 79.1)	<0.001	54.1 (46.5, 62.8)	<0.001	53.4 (47.9, 59.4)	<0.001	52.0 (46.5, 58.2)	<0.001	44.8 (36.6, 54.6)	0.001
	Scattered	119.4 (105.5, 135.0)		92.1 (81.2, 104.3)		89.0 (79.9, 99.1)		82.1 (73.9, 91.2)		75.2 (66.5, 84.8)	
	Heterogeneous	146.0 (123.9, 171.3)		121.6 (105.8, 139.3)		110.6 (99.7, 122.6)		99.0 (87.9, 111.4)		93.6 (82.4, 106.2)	
	Extreme	116.5 (98.4, 137.4)		98.4 (83.1, 116.2)		81.0 (70.3, 93.2)		63.3 (49.7, 80.1)		92.0 (66.6, 125.7)	
D	Fat-Scattered	110.8 (97.9, 125.2)	0.003	84.4 (74.8, 95.1)	<0.001	81.0 (73.1, 89.6)	<0.001	75.6 (68.5, 83.4)	0.001	68.9 (61.7, 76.9)	<0.001
	Heterogeneous-Extreme	139.3 (117.7, 164.1)		117.8 (102.4, 135.3)		107.3 (96.7, 118.9)		96.1 (85.5, 107.9)		93.5 (82.1, 106.3)	
Recommendations for biopsy Number per 1,000 women screened per round (95% CI)											
A	Fat-Scattered	12.2 (9.9, 15.0)	<0.001	11.8 (9.6, 14.5)	<0.001	15.6 (13.7, 17.7)	0.008	16.2 (14.2, 18.4)	0.007	14.2 (12.0, 16.8)	0.07
	Heterogeneous	18.9 (15.8, 22.5)		20.2 (17.3, 23.7)		19.3 (16.9, 22.2)		21.0 (18.0, 24.5)		19.0 (15.5, 23.2)	
	Extreme	20.2 (16.8, 24.3)		19.2 (14.3, 25.7)		13.8 (10.5, 18.2)		13.0 (7.2, 23.3)		16.1 (8.0, 32.1)	
B	Fat	7.5 (5.5, 10.1)	<0.001	8.4 (6.0, 11.7)	<0.001	11.7 (9.5, 14.6)	<0.001	12.8 (10.2, 16.1)	0.003	9.7 (5.8, 16.0)	0.04
	Scattered	13.1 (10.6, 16.1)		12.7 (10.3, 15.6)		16.7 (14.7, 19.0)		17.1 (14.9, 19.6)		15.4 (12.5, 18.8)	
	Heterogeneous-Extreme	19.2 (16.2, 22.7)		20.1 (16.9, 23.7)		18.7 (16.6, 21.2)		20.4 (17.4, 23.8)		18.7 (15.2, 23.0)	

Table 18. Rates of False-Positive and False-Negative Digital Mammography Results and Recommendations for Additional Imaging and Biopsies by Different Breast Density Categories*

		Age, *y*									
		40-49		**50-59**		**60-69**		**70-79**		**80-89**	
C	Fat	7.5 (5.5, 10.1)	<0.001	8.4 (6.0, 11.7)	<0.001	11.7 (9.5, 14.6)	<0.001	12.8 (10.2, 16.1)	0.003	9.7 (5.8, 16.0)	0.06
	Scattered	13.1 (10.6, 16.1)		12.7 (10.3, 15.6)		16.7 (14.7, 19.0)		17.1 (14.9, 19.6)		15.4 (12.5, 18.8)	
	Heterogeneous	18.9 (15.8, 22.5)		20.2 (17.3, 23.7)		19.3 (16.9, 22.2)		21.0 (18.0, 24.5)		19.0 (15.5, 23.2)	
	Extreme	20.2 (16.8, 24.3)		19.2 (14.3, 25.7)		13.8 (10.5, 18.2)		13.0 (7.2, 23.3)		16.1 (8.0, 32.1)	
D	Fat-Scattered	12.2 (9.9, 15.0)	<0.001	11.8 (9.6, 14.5)	<0.001	15.6 (13.7, 17.7)	0.002	16.2 (14.2, 18.4)	0.008	14.2 (12.0, 16.8)	0.03
	Heterogeneous-Extreme	19.2 (16.2, 22.7)		20.1 (16.9, 23.7)		18.7 (16.6, 21.2)		20.4 (17.4, 23.8)		18.7 (15.2, 23.0)	

*2-sided P-values and 95% confidence intervals from a logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.

†Categories include: almost entirely fat=fat; scattered fibroglandular densities=scattered; heterogeneously dense=heterogeneous; and extremely dense=extreme.

Table 19. U.S. Studies of Cumulative False-Positive Mammography and Biopsy Results

Author, year	Study design	Population; age, *years*; participants, *n*	Study years; comparison	Outcome measures	Results
New studies					
Hubbard et al, 2011[143]	Post-intervention series	U.S., 7 mammography registries in the BCSC; 40-59; 169,456	1994-2006; annual vs. biennial screening by age	FP results (no diagnosis of invasive carcinoma or DCIS within 1 year of screening or before the next screening); recalls (BIRADS 0, 3, 4, 5)	Cumulative probability of FP mammography after 10 years, % (95% CI) • Age 40: annual, 61.3 (59.4 to 63.1); biennial, 41.6 (40.6 to 42.5) • Age 50: annual, 61.3 (58.0 to 64.7); biennial, 42.0 (40.4 to 43.7) Cumulative probability of FP biopsy after 10 years, % (95% CI) • Age 40: annual, 7.0 (6.1 to 7.8); biennial, 4.8 (4.4 to 5.2) • Age 50: annual, 9.4 (7.4 to 11.5); biennial, 6.4 (5.6 to 7.2)
Kerlikowske et al, 2013[144]	Post-intervention series	U.S., 7 mammography registries in the BCSC; 40-74; 11,474 with breast cancer, 922,2624 without	1994-2008; annual vs. biennial vs. triennial screening by age, breast density, and menopausal hormone therapy	FP results (no diagnosis of invasive carcinoma or DCIS within 1 year of screening or before the next screening mammogram), recalls (BIRADS 0, 3, 4, 5)	Cumulative probability of FP mammography after 10 years, by breast density,* % (95% CI) • Age 40-49: annual: 36 (34 to 38); 60 (59 to 61); 69 (68 to 70); 66 (64 to 67); biennial: 21 (20 to 22); 39 (38 to 39); 46 (46 to 47); 43 (42 to 44); triennial: 14 (13 to 15); 27 (26 to 27); 33 (31 to 34); 33 (32 to 34). • Age 50-74: annual: 30 (29 to 31); 50 (49 to 51); 60 (59 to 61); 59 (57 to 60); biennial: 17 (17 to 18); 31 (30 to 31); 39 (38 to 39); 38 (37 to 38); triennial: 12 (12 to 13); 22 (21 to 22); 28 (28 to 29); 27 (26 to 28). Cumulative probability of FP biopsy after 10 years, by breast density,* % (95% CI) • Age 40-49: annual: 6 (5 to 7); 9 (8 to 10); 12 (11 to 14); 12 (11 to 14); biennial: 3 (2 to 3); 5 (4 to 5); 7 (6 to 7); 7 (6 to 7); triennial: 2 (2 to 2); 3 (3 to 4); 4 (3 to 4); 3 (2 to 4). • Age 50-74: annual: 5 (5 to 6); 8 (8 to 9); 11 (10 to 12); 11 (10 to 12); biennial: 3 (3 to 3); 5 (4 to 5); 6 (6 to 7); 6 (6 to 7); triennial: 2 (2 to 2); 3 (3 to 4); 5 (4 to 5); 5 (4 to 5). Highest cumulative rates of FP mammography (66% to 69%) or biopsy (12% to 14%): annual mammography; extremely or heterogeneously dense breasts; age 40-49; used combined HT.
2009 review					
Elmore et al, 1998[149]	Post-intervention series	U.S., randomly sampled patients from 11 health centers in an HMO; 40-69	1983-1995; annual vs. biennial screening	FP test results (not a true positive=breast cancer diagnosed on the basis of pathological findings within 1 year of mammography)	Cumulative risk of at least one FP after 10 screening mammograms, % (95% CI) • Age 40-49: 56 (39.5 to 75.8); Age 50-59: 47 (37.8 to 63.0); • Overall: 49 (40.3 to 64.1). Cumulative risk of FP biopsy, % (95% CI) • Overall: 19 (9.8 to 41.2)

*Categories include: fatty; scattered fibroglandular densities; heterogenously dense; extremely dense.

Abbreviations: BCSC=Breast Cancer Surveillance Consortium; BIRADS=Breast Imaging Reporting and Data System; CI=confidence interval; DCIS=ductal carcinoma in situ; FP=false-positive; HMO=health maintenance organization; HT=hormone therapy; n=number; U.S.=United States; vs.=versus.

Table 20. Studies of Overdiagnosis

Author, year	Age, years	Study years	Data source	Comparison groups	Approach, lead time adjustment	Overdiagnosis measures as defined by each study	Overdiagnosis rate of invasive cancer + DCIS	Overdiagnosis rate of invasive cancer	Overdiagnosis rate of DCIS
2014 update									
Bleyer and Welch, 2012[165]	≥40	1976-2008	SEER; United States	Population before vs. after widespread screening	EI; no adjustment	Change in incidence before and after introduction of screening with 3 estimates of baseline incidence. • Best guess: incidence increases 0.25% annually • Extreme: incidence increases 0.50% annually • Very extreme: using highest observed incidence, assume a 0.50% incidence increase	• Best guess: 31% • Extreme: 26% • Very extreme: 22%	NR	NR
Coldman and Phillips, 2013[166]	40-89	1970-2009	Breast cancer registry; Canada	Population before vs. after widespread screening	EI; compensatory drop	• Participation estimate: cumulative incidence with active screening vs. never screened or nonactive screening. • Population estimate: observed vs. expected population cumulative incidence in 2005-2009.	• Participation estimate: 7.3% • Population estimate: 6.7%	• Participation estimate: 5.4% • Population estimate: -0.7%	NR

Table 20. Studies of Overdiagnosis

Author, year	Age, years	Study years	Data source	Comparison groups	Approach, lead time adjustment	Overdiagnosis measures as defined by each study	Overdiagnosis rate of invasive cancer + DCIS	Overdiagnosis rate of invasive cancer	Overdiagnosis rate of DCIS
de Gelder et al, 2011[167]	49-74	2004-2006	Screening program (biennial); Netherlands	Modeled incidence of screening vs. predicted incidence without screening	LT; statistical adjustment; preclinical DCIS: mean 5.2 years; preclinical invasive: 2.6 years	Microsimulation analysis (digital mammography); • Baseline model: 18% are screen-detectable preclinical DCIS; 11% progress to invasive cancer, 5% are clinically diagnosed, 2% regress. • Progressive model: all tumors have preclinical screen-detectable DCIS stage and none regress; 96% invasive with no screening, 4% are clinically diagnosed. • Non-progressive model: no preclinical screen-detected DCIS, majority regress, 2% are clinically diagnosed.	• Baseline model: 2.5% all cases; 8.2% screen-detected • Progressive model: 1.4% all cases; 5.0% screen-detected • Non-progressive model: 7.7% all cases; 25.2% screen-detected	NR	NR
de Gelder et al, 2011[168]*	0-69; 0-74	1990-1998; 1998-2007	Screening program (biennial); Netherlands	Modeled incidence of screening vs. predicted incidence without screening	LT; compensatory drop; mean 2.6 years	Microsimulation screening analysis; excess cancers minus deficit cancers divided by the total number of breast cancers in the absence of screening in women 0-100 years.	1-year estimates 1990-1998: 1.0%; 6.1%; 9.1%; 11.4%; 10.0%; 9.4%; 8.8%; 5.6% 1-year estimates 1998-2007: 4.9%; 10.0%; 7.4%; 4.7%; 4.7%; 4.9%; 4.3%; 4.4%; 2.8%	NR	NR
Duffy et al, 2010[110]	50-69	1977-1998; 1974-2003	Swedish Two-County Trial; U.K. National Breast Screening Program	Active vs. passive screening; population before vs. after widespread screening	EI; compensa-tory drop	• Swedish Trial: Estimated expected incidence trends in the prescreening period vs. observed cases, adjusted for prevalence peak. • U.K. Program: Observed cases of breast cancer, minus any deficit in ages 65-69 or ≥70 years.	• Overall: 4%-7% • Swedish Trial: 4.3 cases per 1,000 women screened for 20 years • U.K. Program: 2.3 cases per 1,000 women screened for 20 years	NR	NR

Table 20. Studies of Overdiagnosis

Author, year	Age, years	Study years	Data source	Comparison groups	Approach, lead time adjustment	Overdiagnosis measures as defined by each study	Overdiagnosis rate of invasive cancer + DCIS	Overdiagnosis rate of invasive cancer	Overdiagnosis rate of DCIS
Falk et al, 2013[169†]	50-69	1995-2009	Norwegian Breast Cancer Screening Program (biennial)	Women screened vs. those never invited or did not attend screening	EI; compensatory drop	Women attending screening adjusted for compliance with screening vs. 3 reference rates: • 40 year olds 1993-1995 • Observed rates of invasive breast cancer 1980-1984 • Cohort of women born 1903-1907	16.5%; 16.3%; 13.9%	11.3%; 11.2%; 9.6%	NR
Gunsoy et al, 2014[180]	40-73	1971-2010	Data from various sources in the U.K.	Women screened vs. not screened	Multiple statistical adjustments	Markov model of the difference between cumulative incidence of invasive + DCIS with denominators: • Cases diagnosed in absence of screening age 40-85 • Cases diagnosed in screening period • Screen-detected breast cancers	• All cases: 4.3 to 8.9% • Screening period: 6.7 to 10.1% • Screen-detected: 11.8 to 13.5% • Highest rates with frequent screening	NR	NR
Hellquist et al, 2012[170]	40-49	1986-2005	Screening for Young Women Trial; Sweden	Population in areas with vs. without screening	EI; statistical adjustment; up to 1.5 years	Incidence in screening group vs. controls. Corrected for prescreening difference, prevalence peak bias (excluded prevalence screen data), trend bias (change in incidence per year of age).	Rate ratio: 1.01 (95% CI 0.94 to 1.08)	Rate ratio: 0.95 (95% CI 0.88 to 1.01)	NR
Jørgensen et al, 2009[171‡]	50-69	1991-2003 vs. 1971-1990	Screening program; Copenhagen and Funen, Denmark	Population in areas with (1991-2003) vs. without (1971-1990) screening	EI; compensatory drop	Ratio of incidence between screened and non-screened areas for the screened age group.	33%	NR	NR

Table 20. Studies of Overdiagnosis

Author, year	Age, years	Study years	Data source	Comparison groups	Approach, lead time adjustment	Overdiagnosis measures as defined by each study	Overdiagnosis rate of invasive cancer + DCIS	Overdiagnosis rate of invasive cancer	Overdiagnosis rate of DCIS
Kalager et al, 2012[172§]	50-69	1996-2005	Norwegian Breast Cancer Screening Program (biennial)	Population in areas with vs. without screening	EI; compensatory drop; Approach 1: 10-year lead time; Approach 2: 5 or 2-year	• Approach 1: Incidence rates in the screening and non-screening groups for women aged 50-79 years. • Approach 2: Excluded all cases of cancer detected in the first screening round, compares incidence in screened women vs. women 2-5 years older.	NR	• Approach 1: entire country: 25%, region 1: 18% • Approach 2: 5-year lead time: 15%, 2-year lead time: 20%	NR
Marmot et al, 2013[163,164]	40-69	1976-2001	Meta-analysis of Canadian National Breast Screening Study and Malmö I Trial	Randomized trials; screening vs. usual care	EI; none	Excess incidence of breast cancer (both invasive cancer and DCIS) in the screening population was compared with the incidence in the absence of screening	• Short case accrual: 19.0% (95% CI, 15.2-22.7%; 3 trials) • Long case accrual: 10.7% (95% CI, 9.3-12.2%; 3 trials)	NR	NR
Martinez-Alonso et al, 2010[173]	40-69	1980-2004	Cancer registry; Catalonia, Spain	Modeled pre vs. post screening incidence	EI; statistical adjustments	Probabilistic model for birth cohorts: 1935, 1940, 1945, 1950; observed vs. expected cumulative incidence.	NR	1935: 0.4% 1940: 23.3% 1945: 30.6% 1950: 46.6%	NR
Miller et al, 2014[69]	40-59	1980-1985	Canadian National Breast Screening Study	Randomized trial; screening vs. usual care	EI; none	Excess of breast cancer cases in mammography arm vs. the control arm of trial.	NR	22% of screen-detected cancer	NR

Table 20. Studies of Overdiagnosis

Author, year	Age, years	Study years	Data source	Comparison groups	Approach, lead time adjustment	Overdiagnosis measures as defined by each study	Overdiagnosis rate of invasive cancer + DCIS	Overdiagnosis rate of invasive cancer	Overdiagnosis rate of DCIS
Morrell et al, 2010[174]	50-69	1999-2001	Screening program (biennial); Australia	Screened vs. unscreened age group or prior to screening implementation	EI; statistical adjustment; 2- or 5-year lead times	Observed annual incidence minus expected annual incidence divided by expected annual incidence; • Interpolation approach: incidence in unscreened women (≤40 or ≥80) modeled by 5-year age group. • Extrapolation approach: incidence for the period prior to the introduction of screening modeled for all 5-year age groups and extrapolated to 1999-2001.	NR	• Interpolation: 2-year: 51%; 5-year: 42%; • Extrapolation: 2-year: 36%, 5-year: 30% • Rates higher for 50-59 vs. 60-69	NR
Njor et al, 2013[175]	56-70	1991-2005	Screening program; Copenhagen and Funen, Denmark	Population in areas with vs. without screening	EI; compensatory drop	Cumulative incidence in screened population vs. expected incidence in unscreened counties	≥8 years followup: Copenhagen, 3% (-14% to 25%), Funen, 0.7% (-9% to 12%)	NR	NR
Puliti, et al, 2009[176]	60-69	1990-NR	Screening program; Florence, Italy	Screening vs. pre-screening	EI; compensatory drop	Ratio of cumulative incidence of breast cancer in the invited group to those in the non-invited group at least 5 years after last screening, assuming 1.2% annual trend in pre-screening incidence.	Rate ratio: 1.01 (95% CI 0.95 to 1.07)	Rate ratio: 0.99 (95% CI 0.94 to 1.05)	NR
Seigneurin et al, 2011[177]	50-69	1991-2006	Cancer registry; Isere, France	Modeled screening incidence	LT; statistical adjustment, 2-4 years	Stochastic simulation model, driven by all-cause mortality, lifetime probability of breast cancer, natural course of breast cancer, and cancer detection; adjusted for sojourn time.	NR	All diagnosed cancers: 1.5%, screen detected: 3.3%	All diagnosed cancers: 28.0%, screen detected: 31.9%

Table 20. Studies of Overdiagnosis

Author, year	Age, years	Study years	Data source	Comparison groups	Approach, lead time adjustment	Overdiagnosis measures as defined by each study	Overdiagnosis rate of invasive cancer + DCIS	Overdiagnosis rate of invasive cancer	Overdiagnosis rate of DCIS
Yen et al, 2012[178]	40-74	1977-2005	Swedish Two County Trial; data from 1 county only (Dalarna)	Active screening vs. passive screening	EI; compensatory drop	Cumulative incidence in active screening vs. usual care groups	Relative risk: 1.00 (95% CI 0.92 to 1.08)	Relative risk: 0.99 (95% CI 0.88 to 1.55)	Relative risk: 1.17 (95% CI 0.88 to 1.55)
Zahl et al, 2012[179]	40-79	1991-2009	Norway Cancer Registry	Screening vs. post-screening	EI; compensatory drop	Define overdiagnosis as increase in number of cancer diagnoses among those who are invited for screening and the reduction in the number of diagnoses among those no longer invited.	~50%	NR	NR
2009 report									
de Koning et al, 2006[155]	50-74	1989-2001	National data from The Netherlands	Screening vs nonscreening (biennial)	Statistical adjustments; assumptions of DCIS progression	Microsimulation model	3% in screened population 8% screen-detected	NR	NR
Duffy et al, 2005[157]	40-74	1977-1985	Swedish Two-county Trial	Active vs. passive screening	Lead time statistical adjustments	Markov multistate model	1% in screened population	NR	NR
	39-59	1982-1996	Gothenburg trial	Screening vs. no screening	Lead time statistical adjustments	Markov multistate model	2% in screened population	NR	NR
Olsen et al, 2006[156]	50-71	1991-1996	Copenhagen, Denmark screening program (biennial)	Incidence in screened women	Statistical adjustments	Chronic disease statistical model of screen-detected overdiagnosis	Prevalence: 7.8%; Incidence: 0.5%	NR	NR
Paci et al, 2004[154]	50-69	1985-1999	Florence, Italy; screening program	Incidence in screening vs. prescreening	EI; corrected for lead time	Observed/expected cases	5%	2%	3%
Paci et al, 2006[153]	50-74	1986-2001	Italy; screening program	Prescreening incidence	EI; corrected for lead time	Observed/expected cases	4.6%; range -0.6% to 9.7% varies by age (highest in 50-54 and 65-74)	3.2%	1.4%

Table 20. Studies of Overdiagnosis

Author, year	Age, years	Study years	Data source	Comparison groups	Approach, lead time adjustment	Overdiagnosis measures as defined by each study	Overdiagnosis rate of invasive cancer + DCIS	Overdiagnosis rate of invasive cancer	Overdiagnosis rate of DCIS
Yen et al, 2003[158]	40-69		Swedish Two-county Trial, United Kingdom, Netherlands, Australia, New York	Screening vs. not screening	LT; statistical adjustment	Six state Markov model	NR	NR	Prevalence: 37% Incidence: 4%
	40-69		Swedish Two-county Trial	Screening vs. not screening	LT; statistical adjustment	Six state Markov model	NR	NR	40-49: 19%, 3% 50-59: 23%, 4% 60-69: 46%, 6%
Zackrisson et al, 2006[159]	55-69	1978-1986	Malmö trial	Randomized screening vs. no screening	EI; compensatory drop	Comparison of incidence in screened vs. unscreened	10% of incidence in control group	7%	3%
Zahl et al, 2004[160]	50-69	1971-2000	Norway and Sweden	Prescreening incidence	EI; compensatory drop	Changes in age-specific incidence rates associated with the introduction of screening programs	NR	30% of incidence in screened population	NR

*An additional 6 model estimates for each year are published in this paper to show the range of estimates varies by selection of the denominator.
†Population overlap with Kalager; may have data to calculate by age group.
‡Same Copenhagen population as Olsen.
§Population overlap with Falk.

Abbreviations: CI=confidence interval; DCIS=ductal carcinoma in situ; EI=excess incidence approach; LT=lead time approach; NR=not reported; SEER=Surveillance, Epidemiology, and End Results Program; U.K.=United Kingdom; vs.=versus.

Table 21. Overdiagnosis Estimates From Randomized, Controlled Trials Without Screening of Control Groups

Trial (reference)	Age, *years*	Overdiagnosis, % (95% CI) Short-case accrual*	Overdiagnosis, % (95% CI) Long-case accrual*
Malmö I[159]	55-69	18.7 (15.1 to 22.4)	10.5 (8.4 to 12.7)
CNBSS-I [76]	40-49	22.7 (18.4 to 27.0)	12.4 (9.9 to 14.9)
CNBSS- 2[78]	50-59	16.0 (12.5 to 19.5)	9.7 (7.5 to 11.9)
Meta-analysis[163]	40-69	19.0 (15.2 to 22.7; I^2=64.8%; p=0.058)	10.7 (9.3 to 12.2; I^2=22.3%; p=0.276)

*Excess cancers as a proportion of cancers diagnosed during the screening period (short-case accrual) or over the followup period (long-case accrual) in women invited for screening.

Abbreviations: CI=confidence interval; CNBSS=Canadian National Breast Screening Study.

Table 22. Systematic Reviews of Psychological Harms From False-Positive vs. Normal Screening Mammography Results

Author, year quality rating	Inclusion criteria	Searches	Number of studies; number of participants	Re-attendance	Anxiety	Depression	Breast cancer worry/distress
Bond et al, 2013[185] Good	Studies in the U.K. comparing psychological and behavioral outcomes of women with FP vs. normal screening mammograms.	Multiple databases through November 2011	7 studies* of psychological harms N=3,168; re-attendance N=151,490	• Lower in FP vs. normal (2 studies) • No difference (2 studies) • Higher in FP vs. normal if given tailored letters (1 study)	No difference (2 studies)	No difference (2 studies)	Higher in FP vs. normal (3 studies)
Hafslund and Nortvedt, 2009[194] Fair	Studies of women not at high risk; ages 40-74 years invited to mammography screening.	Multiple databases January 1995 to July 2007	17 studies† N=18,097	NR	Higher in FP vs. normal (15 studies)	NR	Higher in FP vs. normal (15 studies)
2009 Review							
Brewer et al, 2007[184] Fair	Studies comparing psychological and behavioral outcomes of women with FP vs. normal screening mammograms.	Multiple databases through September 2006	23 studies N=313,967	• Lower in FP vs. normal in U.S. (RR 1.07; 95% CI 1.02 to 1.12; 5 studies) • Lower in normal vs. FP in Canada (RR 0.63; 95%CI 0.50 to 0.80; 2 studies) • No differences in Europe (RR 0.97; 95% CI 0.93 to 1.01; 5 studies)	• Higher in FP vs. normal (4 studies) • No differences (4 studies) • Conflicting results over time (2 studies)	• Lower in FP vs. normal (7 studies) • No differences (1 study) • Conflicting results based on measure (1 study)	• Higher in FP vs. normal (4 studies) • No differences (3 studies) • Conflicting results over time (2 studies)
Brett et al, 2005[183] Fair	Studies of the psychological impact of mammography screening.	Multiple databases 1982 to 2003	54 studies N=NR	NR	Higher in FP vs. normal (14 studies)	NR	Higher in FP vs. normal (9 studies)

*5 of 7 studies were included in at least one of the systematic reviews included in the 2009 review.
†13 of 17 studies were included in at least one of the systematic reviews included in the 2009 review.

Abbreciations: CI=confidence interval; FP=false-positive; N=number; NR=not reported; RR=risk ratio; U.K.=United Kingdom; U.S.=United States; vs.=versus.

Table 23. Summary of Results of New Studies of Psychological Harms

Author, year	Study design	Population	Comparisons, N	Measures	Re-attendance	Anxiety	Depression	Breast cancer worry	General QOL
Bredal et al, 2013[207]	Before-after	Women recalled in a screening program in Norway	A) At recall (n=640) B) 4 weeks later	HADS (score ≥11)	NR	0	0	NR	NR
Brodersen and Siersma, 2013[203]	Nested case-control	Screening programs in Denmark	A) FP (n=272) B) Normal (n=864) C) TP (n=174)	COS-BC	NR	• Immediate: higher A+C vs. B; no difference A vs. C • 3-years after: higher C vs. A+B and A vs. B	NR	0	NR
Espasa et al, 2012[206]	Case-control	Screening program in Spain	A) FP (n=100) B) Normal (n=50)	HADS, structured interview	NR	0	0	Higher FP vs. normal	NR
Fitzpatrick et al, 2011[200]	Retrospective cohort	Screening program in the United Kingdom	A) FP (n=9,746) B) Normal (n=148,589)	Re-attendance	• Decreased: women >55, open biopsy, longer time to diagnosis • Increased: repeat screens, screened in mobile unit	NR	NR	NR	NR
Gibson et al, 2009[198]	Prospective cohort	New Hampshire Mammography Network and New Hampshire Women for Health study	A) FP (n=2,107) B) Normal (n=11,384)	WHQ	NR	NR	Higher for non-white with FP vs. normal	NR	NR
Hafslund et al, 2012[205]	Nested case-control	Screening programs in Norway	A) FP (n=128) B) Normal (n=195)	SF-36, HADS	NR	0	More cases for FP vs. normal	NR	Lower for FP vs. normal
Keyzer-Dekker, 2012[199]	Prospective cohort	Women with abnormal results in The Netherlands	A) 1st screen recalls (n=186) B) Repeat screen recalls (n=296)	STAI, NEO-FFI, CES-D, WHOQOL	NR	0*	0*	NR	NR
Klompen-houwer et al, 2014	Retrospective cohort	Screening program in The Netherlands	A) Normal screen (n=373,474) B) 1st screen recalls (n=6,672) C) repeat screen recalls for different lesion (n=161) D) repeat screen	Re-attendance	• 93.2% vs. 65.4% vs. 56.7% vs. 44.3% • 44.3% for all recalled groups combined	NR	NR	NR	NR

Table 23. Summary of Results of New Studies of Psychological Harms

Author, year	Study design	Population	Comparisons, N	Measures	Re-attendance	Anxiety	Depression	Breast cancer worry	General QOL
			recalls for same lesion (n=89)						
Maxwell et al, 2013[201]	Retrospective cohort	Screening program in the United Kingdom	First screening A) Open biopsy (n=110) b) Needle sampling (n=1,374) C) No tissue sampling (n=2,703)	Re-attendance	Increased for C, but no change for A or B	NR	NR	NR	NR
			Repeat screening A) Open biopsy (n=199) b) Needle sampling (n=1,052) C) No tissue sampling (n=4,009)		Decreased for A and B, but no change for C	NR	NR	NR	NR
Tosteson et al, 2014[204]	Nested case-control	Women participating in DMIST in the United States	A) FP (n=494) immediate B) FP 1-year after	STAI, EuroQOL EQ-5D	NR	Decreased A to B	NR	NR	0
			C) Normal (n=534) immediate D) Normal 1-year after		NR	0	NR	NR	0

*Both groups improved over time.

Abbreviations: 0=comparison studied but not statistically significantly different; CES-D=Center for Epidemiological Studies-Depression Scale; COS-BC=Consequences of Screening in Breast Cancer; DMIST=Digital Mammographic Imaging Screening Trial; FP=false-positive; HADS=Hospital Depression and Anxiety Scale; n=number; NEO-FFI=Neuroticism-Extraversion-Openness-Five Factor Inventory; NR = not reported; QOL=quality of life; SF-36=Short-form 36 Health Survey; STAI=Spielberger State-Trait Anxiety Inventory; TP=true positive; vs.=versus; WHOQOL=World Health Organization Quality of Life Assessment Instrument; WHQ=Women's Health Questionnaire.

Table 24. Models of Radiation Exposure, Breast Cancer Incidence, and Death

Author, year	Study design	Population; age, *years*	Method	Outcome measures	Results
Hendrick, 2010[208]	Modeling Study	U.S. based sources; 40-80	Theoretical estimates are based on long-term followup of acute exposures to higher levels of ionizing radiation and a linear no-threshold extrapolation of risks at low doses. Model assumes 3.7mGy to 4.7 mGy per exam.	Breast cancer cases and mortality	LAR of breast cancer incidence and mortality, per 100,000 • 40 years: 5-7 cases; 1.3-1.7 deaths • 50 years: 2-3 cases; 0.7-0.9 deaths • 80 years: 0.1-0.2 cases; <0.1 deaths LARs of breast cancer incidence and mortality in women undergoing annual screening mammography, per 100,000 • Screening 40-80 years: 72-91 cases; 20-25 deaths • Screening 50-80 years: 31-40 cases; 10-12 deaths
Yaffe and Mainprize, 2011[209]	Modeling study	U.S. based sources; 40-74	Model based on digital mammography and radiation exposure estimates of 3.7 mGy per exam	Estimated lifetime radiation induced breast cancer cases and deaths	Number of radiation induced breast cancer cases and deaths in 100,000 women • Annual screen 40-49 years: 59 cases, 7.6 deaths • Annual 50-59 years: 27 cases, 3.1 deaths • Biennial 50-59 years: 14 cases, 1.6 deaths • Annual 40-59 years: 85 cases, 11 deaths • Annual 40-49 years, biennial to 59 years: 73 cases, 9 deaths • Annual 40-55 years, biennial to 74 years: 86 cases, 11 deaths

Abbreviations: LAR=lifetime attributable risk; mGy=milli Gray (unit of radiation); U.S.=United States.

Table 25. Systematic Reviews of Pain With Mammography

Author, year	Inclusion criteria	Databases; search dates	Number of studies (designs); number of participants	Methods for rating quality and synthesizing results	Results	Quality rating; limitations
Whelehan et al, 2013[211]	Studies of pain or discomfort of screening mammography and re-attendance.	MEDLINE, EMBASE, PsychINFO, CINAHL, ASSIA, Cochrane Database of Systematic Reviews, Sociological Abstracts, SSCI, SCI, and NHS online literature database; October 2012.	20 observational studies (most cross-sectional surveys); causation N=5,741, association N=NR.	Quality based on individual factors;* studies combined separately for causation vs. association; actual vs. intended re-attendance data were considered more valid.	Causation (7 studies) Response rates: 32-79% • Actual non-re-attendance indicating pain as the reason (5 studies): 11-46% • Intended future non-re-attendance due to pain (2 studies): 2.7% and 17.5% Association (15 studies) • Actual re-attendance (10 studies): no difference between women who experienced pain vs. no pain (RR 1.38; 95% CI, 0.94 to 2.02; 5 studies); higher pain scores in non re-attenders vs. re-attenders in 2 of 3 studies (p=0.001 and p<0.05). • Intended re-attendance (5 studies): no differences (3 studies), less intent for women with pain (2 studies) with OR 0.61 (95% CI, 0.38 to 0.98) in one study.	Fair; unclear how study quality was used to formulate conclusions; did not describe characteristics of all included studies; did not assess publication bias.
2009 Review						
Armstrong et al, 2007[14]	Studies of risks of screening mammography for women in their 40s.	MEDLINE, Pre-MEDLINE, and the Cochrane Central Register of Controlled Trials; May 2005.	22 studies (3 RCTs, 5 prospective cohort, 1 retrospective cohort, 13 cross-sectional); N=13,008.	Centre for Evidence-based Medicine criteria; based on study design and rates of attrition; methods of synthesis NR.	• Prevalence of pain from mammography varied from 28-77%. • Degree of pain was associated with stage of menstrual cycle (3 studies), anxiety (2 studies), and pre-mammography anticipation of pain (4 studies).	Fair; no synthesis of data; unclear how study quality was used to formulate conclusions; study designs not pre-specified; did not assess publication bias.

Table 25. Systematic Reviews of Pain With Mammography

Author, year	Inclusion criteria	Databases; search dates	Number of studies (designs); number of participants	Methods for rating quality and synthesizing results	Results	Quality rating; limitations
Miller et al, 2008[210]	RCTs of interventions that reduce or relieve the pain and discomfort of screening mammography.	MEDLINE, EMBASE, CINAHL, and Cochrane Breast Cancer Specialised Register; 2006.	7 RCTs; N=1,771.	Quality (levels A, B, C) based on generation and concealment of allocation sequence, comparability of groups at baseline, intention-to-treat analysis, and double-blinding after allocation; heterogeneity of studies allowed qualitative synthesis only.	**Information provided before mammography vs. usual care (3 trials):** • 44% vs. 24% (p=0.009) experienced less discomfort than expected with verbal information (1 trial). • Pain scores were lower with written information in one trial (mean VAS16.5 vs. 24.5, p<0.05), but no differences were found in another trial. **Breast compression strategies (2 trials):** • Participant vs. technologist compression indicated 57% felt no difference in discomfort, 31% less, 13% more; • No difference with normal vs. one second of reduced compression. **Premedication (1 study)**: acetaminophen vs. none (mean VAS scores 23.7 vs. 22.8, p=0.896). **Breast cushion (1 study):** reduced pain for cushion vs. no cushion (mean VAS pain 20.34 vs. 34.94, p<0.0001).	Good; did not assess publication bias.

*Factors include whether intended or actual re-attendance was measured, survey response rate/participation rate, measures of pain or discomfort, consistency of the timing of outcome measurement, quality of statistical analysis, and robustness of ascertaining re-attendance rate.

Abbreviations: ASSIA=Applied Social Sciences Index and Abstracts; CI=confidence interval; CINAHL=Cumulative Index to Nursing and Allied Health Literature; EMBASE= Excerpta Medica database; N=number; NHS=National Health Services; NR=not reported; OR=odds ratio; RCT=randomized, controlled trial; RR=relative risk; SCI=Science Citation Index; SSCI=Social Sciences Citation Index; VAS=Visual Analogue Scale; vs.=versus.

Table 26. Studies of Harms of Screening With Different Modalities

Author, year	Study design	Population; age, *years*; participants, *n*	Study years; comparison	Outcome measures	Results	Quality rating
Mammography ± tomosynthesis						
Haas et al, 2013[214]	Case series	U.S., multisite hospital and outpatient centers; DM, 7,058; DM + T, 6,100	2011 to 2012; DM vs. DM +T	Recall rate (%); adjusted odds of recall	Recall, DM vs. DM + T by age (% relative change,95% CI): Total 8.4 vs. 12; -29.7 (19.1 to 36.5), p<.01; 40 to 49, 10.4 vs. 16.3; -35.8 (24.2 to 45.7), p<.01; 50 to 59, 7.6 vs. 10.6; -28 (12.7 to 44.6); p<.01; 60 to 69, 7.4 vs. 10.7; -30.3 (12.3 to 44.6), p=.01; ≥70, 6.7 vs 7.9; -15.4; NS Adjusted recall OR, 0.62 (0.55 to 0.70); p<.0001	NR
Friedewald et al, 2014[212]	Post-intervention series	U.S., multicenter; mean age 57; DM, 281,187; DM + T, 173,663	2010 to 2012; DM vs. DM + T	Recall and biopsy rates, per 1,000	Recall, DM vs. DM + T (change, 95% CI): 107/1,000 vs. 91/1,000; -16.1 (-18.0 to -14.2), p<0.001 Biopsy, DM vs. DM + T (change, 95% CI): 18.1/1,000 vs. 19.3/1,000; +1.3 (0.4 to 2.1), p=0.004	NR
Rose et al, 2013[146]	Case series	U.S., multisite community-based breast center; >18 years; 18,202 DM and 10,878 DM + T	2011 to 2012; DM vs. DM + T	Recall rate, %	Recall, DM vs. DM + T by age (% relative change): <50, 10.3% vs. 6.5% (-37.2); 50 to 64, 7.6% vs. 5.1% (-32.9); age >64, 7.9% vs. 4.2% (-46.6); total, 8.7% vs. 5.5% (-37.5); NS	NR
Ciatto et al, 2013[213]	Post-intervention series	Italy; population-based screening program (STORM); ≥48; 7,292	2011 to June 2012; biennial DM vs. DM + T	Recall rate, %	Recall, DM vs. DM + T: total, 141 (2%) vs. 73 (1%), p<0.0001; age <60, 89 (2.2%) vs. 41 (1%); age >60, 52 (2%) vs. 32 (1%)	NR
Skaane et al, 2013[147]	Post-intervention series	Norway, Oslo screening program; 50 to 69; 12,631	2010 to 2011; DM vs. DM+T (biennial screening)	Recall rate, per 1,000	Recall, DM vs. DM + T: 61.1/1,000 vs. 53.1/1,000 (-13%); RR 0.85 (p<0.001)	NR
Mammography ± clinical breast exam						
Chiarelli et al, 2009[215]	Cohort	Canada; 40-69; 290,230	2002 to 2003; biennial M (n=57,715) vs. CBE + M (n=232,515)	Recall rate, %	Recall, M vs. CBE ± M: 6.5% vs. 8.7% (+2.2% for CBE), or 55/10,000 additional FP with CBE	Fair

Abbreviations: CBE=clinical breast exam; CI=confidence interval; DM=digital mammography; FP=false-positive; M=mammography; n=sample size; NR=not reported; NS=not statistically significant; OR=odds ratio; RR=relative risk; STORM=Screening with Tomosynthesis or standard Mammography; T=tomosynthesis; U.S.=United States; vs.=versus.

Table 27. Examples of Specific Adverse Effects of Selected Treatments for Breast Cancer

Treatment	Adverse Effect and Rate*
Surgery	
Mastectomy[216]	Wound infection 3.8%; skin flap necrosis 10% to 18%; chronic chest wall pain >10%. Other adverse effects include phantom breast syndrome, arm morbidity, seroma, pneumothorax, brachial plexopathy, lymphedema.
Lymph node biopsy	Average false-negative 8.4% (range: 0% to 29% across 69 studies);[249] >1% of patients experienced allergic reactions to dye used during the procedure in a trial of 5588 patients.[250] 5% with sentinel node biopsy and 16% to 18% with axillary lymph node dissection following sentinel node biopsy develop clinical lymphedema.[251,252]
Radiation†[217]	
Dose: 50 Gy in 25 fractions over 5 weeks	Based on 1,854 women: among women with breast conserving surgery—breast shrinkage 25%; breast induration 18%; telangiectasia 5%; breast edema 10%; among women who received lymphatic radiotherapy, shoulder stiffness 9%; arm edema 12%. Adverse effects experienced by <5% of patients: symptomatic rib fracture, symptomatic lung fibrosis, ischemic heart disease, brachial plexopathy.
Dose: 41.6 Gy in 13 fractions over 5 weeks	Based on 750 women: among women with breast conserving surgery—breast shrinkage 27%; breast induration 24%; telangiectasia 6%; breast edema 11%; among women who received lymphatic radiotherapy—shoulder stiffness 11%; arm edema 17%. Adverse effects experienced by <5% of patients: symptomatic rib fracture, symptomatic lung fibrosis, ischemic heart disease, brachial plexopathy.
Dose: 40 Gy in 15 fractions over 3 weeks	Based on 1,110 women: among women with breast conserving surgery—breast shrinkage 22%; breast induration 13%; breast edema 5%. Adverse effects experienced by <5% of patients: telangiectasia, symptomatic rib fracture, symptomatic lung fibrosis, ischemic heart disease, brachial plexopathy, shoulder stiffness and arm edema in women who received lymphatic radiotherapy.
Dose: 39 Gy in 13 fractions over 5 weeks	Based on 737 women: among women with breast conserving surgery—breast shrinkage 23%; breast induration 18%; breast edema 7%; among women who received lymphatic radiotherapy—shoulder stiffness 9%; arm edema 7%. Adverse effects experienced by <5% of patients: telangiectasia, symptomatic rib fracture, symptomatic lung fibrosis, ischemic heart disease, brachial plexopathy.
Endocrine therapy	
Anastrozole	**Anastrozole treatment for 5 years**[219,253] (% of patients with common adverse events in a trial of 3125 postmenopausal patients with localized invasive breast cancer): fatigue 19%; nausea and vomiting 13%; hot flushes 36%; mood disturbances 19%; musculoskeletal disorders 36%. Adverse effects experienced by <5% of patients: vaginal bleeding, vaginal discharge, ischemic cardiovascular disease, ischemic cerebrovascular events, venous thromboembolic events, deep venous thromboembolic events, carpal tunnel syndrome. **Goserelin 3.6 mg given subcutaneously every 28 days plus anastrozole 1 mg/day for a mean of 47.8 months**[254] (% of patients each adverse events in a trial of 453 premenopausal patients who had undergone primary surgery for stage I or II breast cancer): arthralgia 24.7%; bone pain 28.3%; fatigue 20.5%; depression, sleep disturbances 21.4%; nausea and vomiting 7.1%; morning stiffness 7.3%; hot flushes 5.5%. Adverse effects experienced by <5% of patients: fracture, cognitive disorder, dizziness, peripheral nerve disease, muscle cramp, fever, hypertonia, tachycardia, thrombosis, leg edema, cutaneous reaction skin disease, impaired vision, uterine polyp, periodontal disease.
Letrozole	**Letrozole 2.5 mg/day for five years**[255] (% of patients with adverse events in a trial of 3975 postmenopausal patients with hormone receptor positive breast cancer): hot flashes 33.5%; night sweats 13.9%; fracture 5.7%; arthralgia 20.3%; myalgia 6.4%. Adverse effects experienced by <5% of patients: cerebrovascular accident or transient ischemic attack, thromboembolic event, cardiac event, other cardiovascular events, vaginal bleeding.

Table 27. Examples of Specific Adverse Effects of Selected Treatments for Breast Cancer

Treatment	Adverse Effect and Rate*
Tamoxifen	**Tamoxifen 10 vs. 20 mg/day orally for 6 months**[256] (% of patients reporting adverse events which occurred in >10% of patients in a trial of 30 women with breast cancer): hot flashes 30%; nausea 17%; pharyngitis 17%; fatigue 13%. **Tamoxifen 20 mg/day orally for 5 years**[218] (% of patients with adverse reactions in a trial of 1422 patients with primary operable breast cancer over the course of 5 years): hot flashes 64%; vaginal discharge 30%; irregular menses 25%; fluid retention 32%; nausea 24%; skin changes 19%; diarrhea 11%; weight gain 38%; weight loss 22%. Adverse effects experienced by <5% of patients: thromboembolic vein, death. Other serious adverse effects of tamoxifen include an increased risk of endometrial cancer and uterine sarcoma.
Exemestane	**Extramestane 25 mg/day orally for 5 years**[257] (% of patients with adverse reactions in a trial of 4852 postmenopausal patients with hormone receptor positive breast cancer): flushes and sweats 35%; hypertension 6%; breast or nipple disorder 6%; vaginal dryness 7%; fractures 5%; joint disorders 36%; muscle disorders 11%; osteoporosis 10%; other musculoskeletal and connective disuse disorders 15%; headache 8%; dizziness 5%; other nervous system disorders 17%; depression 9%; sleep disorder or insomnia 13%; other psychiatric disorders 8%; hyperlipidemia 5%; weight increase 7%. Adverse effect experienced by <5% of patients: arrhythmia, cardiac failure, myocardial ischemia or infarction, other cardiac disorders, embolism, peripheral arterial disease, venous thrombosis, other vascular disorders, endometrial abnormalities, genital or vaginal discharge, postmenopausal bleeding, vulvovaginal disorders, cerebrovascular insufficiency or infarction or thrombosis, nerve compression disorders, loss or reduction of libido, abnormal liver function tests, endocrine disorders, renal and urinary disorders.
Neoadjuvant/adjuvant chemotherapy	
AC (doxorubicin/cyclophosphamide) followed by paclitaxel	**Doxorubicin 60 mg/m^2 by 5 to 15-minute IV infusion and cyclophosphamide 600 mg/m^2 by 30 to 60-minute IV infusion every 3 weeks for 4 cycles followed by 175 mg/m^2 paclitaxel by 1-hour IV infusion weekly for 12 doses**[258] (% of patients with common toxic effects and neuropathies resulting from the paclitaxel component of therapy in 1231 patients with lymph node-positive or high risk, lymph node-negative breast cancer after mastectomy or breast conserving surgery): grade 2, 3, or 4 neuropathy 27%. Adverse effects experienced by <5% of patients: neutropenia, febrile neutropenia, infections, stomatitis, fatigue, myalgia, arthralgia, lacrimation.
TC (docetaxel and cyclophosphamide)	**Docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 as 1-hour IV infusion on day 1 of a 3-week cycle (4 cycles total)**[259] (frequency [%] of side effects in 506 patients with operable stage I to III invasive breast cancer after surgical excision of the primary tumor): anemia <7%; neutropenia 63%; thrombocytopenia <3%; asthenia <79%; edema <35%; fever 24%; infection <20%; myalgia <35%; nausea <55%; phlebitis <12%; stomatitis <35%; vomiting <16%.

Table 27. Examples of Specific Adverse Effects of Selected Treatments for Breast Cancer

Treatment	Adverse Effect and Rate*
TCH (docetaxel/carboplatin/trastuzumab) +/- pertuzumab	**Docetaxel 75 mg/m^2 plus carboplatin administered at area under the plasma concentration curve x6 mg/mL/minute concurrently with trastuzumab at 2mg/kg every 3 weeks for 6 cycles followed by trastuzumab 6 mg/kg every 3 weeks to complete 1 year of treatment**[260] (% of patients with adverse events in a trial of 1056 patients with HER2 positive early-stage breast cancer): irregular menses 26.5%; sensory neuropathy 36%; nail changes 28%; myalgia 38.9%; neutropenia 65.9%; leukopenia 48.2%; febrile neutropenia 9.6% neutropenic infection 11.2%; anemia 5.8% thrombocytopenia: 6.1%. Adverse effect experiences by <5% of patiets: arthralgia, fatigue, hand-foot syndrome, diarrhea, nausea, vomiting, motor neuropathy, renal failure, grade 3 or 4 creatinine elevation, leukemia. **Trastuzumab at an initial dose of 8 mg/kg, followed by 6 mg/kg; pertuzumab at an initial dose of 840 mg, followed by 420 mg, carboplatin was administered at a dose of 6x area under the plasma concentration-time curve and docetaxel was given at 75 mg/m^2** [2 261](% of patients with the most common adverse events during neoadjuvant treatment in a trial of 76 patients with HER2 positive breast cancer): diarrhea 72.4%; alopecia 53.9%; nausea 44.7%; neutropenia 48.7%; vomiting 39/5%; fatigue 42.1%; anemia 36.8%; mucosal inflammation 17.1%; constipation 15.8%; dyspepsia 22.4%; febrile neutropenia 17.1%; leukopenia 11.8%; anemia 17.1%; thrombocytopenia 11.8%. Adverse effects experienced by <5% of patients: drug hypersensitivity, alanine aminotransferase increase. Results reported as % of patients with the most common adverse events during adjuvant treatment in a trial of 67 patients with HER2 positive breast cancer: radiation skin injury 10.4%; arthralgia 9%; hot flushes 6%; diarrhea 9%; fatigue 7.5%; musculoskeletal chest pain 7.5%; peripheral edema 6%; erythema 6%. Adverse effects experienced by <5% of patients: headache, musculoskeletal pain, neutropenia.
Chemotherapy regimens (metastatic cancer)	
Paclitaxel (taxane)	**Paclitaxel 80mg/m^2 weekly via 1 hour infusion until disease progression or limiting toxicity (HER-2 + patients also received trastuzumab 2mg/kg via 30 minute infusion following a 4 mg/kg loading dose administered over 90 minutes)**[262] (% of patients with grade 3 or 4 nonhematologic toxicity in a trial of 577 patients metastatic breast cancer): infection 6%; diarrhea 5%; dyspnea 7%; edema 6%; neurosensory 24%; neuromotor 9%; malaise/fatigue 6%; Hyperglycemia: 5%. Two treatment related deaths attributable to pneumonia, and one secondary malignancy also occurred all in patients without trastuzumab. **Paclitaxel 175mg/m^2 every 3 weeks via 3 hour infusion until disease progression or limiting toxicity (HER-2 + patients also received trastuzumab 2mg/kg via 30 minute infusion following a 4 mg/kg loading dose administered over 90 minutes)**[262] (% of patients with grade 3 or 4 nonhematologic toxicity in a trial of 158 patients metastatic breast cancer): neurosensory 12%; Hyperglycemia: 8%. Adverse effects experienced by <5% of patients: infection, diarrhea, dyspnea, edema, neuromotor, malaise/fatigue. One secondary malignancy also occurred in a patient without trastuzumab.
Docetaxel (taxane)	**Docetaxel 50 mg/m^2 as a 1-hour IV infusion on days 1 and 8 every 3 weeks (100 mg/m^2 per cycle) for a median of 5 cycles**[263] (% of patients with adverse effects in a trial of 88 patients with metastatic breast cancer): neutropenia 94%; thrombocytopenia 11%; anemia 90%; alopecia 91%; asthenia 82%; skin 64%; diarrhea 62%; nausea 54%; vomiting 43%; stomatitis 54%; neurosensory 48%; infection 16%; weight gain 28%; myalgia 18%; hypersensitivity reactions 4%.
Capecitabine (anti metabolite)	**Capecitabine 1250 mg/m^2 twice/day orally for 14 days followed by a 7-day rest period, continued for a maximum of 15 cycles**[264] (% of patients with common adverse events in a trial of 126 patients with anthracycline and taxane pretreated metastatic breast cancer): hand-foot syndrome 71%; nausea 48%; asthenia 35%; vomiting 27%; neutropenia 26%; stomatitis 25%.

*This is not a comprehensive list of all potential adverse effects and reflects only events where rates were available.

Table 27. Examples of Specific Adverse Effects of Selected Treatments for Breast Cancer

†Results reported as % of patients experiencing adverse event during 10 years followup in 1,854 women with completely excised invasive breast cancer after primary surgery followed by chemotherapy and endocrine treatment where prescribed.[217]

Abbreviations: Gy=gray (unit of radiation); HER2= human epidermal growth factor receptor 2; IV = intravenous; kg=kilograms; m=meter; mg=milligram.

Table 28. Summary of Evidence: Screening for Breast Cancer

Main findings from previous USPSTF reviews	Number/type of studies in update	Overall quality*	Limitations	Consistency	Applicability	Summary of findings
Key Question 1. What is the effectiveness of routine mammography screening in reducing breast cancer–specific and all–cause mortality, and how does it differ by age, risk factor, and screening interval?						
Screening reduced breast cancer mortality in RCTs for women age 39-49 (RR 0.85; 95% CrI, 0.75 to 0.96; 8 trials); 50-59 (RR 0.86; 95% CrI, 0.75 to 0.99; 6 trials); and 60-69 (0.68; 95% CrI, 0.54 to 0.87; 2 trials); data were limited for 70-74.	3 RCTs provided updated data in addition to 5 RCTs with older data; 65 observational studies (57 included in 4 systematic reviews + 8 additional studies)	Fair	Trials have methodological limitations; observational studies use various methods that introduce potential bias.	Results are consistent across types of studies	Most studies were conducted in Europe. RCTs used outdated technologies and treatments have changed over time.	• Screening reduced breast cancer mortality in RCTs for women age 40-49 (RR 0.88; 95% CI, 0.73 to 1.003; 9 trials); 50-59 (RR 0.86; 95% CI, 0.68 to 0.97; 7 trials); 60-69 (RR 0.67; 95% CI, 0.54 to 0.83; 5 trials); data were limited for 70-74. • Meta-analysis of observational studies indicated 25% to 38% reduction in breast cancer mortality with screening for age 50-59. • Two observational studies of women in their 40s indicated 25% to 44% reduction in breast cancer mortality for screening participants versus nonparticipants. • All-cause mortality was not reduced with screening. • Results for risk factors and screening intervals were not available.
Key Question 2. What is the effectiveness of routine mammography screening in reducing the incidence of advanced breast cancer and treatment-related morbidity, and how does it differ by age, risk factors, and screening interval?						
Not included.	3 RCTs of screening and cancer stage; 1 Cochrane review of 5 RCTs of screening and uptake of cancer treatment; 4 analyses of BCSC data; 8 observational studies	Fair	Trials have methodological limitations; observational studies use various methods that introduce potential bias.	Results are consistent across types of studies.	Most studies were conducted in Europe. RCTs used outdated technologies and treatments have changed over time.	• Screening reduced cancer stage for age ≥50 (RR, 0.62; 95% CI, 0.46 to 0.83; 3 trials), but not for age 40-49. • Women randomized to screening had more mastectomies, lumpectomies, and radiation therapy, and less hormone therapy than controls. • Women age 40-49 with extremely dense breasts had increased risks for advanced stage cancer and large-size tumors with biennial compared with annual screening.

Table 28. Summary of Evidence: Screening for Breast Cancer

Main findings from previous USPSTF reviews	Number/type of studies in update	Overall quality*	Limitations	Consistency	Applicability	Summary of findings
Key Question 3. How does the effectiveness of routine breast cancer screening in reducing breast cancer–specific and all-cause mortality vary by different screening modality?						
Not included.	No studies evaluated this question.	NA	NA	NA	NA	RCTs of mammography with or without CBE do not compare relative mortality reduction across the different modalities.
Key Question 4. How does the effectiveness of routine breast cancer screening in reducing the incidence of advanced breast cancer and treatment-related morbidity vary by different screening modality?						
Not included.	2 case-series studies	Poor	No RCTs; comparability of groups not known.	Results are consistent.	High clinical relevance.	Tumor size, stage, and node status did not differ between women screened with tomosynthesis + digital mammography compared with those receiving mammography alone in 2 case-series studies.
Key Question 5. What are the harms of routine mammography screening, and how do they differ by age, risk factor, and screening interval?						
Analysis of BCSC data showed that younger women had more false-positives results; the cumulative risk for false-positive mammograms was 21% to 49% after 10 screens, and 56% for age 40-49; cumulative false-positive biopsy rate after 10 screens was 19%. Many women have anxiety and pain with mammography, but it is generally transient and not a deterrent. Estimates of overdiagnosis ranged from 0% to 50% in a review and 8 studies.	Analysis of BCSC data; 3 observational studies of cumulative false positive results; 4 systematic reviews and 10 studies of anxiety; 3 reviews of pain; 1 meta-analysis, 2 reviews, and 27 studies of overdiagnosis; 2 modeling studies of radiation exposure	Poor (radiation) to good (false-positive results)	Limitations vary by outcome; lack of studies for some outcomes (radiation); methodological diversity of studies (overdiagnosis); lack of RCTs; comparability of groups vary in observational studies.	Consistent in general	High clinical relevance.	• Younger women and those with risk factors had more false-positives results, and recommendations for additional imaging and biopsies. • 10-year cumulative rates of false-positive mammography and biopsy results were higher for annual than biennial screening (mammography 61% vs. 41%; biopsy 7% vs. 5%); for women with heterogeneously dense or extremely dense breasts, women in their 40s, and those who used combination hormone therapy. • Women with false-positive results were more distressed than women with negative results, and some women did not return for screening. • Estimates of overdiagnosis based on trials ranged from 11% to 22%; estimates from other studies ranged from 0% to 54%. • Deaths due to radiation induced cancer from screening with digital mammography was estimated through modeling as between 2 to 11 per 100,000 depending on age at onset and screening intervals.

Table 28. Summary of Evidence: Screening for Breast Cancer

Main findings from previous USPSTF reviews	Number/type of studies in update	Overall quality*	Limitations	Consistency	Applicability	Summary of findings
Key Question 6. How do the harms of routine breast cancer screening vary by different screening modality?						
Not included.	6 observational studies	Poor	No RCTs; single studies; comparability of groups not known.	Lack of studies to access consistency	High clinical relevance	Tomosynthesis with mammography reduced recalls, but increased biopsies.

Abbreviations: BCSC= Breast Cancer Surveillance Consortium; CBE=clinical breast exam; CI=confidence interval; CrI=credible interval; NA=not applicable; RCT=randomized controlled trial; RR=relative risk; U.S.=United States; USPSTF=United States Preventive Services Task Force.

Table 29. Summary of Results: Benefits and Harms of Mammography Screening

Benefits of Mammography Screening

Age, years	Reduction in breast cancer deaths from RCTs; RR (95% CI)*	Breast cancer deaths prevented per 10,000 over 10 years (95% CI)*	Reduction in breast cancer deaths from observational studies; RR (95% CI)	Reduction in all-cause deaths from RCTs; RR (95% CI)*	Reduction in advanced breast cancer from RCTs; RR (95% CI)	Reduction in treatment morbidity from RCTs; RR (95% CI)†
40-49	0.88 (0.73 to 1.003) 0.84 (0.70 to 1.002)	4 (0 to 9)	0.74 (0.66 to 0.83); 0.56 (0.45 to 0.67)‡	0.99 (0.94 to 1.06)	0.98 (0.74 to 1.37)	Screening results in more mastectomies 1.20 (1.11 to 1.30) and radiation 1.32 (1.16 to 1.50); the majority of cases from screening are DCIS and early stage.
50-59	0.86 (0.68 to 0.97) 0.86 (0.69 to 1.007)	5 to 8 (0 to 17)		1.02 (0.94 to 1.10)		
60-69	0.67 (0.54 to 0.83) 0.67 (0.55 to 0.91)	12 to 21 (3 to 32)		0.97 (0.90 to 1.04)		
70-74	0.80 (0.51 to 1.28) 0.90 (0.46 to 1.78)	12 to 13 (0 to 32)		0.98 (0.86 to 1.14)		
50-69	0.78 (0.68 to 0.90) 0.81 (0.69 to 0.95)	6 to 13 (1 to 20)	0.75 (0.69 to 0.81)§ 0.69 (0.57 to 0.83)‖		0.62 (0.46 to 0.83)	

*From meta-analyses of screening trials using two different methods of case accrual; long case accrual results are provided first, then short case accrual results.
†Based on trials of screening included in the meta-analysis.
‡Based on a study in Sweden, and a study in Canada (standardized mortality ratio), respectively.
§Based on seven incidence-based mortality studies.
‖Based on eight case-control studies.

Abbreviations: CI=confidence interval; RR=relative risk.

Harms of Mammography Screening

Age, years	False-positive mammography*	Additional imaging recommended*	Biopsy recommended*	10-yr FP mammography rates (annual; biennial)	10-yr FP biopsy rates (annual; biennial)	Overdiagnosis estimates from RCTs % (95% CI)†	Overdiagnosis estimates from screening programs‡	Radiation exposure
40-49	121.2	124.9	16.4	61%; 42%	7%; 5%	10.7 (9.3 to 12.2) 19.0 (15.2 to 22.7)	0 to 54% unadjusted 1 to 10% adjusted	Annual screening 40-55 years, biennial to 74 years: 86 cases, 11 deaths§
50-59	93.2	98.5	15.9	61%; 42%	9%; 6%			
60-69	80.8	88.7	16.5					
70-74	69.6	79.0	17.5					

*Number per 1,000 screened per screening round.
†From meta-analysis of screening trials using two different methods of case accrual; long case accrual results are provided first, then short case accrual results.
‡From EUROSCREEN review based on 13 studies overall and 6 studies adjusted for breast cancer risk and lead time.
§From a model of digital mammography.

Abbreviations: CI=confidence interval; FP=false positive.

Appendix A1. Search Strategies

Database: Ovid MEDLINE(R) without Revisions
Search Strategy:
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1 exp mammography/
2 exp physical examination/
3 exp magnetic resonance imaging/
4 exp ultrasonography/
5 exp mass screening/
6 ((clinical or physical$ or manual$ or routin$ or (regular$ adj2 schedul$)) adj5 (breast$ adj2 exam$)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
7 2 or 3 or 4 or 5 or 6
8 exp breast/
9 exp breast diseases/di, ra, us, pa, ep, mo
10 8 or 9
11 7 and 10
12 1 or 11
13 exp Mortality/
14 exp death/
15 exp survival analysis/
16 exp survivors/
17 mo.fs.
18 exp life tables/
19 exp life expectancy/
20 13 or 14 or 15 or 16 or 17 or 18 or 19
21 12 and 20
22 ((III$ or IV$ or advanc$ or late) adj5 stag$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
23 (tnm adj7 (t3 or t4 or n1 or n2 or n3 or n4 or n5 or n6 or m1)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
24 ((cancer$ or tumor$ or tumour$ or malig$ or adenocarcin$ or nepolas$) adj5 (advanc$ or spread$ or infiltrat$ or metasta$)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
25 22 or 23 or 24
26 12 and 25
27 exp "Outcome Assessment (Health Care)"/

28 12 and 27
29 exp incidence/
30 12 and 29
31 exp Neoplasm Metastasis/
32 exp neoplasm staging/
33 exp neoplasm grading/
34 31 or 32 or 33
35 12 and 34
36 26 or 28 or 30 or 35
37 exp Breast Neoplasms/
38 36 and 37
39 exp Mammography/ae, ct [Adverse Effects, Contraindications]
40 exp Physical Examination/ae, ct
41 exp Mass Screening/ae, ct [Adverse Effects, Contraindications]
42 40 or 41
43 10 and 42
44 13 or 43
45 exp Diagnostic Errors/
46 (overtest$ or overdiagnos$ or over-test$ or over-diagnos$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
47 misdiagnos$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
48 (false$ adj (positiv$ or negativ$)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
49 ((incorrect$ or false$ or wrong$ or bias$ or mistake$ or error$ or erroneous$) adj3 (result$ or finding$ or outcome$ or test$ or diagnos$)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
50 ((inappropriat$ or unnecess$ or unneed$) adj3 (treat$ or surg$ or therap$ or procedur$ or biops$ or interven$ or regimen$)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
51 (observ$ adj3 bias$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
52 iatrogen$.mp.
53 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52

54 12 and 53
55 exp "Wounds and Injuries"/ci, et [Chemically Induced, Etiology]
56 exp Stress, Psychological/
57 exp Prejudice/
58 exp Stereotyping/
59 55 or 56 or 57 or 58
60 12 and 59
61 44 or 54 or 60
62 exp "sensitivity and specificity"/
63 12 and 62
64 exp *Breast Neoplasms/di, pa, ra, us
65 63and 64

Databases: EBM Reviews - Cochrane Central Register of Controlled Trials, Database of Abstracts Reviews of Effects, Health Technology Assessment, and NHS Economic Evaluation Database
Search Strategy:
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1 (mammogra$ or magnetic resonance imag$ or mri or ultrasound$ or ultrasonog$ or screen$ or ((clinical or physical$ or manual$ or routin$ or (regular$ adj2 schedul$)) adj5 exam$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
2 ((Breast$ or mammar$) adj5 (cancer$ or tumor$ or tumour$ or neoplas$ or carcino$ or adenocarcino$ or malig$ or metasta$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
3 (Mortal$ or death$ or dead or dying or die or dies or died or surviv$ or life table$ or life expectanc$).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
4 1 and 2 and 3
5 ((III$ or IV$ or advanc$ or late) adj5 stag$).mp.
6 (tnm adj7 (t3 or t4 or n1 or n2 or n3 or n4 or n5 or n6 or m1)).mp.
7 ((cancer$ or tumor$ or tumour$ or malig$ or adenocarcin$ or nepolas$) adj5 (advanc$ or spread$ or infiltrat$ or metasta$)).mp.
8 ((cancer$ or Neoplas$ or tumor$ or tumour$ or malig$ or carcino$) adj5 (Metasta or staging$ or stage or stages or grading or grades or graded or grade)).mp.
9 ((outcome$ or ((treat$ or therap$) adj3 result$)) adj5 (evaluat$ or compar$ or assess$)).mp.
10 5 or 6 or 7 or 8
11 1 and 2 and 10
12 1 and 2 and 9
13 (overtest$ or overdiagnos$ or over-test$ or over-diagnos$ or overtreat$ or over-treat$).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
14 misdiagnos$.mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]

15 (false$ adj (positiv$ or negativ$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
16 ((incorrect$ or false$ or wrong$ or bias$ or mistake$ or error$ or erroneous$) adj3 (result$ or finding$ or outcome$ or test$ or diagnos$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
17 ((inappropriat$ or unnecess$ or unneed$) adj3 (treat$ or surg$ or therap$ or procedur$ or biops$ or interven$ or regimen$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
18 (observ$ adj3 bias$).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
19 iatrogen$.mp.
20 (diagnos$ adj5 (erroneous$ or error$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
21 ((anguish$ or (emotion$ or psych$ or mental$ or physical$ or social$ or socio$)) adj5 (stress$ or tension$ or pain$ or fear$ or undesir$ or unwant$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
22 (harm$ or advers$).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
23 (prejudic$ or stereotyp$ or stigma$ or unfair$).mp.
24 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25 1 and 2 and 24
26 (((((test$ or diagnos$ or screen$) adj3 (sensitiv$ and Specific)) or (fals$ adj3 (positiv$ or negativ$)) or ((type I or type II) adj5 error$) or (Predict$ or prognos$)) adj5 (Value$ or valid$ or accura$ or correct$)) or (ROC adj2 Curv$) or (Signal adj Noise adj3 Ratio$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
27 1 and 2 and 26

Database: EBM Reviews - Cochrane Database of Systematic Reviews
Search Strategy:
---
1 (mammogra$ or magnetic resonance imag$ or mri or ultrasound$ or ultrasonog$ or screen$ or ((clinical or physical$ or manual$ or routin$ or (regular$ adj2 schedul$)) adj5 exam$)).mp. [mp=title, abstract, full text, keywords, caption text]
2 ((Breast$ or mammar$) adj5 (cancer$ or tumor$ or tumour$ or neoplas$ or carcino$ or adenocarcino$ or malig$ or metasta$)).mp. [mp=title, abstract, full text, keywords, caption text]
3 (Mortal$ or death$ or dead or dying or die or dies or died or surviv$ or life table$ or life expectanc$).mp. [mp=title, abstract, full text, keywords, caption text]
4 1 and 2 and 3
5 ((Breast$ or mammar$) adj5 (cancer$ or tumor$ or tumour$ or neoplas$ or carcino$ or adenocarcino$ or malig$ or metasta$) adj15 (Mortal$ or death$ or dead or dying or die or dies or

died or surviv$ or life table$ or life expectanc$)).mp. [mp=title, short title, abstract, full text, keywords, caption text]
6 1 and 5
7 ((mammogra$ or magnetic resonance imag$ or mri or ultrasound$ or ultrasonog$ or screen$ or ((clinical or physical$ or manual$ or routin$ or (regular$ adj2 schedul$)) adj5 exam$)) adj15 (Mortal$ or death$ or dead or dying or die or dies or died or surviv$ or life table$ or life expectanc$)).mp. [mp=title, short title, abstract, full text, keywords, caption text] (387)
8 2 and 7
9 6 or 8
10 ((mammogra$ or magnetic resonance imag$ or mri or ultrasound$ or ultrasonog$ or screen$ or ((clinical or physical$ or manual$ or routin$ or (regular$ adj2 schedul$)) adj5 exam$)) adj10 ((Breast$ or mammar$) adj5 (cancer$ or tumor$ or tumour$ or neoplas$ or carcino$ or adenocarcino$ or malig$ or metasta$))).mp. [mp=title, short title, abstract, full text, keywords, caption text]
11 3 and 10
12 6 or 9 or 11
13 ((III$ or IV$ or advanc$ or late) adj5 stag$).mp.
14 (tnm adj7 (t3 or t4 or n1 or n2 or n3 or n4 or n5 or n6 or m1)).mp.
15 ((cancer$ or tumor$ or tumour$ or malig$ or adenocarcin$ or nepolas$) adj5 (advanc$ or spread$ or infiltrat$ or metasta$)).mp.
16 ((cancer$ or Neoplas$ or tumor$ or tumour$ or malig$ or carcino$) adj5 (Metasta or staging$ or stage or stages or grading or grades or graded or grade)).mp. (502)
17 ((outcome$ or ((treat$ or therap$) adj3 result$)) adj5 (evaluat$ or compar$ or assess$)).mp.
18 13 or 14 or 15 or 16
19 1 and 2 and 18
20 1 and 2 and 17
21 (overtest$ or overdiagnos$ or over-test$ or over-diagnos$ or overtreat$ or over-treat$).mp. [mp=title, abstract, full text, keywords, caption text]
22 misdiagnos$.mp. [mp=title, abstract, full text, keywords, caption text]
23 (false$ adj (positiv$ or negativ$)).mp. [mp=title, abstract, full text, keywords, caption text]
24 ((incorrect$ or false$ or wrong$ or bias$ or mistake$ or error$ or erroneous$) adj3 (result$ or finding$ or outcome$ or test$ or diagnos$)).mp. [mp=title, abstract, full text, keywords, caption text]
25 ((inappropriat$ or unnecess$ or unneed$) adj3 (treat$ or surg$ or therap$ or procedur$ or biops$ or interven$ or regimen$)).mp. [mp=title, abstract, full text, keywords, caption text]
26 (observ$ adj3 bias$).mp. [mp=title, abstract, full text, keywords, caption text]
27 iatrogen$.mp.
28 (diagnos$ adj5 (erroneous$ or error$)).mp. [mp=title, abstract, full text, keywords, caption text]

29 ((anguish$ or (emotion$ or psych$ or mental$ or physical$ or social$ or socio$)) adj5 (stress$ or tension$ or pain$ or fear$ or undesir$ or unwant$)).mp. [mp=title, abstract, full text, keywords, caption text]
30 (harm$ or advers$).mp. [mp=title, abstract, full text, keywords, caption text]
31 (prejudic$ or stereotyp$ or stigma$ or unfair$).mp.
32 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
33 1 and 2 and 32
34 (((((test$ or diagnos$ or screen$) adj3 (sensitiv$ and Specific)) or (fals$ adj3 (positiv$ or negativ$)) or ((type I or type II) adj5 error$) or (Predict$ or prognos$)) adj5 (Value$ or valid$ or accura$ or correct$)) or (ROC adj2 Curv$) or (Signal adj Noise adj3 Ratio$)).mp. [mp=title, abstract, full text, keywords, caption text]
35 1 and 2 and 34

Appendix A2. Inclusion and Exclusion Criteria

	Include	Exclude
Population	**KQs 1–6:** Women age ≥40 years.	Men, women age <40 years, women with pre-existing breast cancer; clinically significant BRCA mutations, Li-Fraumeni syndrome, Cowden syndrome, hereditary diffuse gastric cancer, or other familial breast cancer syndromes; high-risk breast lesions (DCIS, LCIS, ADH, ALH); or previous large doses of chest radiation (≥20 Gy) before age 30.
Intervention	**KQs 1, 2, 5:** Screening mammography (all methods, i.e., film, digital, tomosynthesis). **KQs 3, 4, 6:** Screening mammography (all methods) combined with other modality; other screening modality (i.e., MRI, ultrasound).	**KQs 1, 2, 5:** Mammography for diagnosis or surveillance **KQs 3, 4, 6:** Breast imaging or examinations for diagnosis or surveillance
Comparisons	**KQs 1, 2, 5:** Mammography in women ages 40–49 vs. 50–59 vs. 60–69 vs. 70–79 years (or other age comparisons); annual mammography vs. biennial vs. triennial vs. alternate intervals vs. none; presence of risk factor vs. none (e.g., family history, extremely dense breast tissue). **KQs 3, 4, 6:** Mammography (all types, i.e., film, digital, tomosynthesis) vs. other modality vs. mammography (all types) combined with other modality, including MRI and ultrasound; interval and age differences by modality.	**KQs 1, 2, 5:** Data not provided by age, interval, or risk factor **KQs 3, 4, 6:** Data not provided by modality, age, or interval
Outcomes: Benefits	**Final health outcomes:** Reduced breast cancer mortality and all-cause mortality. **Intermediate outcomes:** Reduced incidence of advanced breast cancer and treatment-related morbidity (i.e., physical adverse effects of treatment, quality of life measures, and other measures of impairment).	Outcomes not listed as included
Outcomes: Harms	False-positive findings; anxiety; adverse impact on quality of life; false-positive biopsy; false-negative findings; false reassurance; overdiagnosis; overtreatment; radiation exposure.	Outcomes not listed as included
Timing	Immediate, short-term, and long-term outcomes; duration of followup.	No followup
Setting	Settings and populations of women applicable to U.S. primary care practice.	Settings not applicable to U.S. primary care practice
Study Design	**Effectiveness:** RCTs; prospective and retrospective cohort studies. **Harms:** RCTs, prospective and retrospective cohort studies, case-control studies, cross-sectional studies, systematic reviews, meta-analyses, and modeling studies; others considered.	Case reports, case series; studies outside of search dates unless updates of previous trials
Language	English-language abstracts (includes English-language abstracts of non English-language papers) and papers.	Non English-language papers
Contextual Question 1	U.S. rates of specific adverse effects of current treatment regimens for invasive breast cancer and DCIS from published sources and databases, obtained using a best evidence approach.	Non U.S. rates, older regimens (see search dates)

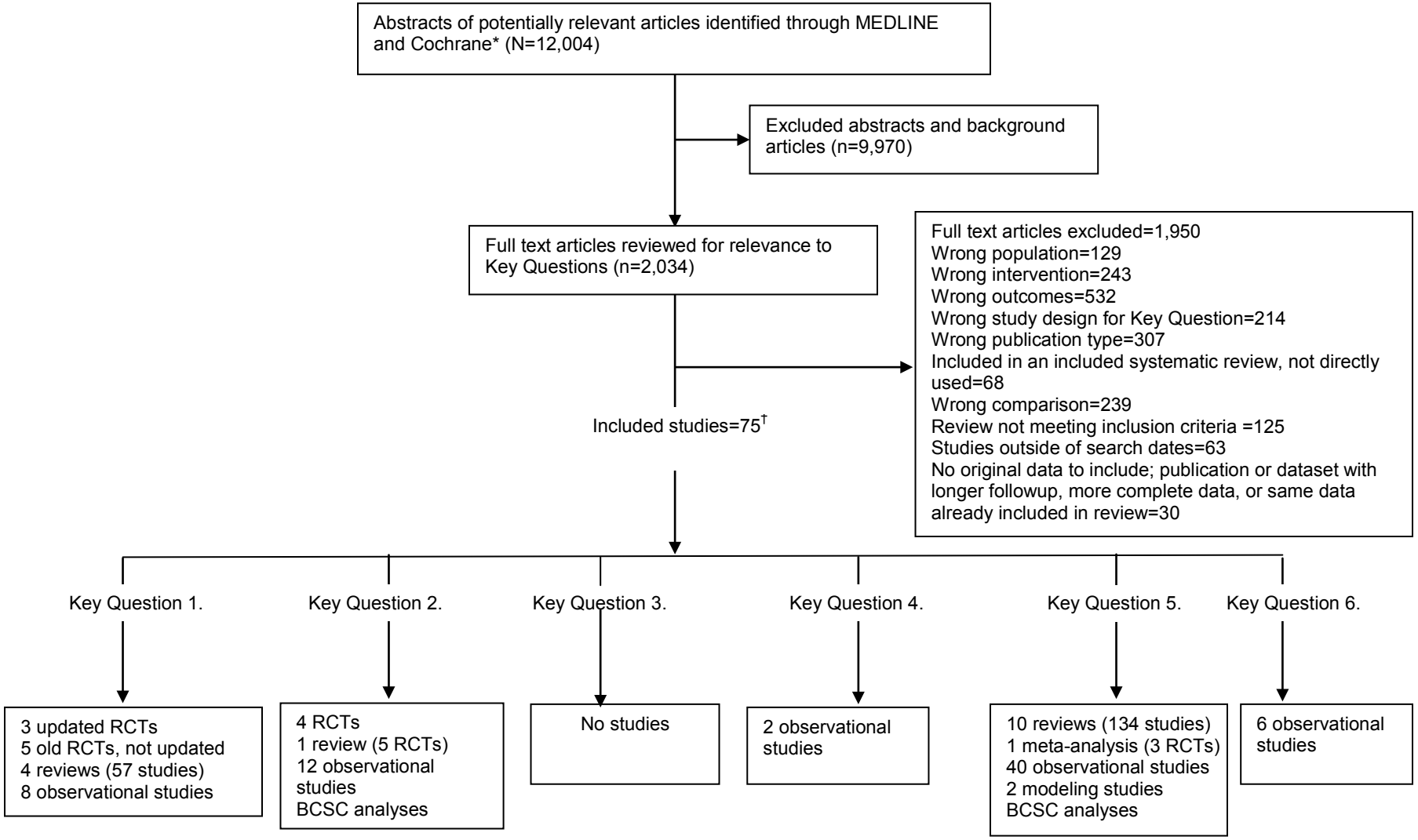
Appendix A2. Inclusion and Exclusion Criteria

	Include	Exclude
Contextual Question 2	Absolute incidence rates of DCIS and localized and advanced invasive breast cancer in screened and nonscreened populations in the United States from published sources and databases, obtained using a best evidence approach.	Non U.S. rates, older estimates (see search dates)
Contextual Question 3	Descriptive papers of how women's perceptions of the benefits and harms of breast cancer screening affect their clinical decision-making regarding breast cancer screening in the United States.	Studies of women in other countries; older studies (see search dates)
Data Sources	Ovid MEDLINE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Breast Cancer Surveillance Consortium database.	Sources not listed as included
Search Dates*	**Effectiveness key questions included in the previous report (KQs 1 & 3):** RCTs published between 2008 and February 2014 and updates of earlier trials. Cohort studies published between 1996 and February 2014. **Effectiveness Key Questions not included in the previous report (KQ 2 & 4):** RCTs and cohort studies published between 1996 and February 2014. **Harms (KQs 5, 6):** Studies published between 2008 and February 2014 and updates of earlier studies. **Contextual questions (1–3):** Studies published between 2010 and February 2014.	Studies published outside of the specified search dates that were not included in previous USPSTF systematic reviews.

*Search dates vary because some key questions (KQs 1, 3, 5, 6) were included in the previous systematic review and require only an update of studies published since the previous search in 2008. Other key questions were not addressed by the previous review and require a search that covers a longer time period (KQ 2 & 4, and cohort studies for KQ 1 & 3). These searches extend to 1996 because this corresponds to the last time the USPSTF evaluated similar data and represents a period when practice was shifting to digital mammography in the United States. The contextual questions have a shorter time period for searches because they require current data.

Abbreviations: ADH=atypical ductal hyperplasia; ALH=atypical lobular hyperplasia; BRCA=breast cancer susceptibility gene; DCIS=ductal carcinoma in situ; Gy=gray (unit of absorbed radiation dose [1 Gy=100 rads]); KQ=key question; LCIS=lobular carcinoma in situ; MRI=magnetic resonance imaging; RCT=randomized, controlled trial; U.S.=United States; USPSTF=U.S. Preventive Services Task Force; vs.=versus.

Appendix A3. Literature Flow by Key Question



*Cochrane databases include the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews.
†Publications were used for multiple key questions; trials reported data in multiple publications; 84 publications were included.

Abbreviations: BCSC=Breast Cancer Surveillance Consortium; n=sample size; RCT=randomized controlled trial.

Appendix A4. List of Excluded Studies

3D mammography shows promise as next breast screening technique. Oncology. 2003;17(6):814, 900.
Exclusion: wrong publication type.

16-year mortality from breast cancer in the UK Trial of Early Detection of Breast Cancer. Lancet. 1999;353(9168):1909-14.
Exclusion: studies outside of search dates.

Advances in breast imaging. Although mammography remains standard for breast cancer screening, several newer technologies are helping to fine-tune diagnosis. Harv Womens Health Watch. 2010;17(9):1-3.
Exclusion: wrong publication type.

Breast carcinoma stage in relation to time interval since last mammography: a registry-based study. The Romagna Cancer Registry and Collaborators. Cancer. 1997;80(8):1432-7.
Exclusion: wrong intervention.

Breast MRI for detection or diagnosis of primary or recurrent breast cancer. Technol Eval Cent Asses Program Exec Summ. 2004;Executive Summary. 19(1):1-9.
Exclusion: review not meeting inclusion criteria.

Breast-cancer screening with mammography in women aged 40-49 years. Swedish Cancer Society and the Swedish National Board of Health and Welfare. Int J Cancer. 1996;68(6):693-9.
Exclusion: wrong publication type.

Computer-aided detection of malignancy with magnetic resonance imaging of the breast. Technol Eval Cent Asses Program Exec Summ. 2006;Executive Summary. 21(4):1-3.
Exclusion: wrong study design for key question.

Computer-aided detection with full-field digital mammography. Technol Eval Cent Asses Program Exec Summ. 2006;Executive Summary. 21(3):1-3.
Exclusion: review not meeting inclusion criteria.

Full-field digital mammography. Technol Eval Cent Asses Program Exec Summ. 2006;Executive Summary. 20(16):1-3.
Exclusion: wrong comparison.

Magnetic resonance imaging of the breast: differential diagnosis of a breast lesion to avoid biopsy. Tecnologica MAP Suppl. 2001:30-2.
Exclusion: wrong outcomes.

Mammograms for older women. Health News. 2000;6(12):7.
Exclusion: wrong publication type.

Mammographic screening for breast cancer: few new data. Prescrire Int. 2008;17(93):24-7.
Exclusion: wrong publication type.

Mammography benefits appear to have no age limit. Mayo Clin Womens Healthsource. 2008;12(11):3.
Exclusion: wrong publication type.

The Million Women Study: design and characteristics of the study population. The Million Women Study Collaborative Group. Breast Cancer Res. 1999;1(1):73-80.
Exclusion: wrong publication type.

Obesity increases risk of death from breast cancer. Clin J Oncol Nurs. 2002;6(3):125.
Exclusion: wrong publication type.

Screening mammography. Prescrire Int. 2006;15(85):192-3.
Exclusion: wrong publication type.

Summaries for patients. Does use of screening mammography explain racial and ethnic differences in death from breast cancer?.[Original report in Ann Intern Med. 2006 Apr 18;144(8):541-53; PMID: 16618951]. Ann Intern Med. 2006;144(8):I18.
Exclusion: wrong publication type.

Summaries for patients. Mammograms in women age 40 to 49: results of the Canadian Breast Cancer Screening study.[Original report in Ann Intern Med. 2002 Sep 3;137(5 Part 1):305-12; PMID: 12204013]. Ann Intern Med. 2002;137(5 Part 1):I28.
Exclusion: wrong publication type.

Summaries for patients. Screening for breast cancer: recommendations from the U.S. Preventive Services Task Force.[Original report in Ann Intern Med. 2002 Sep 3;137(5 Part 1):347-60; PMID: 12204020]. Ann Intern Med. 2002;137(5 Part 1):I47.
Exclusion: wrong publication type.

Summaries for patients. Screening for breast cancer: U.S. Preventive Services Task Force recommendations.[Original report in Ann Intern Med. 2009 Nov 17;151(10):716-26, W-236; PMID: 19920272]. Ann Intern Med. 2009;151(10):I44.
Exclusion: wrong publication type.

Appendix A4. List of Excluded Studies

Summaries for patients: the accuracy of film versus digital screening mammography.[Original report in Ann Intern Med. 2011 Oct 18;155(8):493-502; PMID: 22007043]. Ann Intern Med. 2011;155(8):I30.
Exclusion: wrong publication type.

Summaries for patients: the benefits and harms of more and less frequent screening mammography.[Original report in Ann Intern Med. 2011 Oct 18;155(8):481-92; PMID: 22007042]. Ann Intern Med. 2011;155(8):I14.
Exclusion: wrong publication type.

Abbey CK, Eckstein MP, Boone JM. An equivalent relative utility metric for evaluating screening mammography. Med Decis Making. 2010;30(1):113-22.
Exclusion: wrong outcomes.

Abdolell M, Tsuruda K, Schaller G, et al. Statistical evaluation of a fully automated mammographic breast density algorithm. Comput Math Methods Med. 2013;2013:651091.
Exclusion: wrong outcomes.

Abdullah N, Mesurolle B, El-Khoury M, et al. Breast imaging reporting and data system lexicon for US: interobserver agreement for assessment of breast masses. Radiology. 2009;252(3):665-72.
Exclusion: wrong outcomes.

Abraham L, Geller BM, Yankaskas BC, et al. Accuracy of self-reported breast cancer among women undergoing mammography. Breast Cancer Res Treat. 2009;118(3):583-92.
Exclusion: wrong outcomes.

Absetz P, Aro AR, Sutton SR. Experience with breast cancer, pre-screening perceived susceptibility and the psychological impact of screening. Psychooncology. 2003;12(4):305-18.
Exclusion: included in an included systematic review, not directly used.

Achat H, Close G, Taylor R. Who has regular mammograms? Effects of knowledge, beliefs, socioeconomic status, and health-related factors. Prev Med. 2005;41(1):312-20.
Exclusion: wrong outcomes.

Agliozzo S, De Luca M, Bracco C, et al. Computer-aided diagnosis for dynamic contrast-enhanced breast MRI of mass-like lesions using a multiparametric model combining a selection of morphological, kinetic, and spatiotemporal features. Med Phys. 2012;39(4):1704-15.
Exclusion: wrong outcomes.

Agner SC, Soman S, Libfeld E, et al. Textural kinetics: a novel dynamic contrast-enhanced (DCE)-MRI feature for breast lesion classification. J Digit Imaging. 2011;24(3):446-63.
Exclusion: wrong outcomes.

Aiken LS, Jackson KM. Mammography benefits for women under 50: a closer look at the controversy. Womens Health. 1996;2(4):235-42; discussion 61-6.
Exclusion: wrong publication type.

Akcil M, Karaagaoglu E, Demirhan B. Diagnostic accuracy of fine-needle aspiration cytology of palpable breast masses: an SROC curve with fixed and random effects linear meta-regression models. Diagn Cytopathol. 2008;36(5):303-10.
Exclusion: wrong outcomes.

Alcusky M, Philpotts L, Bonafede M, et al. The patient burden of screening mammography recall. J Womens Health (Larchmt). 2014;23 Suppl 1:S11-9.
Exclusion: wrong outcomes.

Al-Damegh SA. Emerging issues in medical imaging. Indian J Med Ethics. 2005;2(4):123-5.
Exclusion: wrong publication type.

Alexander FE. The Edinburgh Randomized Trial of Breast Cancer Screening. J Natl Cancer Inst. 1997;Monographs.(22):31-5.
Exclusion: studies outside of search dates.

Alexander FE, Anderson TJ, Brown HK, et al. 14 years of follow-up from the Edinburgh randomised trial of breast-cancer screening. Lancet. 1999;353(9168):1903-8.
Exclusion: studies outside of search dates.

Alexander FE, Anderson TJ, Hubbard AL. Screening status in relation to biological and chronological characteristics of breast cancers: a cross sectional survey. J Med Screen. 1997;4(3):152-7.
Exclusion: wrong study design for key question.

Appendix A4. List of Excluded Studies

Alexander FE, Brown HK, Prescott RJ. Improved classification of socio-economic status explains differences in all-cause mortality in a randomised trial of breast cancer screening. J Epidemiol Biostat. 1998;3(2):219-24.
Exclusion: wrong outcomes.

Al-Foheidi M, Al-Mansour MM, Ibrahim EM. Breast cancer screening: review of benefits and harms, and recommendations for developing and low-income countries. Med Oncol. 2013;30(2):471.
Exclusion: review not meeting inclusion criteria.

Alhabshi SMI, Rahmat K, Abdul Halim N, et al. Semi-quantitative and qualitative assessment of breast ultrasound elastography in differentiating between malignant and benign lesions. Ultrasound Med Biol. 2013;39(4):568-78.
Exclusion: wrong intervention.

Alimoglu E, Alimoglu MK, Ceken K, et al. Bi-RADS category 3 nonpalpable breast masses on sonography: long-term results of a prospective cohort study. J Clin Ultrasound. 2012;40(3):125-34.
Exclusion: wrong population.

Alimoglu E, Alimoglu MK, Kabaalioglu A, et al. [Mammography-related pain and anxiety]. Tani Girisim Radyol. 2004;10(3):213-7.
Exclusion: included in an included systematic review, not directly used.

Alimoglu E, Bayraktar SD, Bozkurt S, et al. Follow-up versus tissue diagnosis in BI-RADS category 3 solid breast lesions at US: A cost-consequence analysis. Diagn Interv Radiol. 2012;18(1):3-10.
Exclusion: wrong outcomes.

Allen MW, Hendi P, Schwimmer J, et al. Decision analysis for the cost effectiveness of sestamibi scintimammography in minimizing unnecessary biopsies. Q J Nucl Med. 2000;44(2):168-85.
Exclusion: wrong study design for key question.

Allgood PC, Duffy SW, Warren R, et al. Audit of negative assessments in a breast-screening programme in women who later develop breast cancer-implications for survival. Breast. 2006;15(4):503-9.
Exclusion: wrong outcomes.

Allgood PC, Warwick J, Warren RML, et al. A case-control study of the impact of the East Anglian breast screening programme on breast cancer mortality. Br J Cancer. 2008;98(1):206-9.
Exclusion: included in an included systematic review, not directly used.

Alsaker MDK, Janszky I, Opdahl S, et al. Weight change in adulthood and risk of postmenopausal breast cancer: the HUNT study of Norway. Br J Cancer. 2013;109(5):1310-7.
Exclusion: wrong outcomes.

Alto H. Geomatics for precise 3D breast imaging. Technol Cancer Res Treat. 2005;4(1):29-38.
Exclusion: wrong intervention.

American Cancer Society. Cancer facts and figures 2007. Available at: http://www.cancer.org/acs/groups/content/@nho/documents/document/caff2007pwsecuredpdf.pdf. Accessed September 19, 2014.
Exclusion: wrong comparison.

Amirikia KC, Mills P, Bush J, et al. Higher population-based incidence rates of triple-negative breast cancer among young African-American women : Implications for breast cancer screening recommendations. Cancer. 2011;117(12):2747-53.
Exclusion: wrong outcomes.

Andersen KG GR, Kroman N, Flyger H, Kehlet H. Persistent pain after targeted intraoperative radiotherapy (TARGIT) or external breast radiotherapy for breast cancer: A randomized trial. Breast. 2012;21(1):46-9.
Exclusion: wrong outcomes.

Andersen MR, Hager M, Su C, et al. Analysis of the cost-effectiveness of mammography promotion by volunteers in rural communities. Health Educ Behav. 2002;29(6):755-70.
Exclusion: wrong outcomes.

Andersen SB, Vejborg I, von Euler-Chelpin M. Participation behaviour following a false positive test in the Copenhagen mammography screening programme. Acta Oncol. 2008;47(4):550-5.
Exclusion: wrong outcomes.

Anderson E, Berg J, Black R, et al. Prospective surveillance of women with a family history of breast cancer: auditing the risk threshold. Br J Cancer. 2008;98(4):840-4.
Exclusion: wrong comparison.

Anderson WF, Jatoi I, Devesa SS. Assessing the impact of screening mammography: Breast cancer incidence and mortality rates in Connecticut (1943-2002). Breast Cancer Res Treat. 2006;99(3):333-40.

Appendix A4. List of Excluded Studies

Exclusion: wrong comparison.

Anderson WF, Matsuno RK, Sherman ME, et al. Estimating age-specific breast cancer risks: a descriptive tool to identify age interactions. Cancer Causes Control. 2007;18(4):439-47.
Exclusion: wrong study design for key question.

Anonymous. Digital mammography more sensitive for younger women. J Natl Med Assoc. 2006;98(1):101.
Exclusion: wrong outcomes.

Antonio ALM, Crespi CM. Predictors of interobserver agreement in breast imaging using the Breast Imaging Reporting and Data System. Breast Cancer Res Treat. 2010;120(3):539-46.
Exclusion: review not meeting inclusion criteria.

Anttila A, Koskela J, Hakama M. Programme sensitivity and effectiveness of mammography service screening in Helsinki, Finland. J Med Screen. 2002;9(4):153-8.
Exclusion: included in an included systematic review, not directly used.

Anttila A, Sarkeala T, Hakulinen T, et al. Impacts of the Finnish service screening programme on breast cancer rates. BMC Public Health. 2008;8:38.
Exclusion: wrong comparison.

Anttinen J, Kautiainen H, Kuopio T. Role of mammography screening as a predictor of survival in postmenopausal breast cancer patients. Br J Cancer. 2006;94(1):147-51.
Exclusion: wrong population.

Aro AR, Absetz-Ylöstalo P, Eerola T, et al. Pain and discomfort during mammography. European Journal of Cancer Part A. 1996;32(10):1674-9.
Exclusion: included in an included systematic review, not directly used.

Aro AR, Pilvikki Absetz S, van Elderen TM, et al. False-positive findings in mammography screening induces short-term distress - breast cancer-specific concern prevails longer. Eur J Cancer. 2000;36(9):1089-97.
Exclusion: studies outside of search dates.

Aro AR, Pilvikki Absetz S, Van Elderen TM, et al. False-positive findings in mammography screening induces short-term distress - Breast cancer-specific concern prevails longer. Eur J Cancer. 2000;36(9):1089-97.
Exclusion: included in an included systematic review, not directly used.

Arora N, Martins D, Ruggerio D, et al. Effectiveness of a noninvasive digital infrared thermal imaging system in the detection of breast cancer. Am J Surg. 2008;196(4):523-6.
Exclusion: wrong intervention.

Ascunce EN, Moreno-Iribas C, Barcos Urtiaga A, et al. Changes in breast cancer mortality in Navarre (Spain) after introduction of a screening programme. J Med Screen. 2007;14(1):14-20.
Exclusion: included in an included systematic review, not directly used.

Ascunce N, Ederra M, Delfrade J, et al. Impact of intermediate mammography assessment on the likelihood of false-positive results in breast cancer screening programmes. Eur Radiol. 2012;22(2):331-40.
Exclusion: wrong comparison.

Atkins CD. Potential hazards of mammography. J Clin Oncol. 2007;25(5):604; author reply 5.
Exclusion: wrong publication type.

Aubard Y, Genet D, Eyraud JL, et al. Impact of screening on breast cancer detection. Retrospective comparative study of two periods ten years apart. Eur J Gynaecol Oncol. 2002;23(1):37-41.
Exclusion: wrong comparison.

Austoker J. Breast self examination. BMJ. 2003;326(7379):1-2.
Exclusion: wrong intervention.

Autier P. Breast cancer screening. Eur J Cancer. 2011;47 Suppl 3:S133-46.
Exclusion: review not meeting inclusion criteria.

Autier P, Boniol M. The incidence of advanced breast cancer in the West Midlands, United Kingdom. Eur J Cancer Prev. 2012;21(3):217-21.
Exclusion: wrong study design for key question.

Autier P, Boniol M, Gavin A, et al. Breast cancer mortality in neighbouring European countries with different levels of screening but similar access to treatment: trend analysis of WHO mortality database. BMJ. 2011;343:d4411.
Exclusion: included in an included systematic review, not directly used.

Appendix A4. List of Excluded Studies

Autier P, Boniol M, Middleton R, et al. Advanced breast cancer incidence following population-based mammographic screening. Ann Oncol. 2011;22(8):1726-35.
Exclusion: review not meeting inclusion criteria.

Autier P, Koechlin A, Smans M, et al. Mammography screening and breast cancer mortality in Sweden. J Natl Cancer Inst. 2012;104(14):1080-93.
Exclusion: wrong study design for key question.

Autier P, Shannoun F, Scharpantgen A, et al. A breast cancer screening programme operating in a liberal health care system: the Luxembourg Mammography Programme, 1992-1997. Int J Cancer. 2002;97(6):828-32.
Exclusion: wrong publication type.

Avis NE, Smith KW, Link CL, et al. Increasing mammography screening among women over age 50 with a videotape intervention. Prev Med. 2004;39(3):498-506.
Exclusion: studies outside of search dates.

Ayer T, Chhatwal J, Alagoz O, et al. Informatics in radiology: comparison of logistic regression and artificial neural network models in breast cancer risk estimation. Radiographics. 2010;30(1):13-22.
Exclusion: wrong outcomes.

Ayoola A, Alagarsamy S, Jaboin J, et al. Increase in mastectomies performed in patients in the community setting undergoing MRI. Breast J. 2011;17(3):256-9.
Exclusion: wrong population.

Azavedo E, Zackrisson S, Mejare I, et al. Is single reading with computer-aided detection (CAD) as good as double reading in mammography screening? A systematic review. BMC Medical Imaging. 2012;12:22.
Exclusion: wrong outcomes.

Bae MS, Moon WK, Chang JM, et al. Breast cancer detected with screening US: reasons for nondetection at mammography. Radiology. 2014;270(2):369-77.
Exclusion: wrong outcomes.

Baeten SA, Baltussen RMPM, Uyl-de Groot CA, et al. Reducing disparities in breast cancer survival--the effect of large-scale screening of the uninsured. Breast J. 2011;17(5):548-9.
Exclusion: wrong publication type.

Bailar JC, 3rd, MacMahon B. Randomization in the Canadian National Breast Screening Study: a review for evidence of subversion. CMAJ. 1997;156(2):193-9.
Exclusion: wrong publication type.

Bailey SL, Sigal BM, Plevritis SK. A simulation model investigating the impact of tumor volume doubling time and mammographic tumor detectability on screening outcomes in women aged 40-49 years. J Natl Cancer Inst. 2010;102(16):1263-71.
Exclusion: wrong study design for key question.

Baines CJ. The mammography controversy: full steam ahead versus reasonable caution. AJR Am J Roentgenol. 2013;200(1):W96-7.
Exclusion: wrong publication type.

Baines CJ. Mammography screening: are women really giving informed consent? (Countering the counterpoint). J Natl Cancer Inst. 2003;95(20):1512-3.
Exclusion: wrong publication type.

Baines CJ. Mammography screening: are women really giving informed consent?.[Erratum appears in J Natl Cancer Inst. 2003 Nov 19;95(22):1728]. J Natl Cancer Inst. 2003;95(20):1508-11.
Exclusion: wrong publication type.

Baines CJ, McFarlane DV, Miller AB. The role of the reference radiologist; estimates of inter-observer agreement and potential delay in cancer detection in the national breast screening study. Invest Radiol. 1990;25(9):971-6.
Exclusion: wrong comparison.

Baines CJ, Miller AB. Mammography versus clinical examination of the breasts. J Natl Cancer Inst. 1997;Monographs.(22):125-9.
Exclusion: review not meeting inclusion criteria.

Baines CJ, Miller AB, Kopans DB, et al. Canadian National Breast Screening Study: assessment of technical quality by external review. AJR Am J Roentgenol. 1990;155(4):743-7; discussion 8-9.
Exclusion: wrong outcomes.

Baines CJ, Vidmar M, McKeown-Eyssen G, et al. Impact of menstrual phase on false-negative mammograms in the Canadian National Breast Screening Study. Cancer. 1997;80(4):720-4.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Appendix A4. List of Excluded Studies

Baker DR. Magnetic resonance imaging of occult breast cancer. Clin Breast Cancer. 2000;1(1):66-7.
Exclusion: wrong study design for key question.

Baker JA, Rosen EL, Crockett MM, et al. Accuracy of segmentation of a commercial computer-aided detection system for mammography. Radiology. 2005;235(2):385-90.
Exclusion: wrong outcomes.

Baker S, Wall M, Bloomfield A. Breast cancer screening for women aged 40 to 49 years--what does the evidence mean for New Zealand? N Z Med J. 2005;118(1221):U1628.
Exclusion: review not meeting inclusion criteria.

Baker S, Wall M, Bloomfield A. What is the most appropriate breast-cancer screening interval for women aged 45 to 49 years in New Zealand? N Z Med J. 2005;118(1221):U1636.
Exclusion: review not meeting inclusion criteria.

Baker SG. Modelling the cumulative risk of a false-positive screening test. Stat Methods Med Res. 2011;20(3):291-3; author reply 3-4.
Exclusion: wrong publication type.

Baker SG, Kramer BS, Prorok PC. Comparing breast cancer mortality rates before-and-after a change in availability of screening in different regions: extension of the paired availability design. BMC Med Res Methodol. 2004;4:12.
Exclusion: wrong study design for key question.

Bakic PR, Carton A-K, Kontos D, et al. Breast percent density: estimation on digital mammograms and central tomosynthesis projections. Radiology. 2009;252(1):40-9.
Exclusion: wrong outcomes.

Balducci L, Phillips DM. Breast cancer in older women. Am Fam Physician. 1998;58(5):1163-72.
Exclusion: review not meeting inclusion criteria.

Ballard-Barbash R, Klabunde C, Paci E, et al. Breast cancer screening in 21 countries: delivery of services, notification of results and outcomes ascertainment. Eur J Cancer Prev. 1999;8(5):417-26.
Exclusion: wrong outcomes.

Ballard-Barbash R, Taplin SH, Yankaskas BC, et al. Breast Cancer Surveillance Consortium: a national mammography screening and outcomes database. AJR Am J Roentgenol. 1997;169(4):1001-8.
Exclusion: wrong publication type.

Baltic S. Analysis of mammography trials renews debate on mortality reduction. J Natl Cancer Inst. 2001;93(22):1678-9.
Exclusion: wrong publication type.

Baltzer PAT, Freiberg C, Beger S, et al. Clinical MR-mammography: are computer-assisted methods superior to visual or manual measurements for curve type analysis? A systematic approach. Acad Radiol. 2009;16(9):1070-6.
Exclusion: wrong intervention.

Baltzer PAT, Renz DM, Kullnig PE, et al. Application of computer-aided diagnosis (CAD) in MR-mammography (MRM): do we really need whole lesion time curve distribution analysis? Acad Radiol. 2009;16(4):435-42.
Exclusion: wrong intervention.

Banik S, Rangayyan RM, Desautels JEL. Detection of architectural distortion in prior mammograms. IEEE Trans Med Imaging. 2011;30(2):279-94.
Exclusion: wrong outcomes.

Banks E. Hormone replacement therapy and the sensitivity and specificity of breast cancer screening: a review. J Med Screen. 2001;8(1):29-34.
Exclusion: review not meeting inclusion criteria.

Banks E, Reeves G, Beral V, et al. Predictors of outcome of mammography in the National Health Service Breast Screening Programme. J Med Screen. 2002;9(2):74-82.
Exclusion: wrong comparison.

Banks E, Reeves G, Beral V, et al. Hormone replacement therapy and false positive recall in the Million Women Study: patterns of use, hormonal constituents and consistency of effect. Breast Cancer Res. 2006;8(1):R8.
Exclusion: wrong outcomes.

Banning M. Perceptions of breast health awareness in Black British women. Eur J Oncol Nurs. 2011;15(2):173-7.
Exclusion: wrong outcomes.

Barchielli A, Federico M, De Lisi V, et al. In situ breast cancer: incidence trend and organised screening programmes in Italy. Eur J Cancer. 2005;41(7):1045-50.
Exclusion: wrong outcomes.

Appendix A4. List of Excluded Studies

Barchielli A, Paci E. Trends in breast cancer mortality, incidence, and survival, and mammographic screening in Tuscany, Italy. Cancer Causes Control. 2001;12(3):249-55.
Exclusion: included in an included systematic review, not directly used.

Barchielli A, Paci E, Giorgi D. Recent trends of in situ carcinoma of the breast and mammographic screening in the Florence area, Italy. Cancer Causes Control. 1999;10(4):313-7.
Exclusion: wrong comparison.

Bare M, Sentis M, Galceran J, et al. Interval breast cancers in a community screening programme: frequency, radiological classification and prognostic factors. Eur J Cancer Prev. 2008;17(5):414-21.
Exclusion: wrong outcomes.

Barlow WE, Chi C, Carney PA, et al. Accuracy of screening mammography interpretation by characteristics of radiologists. J Natl Cancer Inst. 2004;96(24):1840-50.
Exclusion: wrong outcomes.

Barlow WE, White E, Ballard-Barbash R, et al. Prospective breast cancer risk prediction model for women undergoing screening mammography. J Natl Cancer Inst. 2006;98(17):1204-14.
Exclusion: wrong study design for key question.

Barnett JB. The relationship between obesity and breast cancer risk and mortality. Nutr Rev. 2003;61(2):73-6.
Exclusion: wrong study design for key question.

Barratt AL, Les Irwig M, Glasziou PP, et al. Benefits, harms and costs of screening mammography in women 70 years and over: a systematic review. Med J Aust. 2002;176(6):266-71.
Exclusion: review not meeting inclusion criteria.

Barth RJ, Jr., Gibson GR, Carney PA, et al. Detection of breast cancer on screening mammography allows patients to be treated with less-toxic therapy. AJR Am J Roentgenol. 2005;184(1):324-9.
Exclusion: wrong outcomes.

Barton MB, Elmore JG. Pointing the way to informed medical decision making: test characteristics of clinical breast examination. J Natl Cancer Inst. 2009;101(18):1223-5.
Exclusion: wrong publication type.

Barton MB, Harris R, Fletcher SW. The rational clinical examination. Does this patient have breast cancer? The screening clinical breast examination: should it be done? How? JAMA. 1999;282(13):1270-80.
Exclusion: wrong intervention.

Barton MB, Morley DS, Moore S, et al. Decreasing women's anxieties after abnormal mammograms: a controlled trial. J Natl Cancer Inst. 2004;96(7):529-38.
Exclusion: wrong outcomes.

Bassett L, Butler D. Mammography and early breast cancer detection. Am Fam Physician. 1991;43(2):547-57.
Exclusion: wrong publication type.

Bastardis-Zakas K, Iatrakis G, Navrozoglou I, et al. Maximizing the benefits of screening mammography for women 40-49 years old. Clin Exp Obstet Gynecol. 2010;37(4):278-82.
Exclusion: review not meeting inclusion criteria.

Baum M. Breast cancer screening comes full circle. J Natl Cancer Inst. 2004;96(20):1490-1.
Exclusion: wrong publication type.

Baydush AH, Catarious DM, Abbey CK, et al. Computer aided detection of masses in mammography using subregion Hotelling observers. Med Phys. 2003;30(7):1781-7.
Exclusion: wrong study design for key question.

Bazzocchi M, Mazzarella F, Del Frate C, et al. CAD systems for mammography: a real opportunity? A review of the literature. Radiol Med (Torino). 2007;112(3):329-53.
Exclusion: wrong study design for key question.

BCA BCA. Health is Not Just Healthcare: Inequities in Breast Cancer. 2013
Exclusion: wrong publication type.

Beam CA, Layde PM, Sullivan DC. Variability in the interpretation of screening mammograms by US radiologists. Findings from a national sample. Arch Intern Med. 1996;156(2):209-13.
Exclusion: wrong outcomes.

Becker N, Hakama M, Nyström L. Evaluation of effectiveness of quality-assured mammography screening in Germany: sample size considerations and design options. Eur J Cancer Prev. 2007;16(3):225-31.
Exclusion: wrong study design for key question.

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Beckett JR, Kotre CJ, Michaelson JS. Analysis of benefit:risk ratio and mortality reduction for the UK Breast Screening Programme. Br J Radiol. 2003;76(905):309-20.
Exclusion: wrong study design for key question.

Beckmann KR, Roder DM, Hiller JE, et al. Do breast cancer risk factors differ among those who do and do not undertake mammography screening? J Med Screen. 2013;20(4):208-19.
Exclusion: wrong outcomes.

Beemsterboer PM, Warmerdam PG, Boer R, et al. Radiation risk of mammography related to benefit in screening programmes: a favourable balance? J Med Screen. 1998;5(2):81-7.
Exclusion: studies outside of search dates.

Behjatnia B, Sim J, Bassett LW, et al. Does size matter? Comparison study between MRI, gross, and microscopic tumor sizes in breast cancer in lumpectomy specimens. Int J Clin Exp Pathol. 2010;3(3):303-9.
Exclusion: wrong intervention.

Benndorf M, Baltzer PAT, Vag T, et al. Breast MRI as an adjunct to mammography: Does it really suffer from low specificity? A retrospective analysis stratified by mammographic BI-RADS classes. Acta Radiol. 2010;51(7):715-21.
Exclusion: wrong outcomes.

Bennett IC, Muller J, Cockburn L, et al. Outcomes of multimodality breast screening for women at increased risk of familial breast cancer. World J Surg. 2010;34(5):979-86.
Exclusion: wrong population.

Bennett IC, Robert DA, Osborne JM, et al. Discomfort during mammography: A survey of women attending a breast screening center. Breast Dis. 1994;7(1):35-41.
Exclusion: included in an included systematic review, not directly used.

Bennett ML, Welman CJ, Celliers LM. How reassuring is a normal breast ultrasound in assessment of a screen-detected mammographic abnormality? A review of interval cancers after assessment that included ultrasound evaluation. Clin Radiol. 2011;66(10):928-39.
Exclusion: wrong outcomes.

Bennett RL, Blanks RG, Moss SM. Does the accuracy of single reading with CAD (computer-aided detection) compare with that of double reading?: A review of the literature. Clin Radiol. 2006;61(12):1023-8.
Exclusion: review not meeting inclusion criteria.

Bennett RL, Blanks RG, Patnick J, et al. Results from the UK NHS Breast Screening Programme 2000-05. J Med Screen. 2007;14(4):200-4.
Exclusion: wrong study design for key question.

Bennett RL, Evans AJ, Kutt E, et al. Pathological and mammographic prognostic factors for screen detected cancers in a multi-centre randomised, controlled trial of mammographic screening in women from age 40 to 48 years. Breast. 2011;20(6):525-8.
Exclusion: wrong comparison.

Bennett RL, Moss SM. Screening outcomes in women over age 70 who self-refer in the NHSBSP in England. J Med Screen. 2011;18(2):91-5.
Exclusion: wrong comparison.

Bennett RL, Sellars SJ, Blanks RG, et al. An observational study to evaluate the performance of units using two radiographers to read screening mammograms. Clin Radiol. 2012;67(2):114-21.
Exclusion: wrong outcomes.

Bennett RL, Sellars SJ, Moss SM. Interval cancers in the NHS breast cancer screening programme in England, Wales and Northern Ireland. Br J Cancer. 2011;104(4):571-7.
Exclusion: wrong outcomes.

Beral V, Alexander M, Duffy S, et al. The number of women who would need to be screened regularly by mammography to prevent one death from breast cancer. J Med Screen. 2011;18(4):210-2.
Exclusion: wrong publication type.
Beral V, Banks E, Reeves G, et al. Hormone replacement therapy and high incidence of breast cancer between mammographic screens. Lancet. 1997;349(9058):1103-4.
Exclusion: wrong publication type.

Berg AO. The mammography debate. Am Fam Physician. 2002;66(12):2211-2.
Exclusion: wrong publication type.

Berg AO. Mammography screening: are women really giving informed consent? (Counterpoint). J Natl Cancer Inst. 2003;95(20):1511-2; discussion 2-3.
Exclusion: wrong publication type.

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Berg WA. Supplemental screening sonography in dense breasts. Radiol Clin North Am. 2004;42(5):845-51, vi.
Exclusion: review not meeting inclusion criteria.

Berg WA, Blume JD, Cormack JB, et al. Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer.[Erratum appears in JAMA. 2010 Apr 21;303(15):1482]. JAMA. 2008;299(18):2151-63.
Exclusion: wrong population.

Berg WA, Mendelson EB. Technologist-performed handheld screening breast US imaging: how is it performed and what are the outcomes to date? Radiology. 2014;272(1):12-27.
Exclusion: wrong publication type.

Berg WA, Zhang Z, Lehrer D, et al. Detection of breast cancer with addition of annual screening ultrasound or a single screening MRI to mammography in women with elevated breast cancer risk. JAMA. 2012;307(13):1394-404.
Exclusion: wrong population.

Bernardi D, Caumo F, Macaskill P, et al. Effect of integrating 3D-mammography (digital breast tomosynthesis) with 2D-mammography on radiologists' true-positive and false-positive detection in a population breast screening trial. Eur J Cancer. 2014;50(7):1232-8.
Exclusion: wrong intervention.

Bernardi D, Ciatto S, Pellegrini M, et al. Prospective study of breast tomosynthesis as a triage to assessment in screening. Breast Cancer Res Treat. 2012;133(1):267-71.
Exclusion: wrong population.

Berrington de Gonzalez A. Estimates of the potential risk of radiation-related cancer from screening in the UK. J Med Screen. 2011;18(4):163-4.
Exclusion: wrong publication type.

Berrington de Gonzalez A, Reeves G. Mammographic screening before age 50 years in the UK: comparison of the radiation risks with the mortality benefits. Br J Cancer. 2005;93(5):590-6.
Exclusion: studies outside of search dates.

Berry DA. Benefits and risks of screening mammography for women in their forties: a statistical appraisal. J Natl Cancer Inst. 1998;90(19):1431-9.
Exclusion: wrong publication type.

Berry DA. The screening mammography paradox: better when found, perhaps better not to find. Br J Cancer. 2008;98(11):1729-30.
Exclusion: wrong publication type.

Berry DA, Cronin KA, Plevritis SK, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. N Engl J Med. 2005;353(17):1784-92.
Exclusion: wrong study design for key question.

Berry DA, Inoue L, Shen Y, et al. Modeling the impact of treatment and screening on U.S. breast cancer mortality: a Bayesian approach. J Natl Cancer Inst. 2006;Monographs.(36):30-6.
Exclusion: wrong study design for key question.

Bick U, Diekmann F. Digital mammography: what do we and what don't we know? Eur Radiol. 2007;17(8):1931-42.
Exclusion: wrong publication type.

Bick U, Engelken F, Diederichs G, et al. MRI of the breast as part of the assessment in population-based mammography screening. Fortschr Geb Rontgenstr Nuklearmed. 2013;185(9):849-56.
Exclusion: wrong outcomes.

Biesheuvel C, Barratt A, Howard K, et al. Effects of study methods and biases on estimates of invasive breast cancer overdetection with mammography screening: a systematic review. Lancet Oncol. 2007;8(12):1129-38.
Exclusion: review not meeting inclusion criteria.

Bijwaard H, Brenner A, Dekkers F, et al. Breast cancer risk from different mammography screening practices. Radiat Res. 2010;174(3):367-76.
Exclusion: wrong population.

Bitterman A, Bleicher RJ, Cabot MC, et al. Sentinel lymphadenectomy: a new alternative for managing early breast cancer. Isr Med Assoc J. 2002;4(10):803-9.
Exclusion: wrong publication type.

Black WC, Fletcher SW. Effects of estrogen on screening mammography: another complexity. J Natl Cancer Inst. 1996;88(10):627-8.
Exclusion: wrong publication type.

Black WC, Haggstrom DA, Welch HG. All-cause mortality in randomized trials of cancer screening. J Natl Cancer Inst. 2002;94(3):167-73.
Exclusion: review not meeting inclusion criteria.

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Blair S, McElroy M, Middleton MS, et al. The efficacy of breast MRI in predicting breast conservation therapy. J Surg Oncol. 2006;94(3):220-5.
Exclusion: wrong intervention.

Blamey RW, Wilson AR, Patnick J. ABC of breast diseases: screening for breast cancer. BMJ. 2000;321(7262):689-93.
Exclusion: review not meeting inclusion criteria.

Blanchard K, Colbert JA, Kopans DB, et al. Long-term risk of false-positive screening results and subsequent biopsy as a function of mammography use. Radiology. 2006;240(2):335-42.
Exclusion: studies outside of search dates.

Blanchard K, Colbert JA, Puri D, et al. Mammographic screening: patterns of use and estimated impact on breast carcinoma survival. Cancer. 2004;101(3):495-507.
Exclusion: wrong study design for key question.

Blanks RG, Bennett RL, Patnick J, et al. The effect of changing from one to two views at incident (subsequent) screens in the NHS breast screening programme in England: impact on cancer detection and recall rates. Clin Radiol. 2005;60(6):674-80.
Exclusion: wrong outcomes.

Blanks RG, Day NE, Moss SM. Monitoring the performance of breast screening programmes: use of indirect standardisation in evaluating the invasive cancer detection rate. J Med Screen. 1996;3(2):79-81.
Exclusion: wrong outcomes.

Blanks RG, Moss SM, McGahan CE, et al. Effect of NHS breast screening programme on mortality from breast cancer in England and Wales, 1990-8: comparison of observed with predicted mortality. BMJ. 2000;321(7262):665-9.
Exclusion: included in an included systematic review, not directly used.

Blanks RG, Moss SM, Patnick J. Results from the UK NHS breast screening programme 1994-1999. J Med Screen. 2000;7(4):195-8.
Exclusion: wrong comparison.

Bliss JM, Gray R. Breast cancer and hormone-replacement therapy: the Million Women Study. Lancet. 2003;362(9392):1328-9; author reply 30-1.
Exclusion: wrong publication type.

Bloom JR, Stewart SL, Hancock SL. Breast cancer screening in women surviving Hodgkin disease. Am J Clin Oncol. 2006;29(3):258-66.
Exclusion: wrong population.

Bluekens AMJ, Holland R, Karssemeijer N, et al. Comparison of digital screening mammography and screen-film mammography in the early detection of clinically relevant cancers: a multicenter study. Radiology. 2012;265(3):707-14.
Exclusion: wrong comparison.

Bluekens AMJ, Karssemeijer N, Beijerinck D, et al. Consequences of digital mammography in population-based breast cancer screening: initial changes and long-term impact on referral rates. Eur Radiol. 2010;20(9):2067-73.
Exclusion: wrong comparison.

Bobo JK, Lee NC, Thames SF. Findings from 752,081 clinical breast examinations reported to a national screening program from 1995 through 1998. J Natl Cancer Inst. 2000;92(12):971-6.
Exclusion: wrong outcomes.

Bock K, Borisch B, Cawson J, et al. Effect of population-based screening on breast cancer mortality.[Erratum appears in Lancet. 2013 Feb 16;381(9866):536]. Lancet. 2011;378(9805):1775-6.
Exclusion: wrong publication type.

Boer R, de Koning HJ, van der Maas PJ. A longer breast carcinoma screening interval for women age older than 65 years? Cancer. 1999;86(8):1506-10.
Exclusion: wrong study design for key question.

Boetes C, Veltman J, van Die L, et al. The role of MRI in invasive lobular carcinoma. Breast Cancer Res Treat. 2004;86(1):31-7.
Exclusion: wrong intervention.

Boggs DA, Rosenberg L, Pencina MJ, et al. Validation of a breast cancer risk prediction model developed for Black women. J Natl Cancer Inst. 2013;105(5):361-7.
Exclusion: wrong outcomes.

Bogner HR, Wittink MN. Depression as a risk factor for underuse of mammography. J Womens Health (Larchmt). 2004;13(6):739-42.
Exclusion: wrong publication type.

Bolivar AV, Gomez SS, Merino P, et al. Computer-aided detection system applied to full-field digital mammograms. Acta Radiol. 2010;51(10):1086-92.
Exclusion: wrong outcomes.

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Bondy ML, Newman LA. Assessing breast cancer risk: evolution of the Gail Model. J Natl Cancer Inst. 2006;98(17):1172-3.
Exclusion: wrong publication type.

Bonneux L. Mortality reduction by breast-cancer screening. Lancet. 2003;362(9379):245.
Exclusion: wrong publication type.

Boone JM, Lindfors KK, Seibert JA. Determining sensitivity of mammography from screening data, cancer incidence, and receiver-operating characteristic curve parameters. Med Decis Making. 2002;22(3):228-37.
Exclusion: wrong outcomes.

Borch KB, Lund E, Braaten T, et al. Physical activity and the risk of postmenopausal breast cancer - the Norwegian Women and Cancer Study. J Negat Results Biomed. 2014;13:3.
Exclusion: wrong outcomes.

Bordas P, Jonsson H, Nyström L, et al. Early breast cancer deaths in women aged 40-74 years diagnosed during the first 5 years of organised mammography service screening in north Sweden. Breast. 2004;13(4):276-83.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Bordas P, Jonsson H, Nyström L, et al. Interval cancer incidence and episode sensitivity in the Norrbotten Mammography Screening Programme, Sweden. J Med Screen. 2009;16(1):39-45.
Exclusion: wrong outcomes.

Bordoni A, Probst-Hensch NM, Mazzucchelli L, et al. Assessment of breast cancer opportunistic screening by clinical-pathological indicators: a population-based study. Br J Cancer. 2009;101(11):1925-31.
Exclusion: wrong outcomes.

Borrayo EA, Hines L, Byers T, et al. Characteristics associated with mammography screening among both Hispanic and non-Hispanic white women. J Womens Health (Larchmt). 2009;18(10):1585-894.
Exclusion: wrong outcomes.

Bourez RLJH, Rutgers EJT, Van De Velde CJH. Will we need lymph node dissection at all in the future? Clin Breast Cancer. 2002;3(5):315-22; discussion 23-5.
Exclusion: wrong outcomes.

Boyd NF, Jong RA, Yaffe MJ, et al. A critical appraisal of the Canadian National Breast Cancer Screening Study. Radiology. 1993;189(3):661-3.
Exclusion: wrong publication type.

Boyd NF, Melnichouk O, Martin LJ, et al. Mammographic density, response to hormones, and breast cancer risk. J Clin Oncol. 2011;29(22):2985-92.
Exclusion: wrong outcomes.

Boyer B, Balleyguier C, Granat O, et al. CAD in questions/answers Review of the literature. Eur J Radiol. 2009;69(1):24-33.
Exclusion: wrong publication type.

Bradley CJ, Given CW, Roberts C. Late stage cancers in a Medicaid-insured population. Med Care. 2003;41(6):722-8.
Exclusion: wrong population.

Braillon A, Bewley S. Lost opportunity to usefully examine French breast cancer screening mortality. Cancer epidemiol. 2011;35(3):306; author reply 7-8.
Exclusion: wrong publication type.

Braithwaite D, Zhu W, Hubbard RA, et al. Screening outcomes in older US women undergoing multiple mammograms in community practice: does interval, age, or comorbidity score affect tumor characteristics or false positive rates? J Natl Cancer Inst. 2013;105(5):334-41.
Exclusion: wrong comparison.

Brandt KR, Craig DA, Hoskins TL, et al. Can digital breast tomosynthesis replace conventional diagnostic mammography views for screening recalls without calcifications? A comparison study in a simulated clinical setting. AJR Am J Roentgenol. 2013;200(2):291-8.
Exclusion: wrong intervention.

Bredart A, Kop JL, Fall M, et al. Anxiety and specific distress in women at intermediate and high risk of breast cancer before and after surveillance by magnetic resonance imaging and mammography versus standard mammography. Psychooncology. 2012;21(11):1185-94.
Exclusion: wrong population.

Breen N, Yabroff KR, Meissner HI. What proportion of breast cancers are detected by mammography in the United States? Cancer Detect Prev. 2007;31(3):220-4.
Exclusion: wrong study design for key question.

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Brekelmans CT, Bartels CC, Crepin E, et al. Breast cancer screening in high-risk women. Rotterdam Committee of Medical and Genetic Counseling. Dis Markers. 1999;15(1-3):34-6.
Exclusion: wrong population.

Brekelmans CT, van Gorp JM, Peeters PH, et al. Histopathology and growth rate of interval breast carcinoma. Characterization of different subgroups. Cancer. 1996;78(6):1220-8.
Exclusion: wrong outcomes.

Brem RF, Baum J, Lechner M, et al. Improvement in sensitivity of screening mammography with computer-aided detection: a multiinstitutional trial. AJR Am J Roentgenol. 2003;181(3):687-93.
Exclusion: wrong outcomes.

Brem RF, Hoffmeister JW, Rapelyea JA, et al. Impact of breast density on computer-aided detection for breast cancer.[Erratum appears in AJR Am J Roentgenol. 2005 Jun;184(6):1968]. AJR Am J Roentgenol. 2005;184(2):439-44.
Exclusion: wrong outcomes.

Brem RF, Ioffe M, Rapelyea JA, et al. Invasive lobular carcinoma: detection with mammography, sonography, MRI, and breast-specific gamma imaging. AJR Am J Roentgenol. 2009;192(2):379-83.
Exclusion: wrong population.

Brenner DJ, Sawant SG, Hande MP, et al. Routine screening mammography: how important is the radiation-risk side of the benefit-risk equation? Int J Radiat Biol. 2002;78(12):1065-7.
Exclusion: wrong population.

Brenner RJ. False-negative mammograms. Medical, legal, and risk management implications. Radiol Clin North Am. 2000;38(4):741-57.
Exclusion: wrong publication type.

Brett J, Austoker J. Women who are recalled for further investigation for breast screening: Psychological consequences 3 years after recall and factors affecting re-attendance. J Public Health Med. 2001;23(4):292-300.
Exclusion: included in an included systematic review, not directly used.

Brett J, Austoker J. Women who are recalled for further investigation for breast screening: Psychological consequences 3 years after recall and factors affecting re-attendance. J Public Health Med. 2001;23(4):292-300.
Exclusion: included in an included systematic review, not directly used.

Brett J, Austoker J, Ong G. Do women who undergo further investigation for breast screening suffer adverse psychological consequences? A multi-centre follow-up study comparing different breast screening result groups five months after their last breast screening appointment. J Public Health Med. 1998;20(4):396-403.
Exclusion: studies outside of search dates.

Brett J, Austoker J, Ong G. Do women who undergo further investigation for breast screening suffer adverse psychological consequences? A multi-centre follow-up study comparing different breast screening result groups five months after their last breast screening appointment. J Public Health Med. 1998;20(4):396-403.
Exclusion: included in an included systematic review, not directly used.

Brewster AM, Thompson P, Sahin AA, et al. Copy number imbalances between screen- and symptom-detected breast cancers and impact on disease-free survival. Cancer Prev Res (Phila). 2011;4(10):1609-16.
Exclusion: wrong comparison.

Brewster D, Everington D, Harkness E, et al. Incidence of and mortality from breast cancer since introduction of screening. Scottish figures show higher incidence and similar mortality. BMJ. 1996;312(7031):639-40.
Exclusion: wrong publication type.

Brewster DH, Sharpe KH, Clark DI, et al. Declining breast cancer incidence and decreased HRT use. Lancet. 2009;373(9662):459-60; author reply 61.
Exclusion: wrong publication type.

Brewster DH, Stockton DL. Ascertainment of breast cancer by the Scottish Cancer Registry: an assessment based on comparison with five independent breast cancer trials databases. Breast. 2008;17(1):104-6.
Exclusion: wrong study design for key question.

Briedis D, Siu KKW, Paganin DM, et al. Analyser-based mammography using single-image reconstruction. Phys Med Biol. 2005;50(15):3599-611.
Exclusion: wrong study design for key question.

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Brodersen J, Jorgensen KJ, Gotzsche PC. The benefits and harms of screening for cancer with a focus on breast screening. Pol Arch Med Wewn. 2010;120(3):89-94.
Exclusion: review not meeting inclusion criteria.

Broeders M, Moss S, Nyström L, et al. The impact of mammographic screening on breast cancer mortality in Europe: a review of observational studies. J Med Screen. 2012;19 Suppl 1:14-25.
Exclusion: review not meeting inclusion criteria.

Broeders MJ, Peer PG, Straatman H, et al. Diverging breast cancer mortality rates in relation to screening? A comparison of Nijmegen to Arnhem and the Netherlands, 1969-1997. Int J Cancer. 2001;92(2):303-8.
Exclusion: wrong outcomes.

Broeders MJM, Verbeek ALM, Straatman H, et al. Repeated mammographic screening reduces breast cancer mortality along the continuum of age. J Med Screen. 2002;9(4):163-7.
Exclusion: wrong study design for key question.

Brouckaert O, Schoneveld A, Truyers C, et al. Breast cancer phenotype, nodal status and palpability may be useful in the detection of overdiagnosed screening-detected breast cancers. Ann Oncol. 2013;24(7):1847-52.
Exclusion: wrong outcomes.

Brown M, Eccles C, Wallis MG. Geographical distribution of breast cancers on the mammogram: an interval cancer database. Br J Radiol. 2001;74(880):317-22.
Exclusion: wrong outcomes.

Brown SBF, Morrison DS, Cooke TG. Increasing incidence of breast cancer: distinguishing between the effects of birth cohort and a national breast screening programme. Breast Cancer Res Treat. 2009;116(3):603-7.
Exclusion: wrong outcomes.

Bruening W, Uhl S, Fontanarosa J, et al. Noninvasive Diagnostic Tests for Breast Abnormalities: Update of a 2006 Review. AHRQ Comparative Effectiveness Reviews. 2012
Exclusion: review not meeting inclusion criteria.

Bucchi L, Barchielli A, Ravaioli A, et al. Screen-detected vs clinical breast cancer: the advantage in the relative risk of lymph node metastases decreases with increasing tumour size. Br J Cancer. 2005;92(1):156-61.
Exclusion: wrong study design for key question.

Bucchi L, Foca F, Ravaioli A, et al. Receipt of adjuvant systemic therapy among patients with high-risk breast cancer detected by mammography screening. Breast Cancer Res Treat. 2009;113(3):559-66.
Exclusion: wrong outcomes.

Bucchi L, Puliti D, Ravaioli A, et al. Breast screening: axillary lymph node status of interval cancers by interval year. Breast. 2008;17(5):477-83.
Exclusion: wrong outcomes.

Buchberger W, DeKoekkoek-Doll P, Springer P, et al. Incidental findings on sonography of the breast: clinical significance and diagnostic workup. AJR Am J Roentgenol. 1999;173(4):921-7.
Exclusion: wrong outcomes.

Buchberger W, Niehoff A, Obrist P, et al. Clinically and mammographically occult breast lesions: detection and classification with high-resolution sonography. Semin Ultrasound CT MR. 2000;21(4):325-36.
Exclusion: wrong intervention.

Buiatti E, Barchielli A, Bartolacci S, et al. Stage-specific incidence of breast cancer before the beginning of organized screening programs in Italy. Cancer Causes Control. 2002;13(1):65-71.
Exclusion: wrong intervention.

Buiatti E, Barchielli A, Bartolacci S, et al. The impact of organised screening programmes on the stage-specific incidence of breast cancer in some Italian areas. Eur J Cancer. 2003;39(12):1776-82.
Exclusion: wrong outcomes.

Buist DSM, Porter PL, Lehman C, et al. Factors contributing to mammography failure in women aged 40-49 years. J Natl Cancer Inst. 2004;96(19):1432-40.
Exclusion: wrong population.

Buist DSM, Walker R, Bowles EJA, et al. Screening mammography use among current, former, and never hormone therapy users may not explain recent declines in breast cancer incidence. Cancer Epidemiol Biomarkers Prev. 2012;21(5):720-7.
Exclusion: wrong outcomes.

Bull AR, Campbell MJ. Assessment of the psychological impact of a breast screening programme. Br J Radiol. 1991;64(762):510-5.

Exclusion: included in an included systematic review, not directly used.

Bulliard JL, De Landtsheer JP, Levi F. Results from the Swiss mammography screening pilot programme. Eur J Cancer. 2003;39(12):1761-9.
Exclusion: wrong comparison.

Bulliard JL, Ducros C, Dayer E, et al. Variation in performance in low-volume mammography screening programmes: experience from Switzerland. Cancer epidemiol. 2011;35(3):293-7.
Exclusion: wrong outcomes.

Bulliard JL, Ducros C, Jemelin C, et al. Effectiveness of organised versus opportunistic mammography screening. Ann Oncol. 2009;20(7):1199-202.
Exclusion: wrong comparison.

Bulpitt CJ, Benos AS, Nicholl CG, et al. Should medical screening of the elderly population be promoted? Gerontology. 1990;36(4):230-45.
Exclusion: review not meeting inclusion criteria.

Burani R, Caimi F, Maggioni C, et al. Quality assessment of the mammographic screening programme in the Azienda Sanitaria locale Provincia Milano 1 -- analysis of interval cancers and discussion of possible causes of diagnostic error. Radiol Med (Torino). 2005;109(3):260-7.
Exclusion: wrong outcomes.

Burhenne LJ, Burhenne HJ. The Canadian National Breast Screening Study: a Canadian critique. AJR Am J Roentgenol. 1993;161(4):761-3.
Exclusion: wrong publication type.

Burke JP, Power C, Gorey TF, et al. A comparative study of risk factors and prognostic features between symptomatic and screen detected breast cancer. Eur J Surg Oncol. 2008;34(2):149-53.
Exclusion: wrong comparison.

Burnside E, Belkora J, Esserman L. The impact of alternative practices on the cost and quality of mammographic screening in the United States. Clin Breast Cancer. 2001;2(2):145-52.
Exclusion: wrong outcomes.

Burnside ES, Sickles EA, Sohlich RE, et al. Differential value of comparison with previous examinations in diagnostic versus screening mammography. AJR Am J Roentgenol. 2002;179(5):1173-7.
Exclusion: wrong outcomes.

Burrell HC, Sibbering DM, Wilson AR, et al. Screening interval breast cancers: mammographic features and prognosis factors. Radiology. 1996;199(3):811-7.
Exclusion: wrong outcomes.

Burstein HJ, Polyak K, Wong JS, et al. Ductal carcinoma in situ of the breast. N Engl J Med. 2004;350(14):1430-41.
Exclusion: wrong population.

Burton RC, Bell RJ, Thiagarajah G, et al. Adjuvant therapy, not mammographic screening, accounts for most of the observed breast cancer specific mortality reductions in Australian women since the national screening program began in 1991. Breast Cancer Res Treat. 2012;131(3):949-55.
Exclusion: wrong comparison.

Buscombe JR, Cwikla JB, Holloway B, et al. Prediction of the usefulness of combined mammography and scintimammography in suspected primary breast cancer using ROC curves. J Nucl Med. 2001;42(1):3-8.
Exclusion: wrong population.

Buyse M, Loi S, van't Veer L, et al. Validation and clinical utility of a 70-gene prognostic signature for women with node-negative breast cancer. J Natl Cancer Inst. 2006;98(17):1183-92.
Exclusion: wrong intervention.

Byng JW, Boyd NF, Little L, et al. Symmetry of projection in the quantitative analysis of mammographic images. Eur J Cancer Prev. 1996;5(5):319-27.
Exclusion: wrong outcomes.

Caban ME, Kuo Y-F, Mahnken JD, et al. Mammography use may partially mediate disparities in tumor size at diagnosis in women with social security disabilities. Women Health. 2007;46(4):1-17.
Exclusion: wrong comparison.

Cabanes A, Vidal E, Pérez-Gómez B, et al. Age-specific breast, uterine and ovarian cancer mortality trends in Spain: changes from 1980 to 2006. Cancer epidemiol. 2009;33(3-4):169-75.
Exclusion: included in an included systematic review, not directly used.

Cady B, Chung MA. Preventing invasive breast cancer: another benefit from mammographic screening. Cancer. 2011;117(14):3064-8.
Exclusion: wrong publication type.

Appendix A4. List of Excluded Studies

Cady B, Michaelson JS, Chung MA. The "tipping point" for breast cancer mortality decline has resulted from size reductions due to mammographic screening. Ann Surg Oncol. 2011;18(4):903-6.
Exclusion: wrong publication type.

Cady B, Stone MD, Schuler JG, et al. The new era in breast cancer. Invasion, size, and nodal involvement dramatically decreasing as a result of mammographic screening. Arch Surg. 1996;131(3):301-8.
Exclusion: wrong study design for key question.

Callaway MP, Boggis CR, Astley SA, et al. The influence of previous films on screening mammographic interpretation and detection of breast carcinoma. Clin Radiol. 1997;52(7):527-9.
Exclusion: wrong outcomes.

Calle EE, Feigelson HS, Hildebrand JS, et al. Postmenopausal hormone use and breast cancer associations differ by hormone regimen and histologic subtype.[Erratum appears in Cancer. 2009 Apr 1;115(7):1587]. Cancer. 2009;115(5):936-45.
Exclusion: wrong outcomes.

Campbell JB. Breast cancer-race, ethnicity, and survival: a literature review. Breast Cancer Res Treat. 2002;74(2):187-92.
Exclusion: review not meeting inclusion criteria.

Caproni N, Marchisio F, Pecchi A, et al. Contrast-enhanced ultrasound in the characterisation of breast masses: utility of quantitative analysis in comparison with MRI. Eur Radiol. 2010;20(6):1384-95.
Exclusion: wrong intervention.

Carcaise-Edinboro P, Bradley CJ, Dahman B. Surveillance mammography for Medicaid/Medicare breast cancer patients. J Cancer Surviv. 2010;4(1):59-66.
Exclusion: wrong intervention.

Carles M, Vilaprinyo E, Cots F, et al. Cost-effectiveness of early detection of breast cancer in Catalonia (Spain). BMC Cancer. 2011;11:192.
Exclusion: wrong outcomes.

Carlos RC. Declining screening mammography rates: a multigenerational loss of opportunity? AJR Am J Roentgenol. 2009;192(2):388-9.
Exclusion: wrong publication type.

Carmichael AR. Obesity as a risk factor for development and poor prognosis of breast cancer. BJOG. 2006;113(10):1160-6.
Exclusion: review not meeting inclusion criteria.

Carney JK, Ewing JF, Finley CA. Progress in breast cancer screening: Vermont's efforts. J Public Health Manag Pract. 1996;2(2):57-63.
Exclusion: studies outside of search dates.

Carney PA, Abraham LA, Miglioretti DL, et al. Factors associated with imaging and procedural events used to detect breast cancer after screening mammography. AJR Am J Roentgenol. 2007;188(2):385-92.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Carney PA, Bogart TA, Geller BM, et al. Association between time spent interpreting, level of confidence, and accuracy of screening mammography. AJR Am J Roentgenol. 2012;198(4):970-8.
Exclusion: wrong outcomes.

Carney PA, Cook AJ, Miglioretti DL, et al. Use of clinical history affects accuracy of interpretive performance of screening mammography. J Clin Epidemiol. 2012;65(2):219-30.
Exclusion: wrong outcomes.

Carney PA, Goodrich ME, O'Mahony DM, et al. Mammography in New Hampshire: characteristics of the women and the exams they receive. J Community Health. 2000;25(3):183-98.
Exclusion: wrong outcomes.

Carney PA, Sickles EA, Monsees BS, et al. Identifying minimally acceptable interpretive performance criteria for screening mammography. Radiology. 2010;255(2):354-61.
Exclusion: wrong outcomes.

Carter KJ, Castro F, Kessler E, et al. Simulation of breast cancer screening: quality assessment of two protocols. J Healthc Qual. 2004;26(6):31-8.
Exclusion: wrong study design for key question.

Carter TI, Reilly JJ. Missed opportunities: clinical antecedents in the diagnosis of advanced breast cancer. Ann Surg Oncol. 2012;19(9):2782-5.
Exclusion: wrong population.

Castells X, Roman M, Romero A, et al. Breast cancer detection risk in screening mammography after a false-positive result. Cancer epidemiol. 2013;37(1):85-90.
Exclusion: wrong outcomes.

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Castro F, Carter KJ, Kessler E, et al. The relation of breast cancer staging to screening protocol compliance: a computer simulation study. Comput Biol Med. 2005;35(2):91-101.
Exclusion: wrong outcomes.

Cates C, Senn S. Screening mammography re-evaluated. Lancet. 2000;355(9205):750; author reply 2.
Exclusion: wrong publication type.

Caumo F, Bernardi D, Ciatto S, et al. Incremental effect from integrating 3D-mammography (tomosynthesis) with 2D-mammography: Increased breast cancer detection evident for screening centres in a population-based trial. Breast. 2014;23(1):76-80.
Exclusion: wrong outcomes.

Caumo F, Brunelli S, Tosi E, et al. On the role of arbitration of discordant double readings of screening mammography: experience from two Italian programmes. Radiol Med (Torino). 2011;116(1):84-91.
Exclusion: wrong outcomes.

Caumo F, Vecchiato F, Pellegrini M, et al. Analysis of interval cancers observed in an Italian mammography screening programme (2000-2006). Radiol Med (Torino). 2009;114(6):907-14.
Exclusion: wrong outcomes.

Caumo F, Vecchiato F, Strabbioli M, et al. Interval cancers in breast cancer screening: comparison of stage and biological characteristics with screen-detected cancers or incident cancers in the absence of screening. Tumori. 2010;96(2):198-201.
Exclusion: wrong outcomes.

Cawson JN, Nickson C, Amos A, et al. Invasive breast cancers detected by screening mammography: a detailed comparison of computer-aided detection-assisted single reading and double reading. J Med Imaging Radiat Oncol. 2009;53(5):442-9.
Exclusion: wrong outcomes.

Cecchini RS, Costantino JP, Cauley JA, et al. Body mass index and the risk for developing invasive breast cancer among high-risk women in NSABP P-1 and STAR breast cancer prevention trials. Cancer Prev Res (Phila). 2012;5(4):583-92.
Exclusion: wrong intervention.

Celaya MO, Berke EM, Onega TL, et al. Breast cancer stage at diagnosis and geographic access to mammography screening (New Hampshire, 1998-2004). Rural Remote Health. 2010;10(2):1361.
Exclusion: wrong comparison.

Centre for R, Dissemination. Clinical and economic outcomes analyses of women developing breast cancer in a managed care organization (Provisional abstract). NHS Economic Evaluation Database. 2014(1)
Exclusion: wrong outcomes.

Centre for R, Dissemination. Costs, effects and cost-effectiveness of breast cancer control in Ghana (Provisional abstract). NHS Economic Evaluation Database. 2014(1)
Exclusion: wrong outcomes.

Centre for R, Dissemination. Tailored breast cancer screening program with microdose mammography, US, and MR imaging: short-term results of a pilot study in 40-49-year-old women (Provisional abstract). NHS Economic Evaluation Database. 2014(1)
Exclusion: wrong publication type.

Chae EY, Kim HH, Cha JH, et al. Evaluation of screening whole-breast sonography as a supplemental tool in conjunction with mammography in women with dense breasts. J Ultrasound Med. 2013;32(9):1573-8.
Exclusion: wrong outcomes.

Chagpar AB, McMasters KM, Saul J, et al. Body mass index influences palpability but not stage of breast cancer at diagnosis. Am Surg. 2007;73(6):555-60; discussion 60.
Exclusion: wrong population.

Chan SWW, Cheung PSY, Chan S, et al. Benefit of ultrasonography in the detection of clinically and mammographically occult breast cancer. World J Surg. 2008;32(12):2593-8.
Exclusion: wrong intervention.

Chang HR, Cole B, Bland KI. Nonpalpable breast cancer in women aged 40-49 years: a surgeon's view of benefits from screening mammography. J Natl Cancer Inst. 1997;Monographs.(22):145-9.
Exclusion: wrong comparison.

Chang JM, Moon WK, Cho N, et al. Breast cancers initially detected by hand-held ultrasound: detection performance of radiologists using automated breast ultrasound data. Acta Radiol. 2011;52(1):8-14.
Exclusion: wrong outcomes.

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Chang R-F, Chang-Chien K-C, Takada E, et al. Breast density analysis in 3-D whole breast ultrasound images. Conf Proc IEEE Eng Med Biol Soc. 2006;1:2795-8.
Exclusion: wrong outcomes.

Chang Y, Schechter CB, van Ravesteyn NT, et al. Collaborative modeling of the impact of obesity on race-specific breast cancer incidence and mortality. Breast Cancer Res Treat. 2012;136(3):823-35.
Exclusion: wrong outcomes.

Chang YH, Zheng B, Gur D. Robustness of computerized identification of masses in digitized mammograms. A preliminary assessment. Invest Radiol. 1996;31(9):563-8.
Exclusion: wrong intervention.

Chay WY, Ong WS, Tan PH, et al. Validation of the Gail model for predicting individual breast cancer risk in a prospective nationwide study of 28,104 Singapore women. Breast Cancer Res. 2012;14(1):R19.
Exclusion: wrong intervention.

Chen C, Orel SG, Schnall MD, et al. Breast conservation treatment for patients presenting with axillary lymphadenopathy from presumed primary breast cancer: the role of breast magnetic resonance imaging for staging. Clin Breast Cancer. 2002;3(3):219-22.
Exclusion: wrong study design for key question.

Chen DR, Jeng LB, Kao A, et al. Comparing thallium-201 spect mammoscintigraphy and ultrasonography to detect breast cancer in mammographical dense breasts. Neoplasma. 2003;50(3):222-6.
Exclusion: wrong intervention.

Chen HH, Thurfjell E, Duffy SW, et al. Evaluation by Markov chain models of a non-randomised breast cancer screening programme in women aged under 50 years in Sweden. J Epidemiol Community Health. 1998;52(5):329-35.
Exclusion: wrong study design for key question.

Chen J-H, Mehta RS, Nalcioglu O, et al. Magnetic resonance imaging evaluation of noninflammatory breast cancer with skin involvement after neoadjuvant chemotherapy.[Erratum appears in Ann Surg Oncol. 2011 Dec;18 Suppl 3:S329 Note: Mehta, Rita S [added]]. Ann Surg Oncol. 2010;17(7):1964-5.
Exclusion: wrong publication type.

Chen L, Chen Y, Diao XH, et al. Comparative study of automated breast 3-D ultrasound and handheld B-mode ultrasound for differentiation of benign and malignant breast masses. Ultrasound Med Biol. 2013;39(10):1735-42.
Exclusion: wrong outcomes.

Chen TH-H, Yen AM-F, Wu GH-M, et al. Multiple detection modalities and disease natural history of breast cancer. Stud Health Technol Inform. 2007;129(Pt 1):78-81.
Exclusion: wrong study design for key question.

Chen TR, Tyan YS, Teng PS, et al. Population dose from medical exposure in Taiwan for 2008. Med Phys. 2011;38(6):3139-48.
Exclusion: wrong publication type.

Chen W, Giger ML, Lan L, et al. Computerized interpretation of breast MRI: investigation of enhancement-variance dynamics. Med Phys. 2004;31(5):1076-82.
Exclusion: wrong outcomes.

Chen W-M, Chang R-F, Moon WK, et al. Breast cancer diagnosis using three-dimensional ultrasound and pixel relation analysis. Ultrasound Med Biol. 2003;29(7):1027-35.
Exclusion: wrong outcomes.

Chen Y, Brock G, Wu D. Estimating key parameters in periodic breast cancer screening-application to the Canadian National Breast Screening Study data. Cancer epidemiol. 2010;34(4):429-33.
Exclusion: wrong study design for key question.

Chen Z, Wu AH, Gauderman WJ, et al. Does mammographic density reflect ethnic differences in breast cancer incidence rates? Am J Epidemiol. 2004;159(2):140-7.
Exclusion: wrong comparison.

Cheng Y-C, Wu N-Y, Ko JS, et al. Breast cancers detected by breast MRI screening and ultrasound in asymptomatic Asian women: 8 years of experience in Taiwan. Oncology. 2012;82(2):98-107.
Exclusion: wrong comparison.

Chiarelli AM, Edwards SA, Prummel MV, et al. Digital compared with screen-film mammography: performance measures in concurrent cohorts within an organized breast screening program. Radiology. 2013;268(3):684-93.
Exclusion: wrong comparison.

Appendix A4. List of Excluded Studies

Chiarelli AM, Edwards SA, Sheppard AJ, et al. Favourable prognostic factors of subsequent screen-detected breast cancers among women aged 50-69. Eur J Cancer Prev. 2012;21(6):499-506.
Exclusion: wrong study design for key question.

Chiarelli AM, Halapy E, Nadalin V, et al. Performance measures from 10 years of breast screening in the Ontario Breast Screening Program, 1990/91 to 2000. Eur J Cancer Prev. 2006;15(1):34-42.
Exclusion: wrong comparison.

Chiarelli AM, Kirsh VA, Klar NS, et al. Influence of patterns of hormone replacement therapy use and mammographic density on breast cancer detection. Cancer Epidemiol Biomarkers Prev. 2006;15(10):1856-62.
Exclusion: wrong outcomes.

Chiarelli AM, Mai V, Halapy EE, et al. Effect of screening result on waiting times to assessment and breast cancer diagnosis: results from the Ontario Breast Screening Program. Can J Public Health. 2005;Revue Canadienne de Sante Publique. 96(4):259-63.
Exclusion: wrong comparison.

Chiarelli AM, Prummel MV, Muradali D, et al. Effectiveness of screening with annual magnetic resonance imaging and mammography: results of the initial screen from the ontario high risk breast screening program. J Clin Oncol. 2014;32(21):2224-30.
Exclusion: wrong population.

Chida K, Komatsu Y, Sai M, et al. Reduced compression mammography to reduce breast pain. Clin Imaging. 2009;33(1):7-10.
Exclusion: wrong outcomes.

Chiu C, Morrell S, Page A, et al. Population-based mammography screening and breast cancer incidence in New South Wales, Australia. Cancer Causes Control. 2006;17(2):153-60.
Exclusion: wrong outcomes.

Chlebowski RT. Nutrition and physical activity influence on breast cancer incidence and outcome. Breast. 2013;22 Suppl 2:S30-7.
Exclusion: wrong publication type.

Chlebowski RT, Anderson G, Manson JE, et al. Estrogen alone in postmenopausal women and breast cancer detection by means of mammography and breast biopsy. J Clin Oncol. 2010;28(16):2690-7.
Exclusion: wrong intervention.

Chlebowski RT, Anderson G, Pettinger M, et al. Estrogen plus progestin and breast cancer detection by means of mammography and breast biopsy. Arch Intern Med. 2008;168(4):370-7; quiz 45.
Exclusion: wrong intervention.

Chlebowski RT, Anderson GL. The influence of time from menopause and mammography on hormone therapy-related breast cancer risk assessment. J Natl Cancer Inst. 2011;103(4):284-5.
Exclusion: wrong publication type.

Chlebowski RT, Hendrix SL, Langer RD, et al. Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women: the Women's Health Initiative Randomized Trial. JAMA. 2003;289(24):3243-53.
Exclusion: wrong intervention.

Chlebowski RT, Johnson KC, Kooperberg C, et al. Calcium plus vitamin D supplementation and the risk of breast cancer. J Natl Cancer Inst. 2008;100(22):1581-91.
Exclusion: wrong intervention.

Chlebowski RT, Kuller LH, Prentice RL, et al. Breast cancer after use of estrogen plus progestin in postmenopausal women. N Engl J Med. 2009;360(6):573-87.
Exclusion: wrong outcomes.

Cho N, Kim SJ, Choi HY, et al. Features of prospectively overlooked computer-aided detection marks on prior screening digital mammograms in women with breast cancer. AJR Am J Roentgenol. 2010;195(5):1276-82.
Exclusion: wrong intervention.

Cho N, Moon WK, Cha JH, et al. Differentiating benign from malignant solid breast masses: comparison of two-dimensional and three-dimensional US. Radiology. 2006;240(1):26-32.
Exclusion: wrong outcomes.

Chou C-P, Pan H-B, Hsu G-C, et al. Assessing the first 3 years of Taiwan's nationwide population-based mammography screening program. Breast J. 2012;18(5):498-9.
Exclusion: wrong publication type.

Christensen LH, Engholm G, Cortes R, et al. Reduced mortality for women with mammography-detected breast cancer in east Denmark and south Sweden. Eur J Cancer. 2006;42(16):2773-80.

Exclusion: wrong comparison.

Christiansen CL, Wang F, Barton MB, et al. Predicting the cumulative risk of false-positive mammograms. J Natl Cancer Inst. 2000;92(20):1657-66.
Exclusion: studies outside of search dates.

Chu KC, Tarone RE, Kessler LG, et al. Recent trends in U.S. breast cancer incidence, survival, and mortality rates. J Natl Cancer Inst. 1996;88(21):1571-9.
Exclusion: wrong outcomes.

Chuwa EWL, Yeo AWY, Koong HN, et al. Early detection of breast cancer through population-based mammographic screening in Asian women: a comparison study between screen-detected and symptomatic breast cancers. Breast J. 2009;15(2):133-9.
Exclusion: wrong population.

Ciatto S. Recommending mammography screening beyond 80 years of age: a time for caution. Womens Health (Lond Engl). 2008;4(4):333-5.
Exclusion: wrong publication type.

Ciatto S, Ambrogetti D, Collini G, et al. Computer-aided detection (CAD) of cancers detected on double reading by one reader only. Breast. 2006;15(4):528-32.
Exclusion: wrong intervention.

Ciatto S, Bernardi D, Pellegrini M, et al. Proportional incidence and radiological review of large (T2+) breast cancers as surrogate indicators of screening programme performance. Eur Radiol. 2012;22(6):1250-4.
Exclusion: wrong outcomes.

Ciatto S, Catarzi S, Lamberini MP, et al. Interval breast cancers in screening: the effect of mammography review method on classification. Breast. 2007;16(6):646-52.
Exclusion: wrong intervention.

Ciatto S, Houssami N, Ambrogetti D, et al. Minority report - false negative breast assessment in women recalled for suspicious screening mammography: imaging and pathological features, and associated delay in diagnosis. Breast Cancer Res Treat. 2007;105(1):37-43.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Ciatto S, Houssami N, Apruzzese A, et al. Reader variability in reporting breast imaging according to BI-RADS assessment categories (the Florence experience). Breast. 2006;15(1):44-51.
Exclusion: wrong outcomes.

Ciatto S, Visioli C, Paci E, et al. Breast density as a determinant of interval cancer at mammographic screening. Br J Cancer. 2004;90(2):393-6.
Exclusion: wrong comparison.

Clark R. Re: Accuracy of screening mammography interpretation by characteristics of radiologists. J Natl Cancer Inst. 2005;97(12):936.
Exclusion: wrong publication type.

Coates RJ, Uhler RJ, Brogan DJ, et al. Patterns and predictors of the breast cancer detection methods in women under 45 years of age (United States). Cancer Causes Control. 2001;12(5):431-42.
Exclusion: wrong population.

Coates RJ, Uhler RJ, Hall HI, et al. Risk of breast cancer in young women in relation to body size and weight gain in adolescence and early adulthood. Br J Cancer. 1999;81(1):167-74.
Exclusion: wrong population.

Coburn NG, Chung MA, Fulton J, et al. Decreased breast cancer tumor size, stage, and mortality in Rhode Island: an example of a well-screened population. Cancer Control. 2004;11(4):222-30.
Exclusion: wrong study design for key question.

Cockburn J, De Luise T, Hurley S, et al. Development and validation of the PCQ: A questionnaire to measure the psychological consequences of screening mammography. Social Science and Medicine. 1992;34(10):1129-34.
Exclusion: included in an included systematic review, not directly used.

Cockburn J, Staples M, Hurley SF, et al. Psychological consequences of screening mammography. J Med Screen. 1994;1(1):7-12.
Exclusion: studies outside of search dates.

Cockburn J, Staples M, Hurley SF, et al. Psychological consequences of screening mammography. J Med Screen. 1994;1(1):7-12.
Exclusion: included in an included systematic review, not directly used.

Appendix A4. List of Excluded Studies

Codd MB, Buttimer J, Comber H, et al. Mortality from breast cancer in Ireland prior to the introduction of population-based mammographic screening. Ir J Med Sci. 1999;168(2):87-92.
Exclusion: wrong outcomes.

Cohen MM, Kaufert PA, MacWilliam L, et al. Using an alternative data source to examine randomization in the Canadian National Breast Screening Study. J Clin Epidemiol. 1996;49(9):1039-44.
Exclusion: studies outside of search dates.

Coldman A, Phillips N. Population studies of the effectiveness of mammographic screening. Prev Med. 2011;53(3):115-7.
Exclusion: review not meeting inclusion criteria.

Coldman A, Phillips N, Warren L, et al. Breast cancer mortality after screening mammography in British Columbia women. Int J Cancer. 2007;120(5):1076-80.
Exclusion: wrong comparison.

Coldman AJ, Major D, Doyle GP, et al. Organized breast screening programs in Canada: effect of radiologist reading volumes on outcomes. Radiology. 2006;238(3):809-15.
Exclusion: wrong outcomes.

Coldman AJ, Phillips N. Breast cancer survival and prognosis by screening history. Br J Cancer. 2014;110(3):556-9.
Exclusion: wrong intervention.

Coldman AJ, Phillips N. False-positive screening mammograms and biopsies among women participating in a Canadian provincial breast screening program. Can J Public Health. 2012;Revue Canadienne de Sante Publique. 103(6):e420-4.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Coldman AJ, Phillips N, Speers C. A retrospective study of the effect of participation in screening mammography on the use of chemotherapy and breast conserving surgery. Int J Cancer. 2007;120(10):2185-90.
Exclusion: wrong population.

Cole EB, Toledano AY, Lundqvist M, et al. Comparison of radiologist performance with photon-counting full-field digital mammography to conventional full-field digital mammography. Acad Radiol. 2012;19(8):916-22.
Exclusion: wrong outcomes.

Cole EB, Zhang Z, Marques HS, et al. Assessing the stand-alone sensitivity of computer-aided detection with cancer cases from the Digital Mammographic Imaging Screening Trial. AJR Am J Roentgenol. 2012;199(3):W392-401.
Exclusion: wrong intervention.

Collins S, Woodman CB, Threlfall A, et al. Survival rates from interval cancer in NHS breast screening programme. BMJ. 1998;316(7134):832-3.
Exclusion: wrong publication type.

Cong XJ, Shen Y, Miller AB. Estimation of age-specific sensitivity and sojourn time in breast cancer screening studies. Stat Med. 2005;24(20):3123-38.
Exclusion: wrong study design for key question.

Conner P. Breast response to menopausal hormone therapy--aspects on proliferation, apoptosis and mammographic density. Ann Med. 2007;39(1):28-41.
Exclusion: review not meeting inclusion criteria.

Consedine NS. A false-positive on screening mammography has a negative psychosocial impact up to 3 years after receiving the all clear. Evid Based Ment Health. 2013;16(4):115.
Exclusion: wrong publication type.

Cook AJ, Elmore JG, Miglioretti DL, et al. Decreased accuracy in interpretation of community-based screening mammography for women with multiple clinical risk factors. J Clin Epidemiol. 2010;63(4):441-51.
Exclusion: wrong outcomes.

Cooper GS, Yuan Z, Bowlin SJ, et al. An ecological study of the effectiveness of mammography in reducing breast cancer mortality. Am J Public Health. 1998;88(2):281-4.
Exclusion: wrong study design for key question.

Cooper GS, Yuan Z, Jethva RN, et al. Use of Medicare claims data to measure county-level variation in breast carcinoma incidence and mammography rates. Cancer Detect Prev. 2002;26(3):197-202.
Exclusion: wrong study design for key question.

Cornford E, Reed J, Murphy A, et al. Optimal screening mammography reading volumes; evidence from real life in the East Midlands region of the NHS Breast Screening Programme. Clin Radiol. 2011;66(2):103-7.
Exclusion: wrong outcomes.

Appendix A4. List of Excluded Studies

Cornford EJ, Evans AJ, James JJ, et al. The pathological and radiological features of screen-detected breast cancers diagnosed following arbitration of discordant double reading opinions. Clin Radiol. 2005;60(11):1182-7.
Exclusion: wrong comparison.

Corsetti V, Ferrari A, Ghirardi M, et al. Role of ultrasonography in detecting mammographically occult breast carcinoma in women with dense breasts. Radiol Med (Torino). 2006;111(3):440-8.
Exclusion: studies outside of search dates.

Corsetti V, Houssami N, Ferrari A, et al. Breast screening with ultrasound in women with mammography-negative dense breasts: evidence on incremental cancer detection and false positives, and associated cost. Eur J Cancer. 2008;44(4):539-44.
Exclusion: wrong comparison.

Corsetti V, Houssami N, Ghirardi M, et al. Evidence of the effect of adjunct ultrasound screening in women with mammography-negative dense breasts: interval breast cancers at 1 year follow-up. Eur J Cancer. 2011;47(7):1021-6.
Exclusion: wrong comparison.

Couto E, Banks E, Reeves G, et al. Family history and breast cancer tumour characteristics in screened women. Int J Cancer. 2008;123(12):2950-4.
Exclusion: wrong study design for key question.

Cowan WK, Angus B, Gray JC, et al. A study of interval breast cancer within the NHS breast screening programme. J Clin Pathol. 2000;53(2):140-6.
Exclusion: wrong outcomes.

Cowan WK, Kelly P, Sawan A, et al. The pathological and biological nature of screen-detected breast carcinomas: a morphological and immunohistochemical study. J Pathol. 1997;182(1):29-35.
Exclusion: wrong comparison.

Cox B. The effect of service screening on breast cancer mortality rates. Eur J Cancer Prev. 2008;17(4):306-11.
Exclusion: wrong study design for key question.

Cox B. Variation in the effectiveness of breast screening by year of follow-up. J Natl Cancer Inst. 1997;Monographs.(22):69-72.
Exclusion: review not meeting inclusion criteria.

Crawford MD, Biankin AV, Rickard MT, et al. The operative management of screen-detected breast cancers. Aust N Z J Surg. 2000;70(3):168-73.
Exclusion: wrong comparison.

Crispo A, Barba M, D'Aiuto G, et al. Molecular profiles of screen detected vs. symptomatic breast cancer and their impact on survival: results from a clinical series. BMC Cancer. 2013;13:15.
Exclusion: wrong outcomes.

Crocetti E, Buzzoni C, Falcini F, et al. Disentangling the roles of mammographic screening and HRT in recent breast cancer incidence trends in italy by analyses based on calendar time and time since screening activation. Breast J. 2010;16(4):350-5.
Exclusion: wrong outcomes.

Cronin KA, Yu B, Krapcho M, et al. Modeling the dissemination of mammography in the United States. Cancer Causes Control. 2005;16(6):701-12.
Exclusion: wrong study design for key question.

Crosignani PG, Rubin BL. Screening before and during the use of oral contraceptives and hormone replacement therapy. The ESHRE Capri Workshop Group. Hum Reprod. 2000;15(2):485-92.
Exclusion: wrong publication type.

Crouchley K, Wylie E, Khong E. Hormone replacement therapy and mammographic screening outcomes in Western Australia. J Med Screen. 2006;13(2):93-7.
Exclusion: wrong comparison.

Crump SR, Shipp MP, McCray GG, et al. Abnormal mammogram follow-up: do community lay health advocates make a difference? Health Promot Pract. 2008;9(2):140-8.
Exclusion: wrong intervention.

Crystal P, Strano SD, Shcharynski S, et al. Using sonography to screen women with mammographically dense breasts. AJR Am J Roentgenol. 2003;181(1):177-82.
Exclusion: wrong population.

Cui Y, Whiteman MK, Flaws JA, et al. Body mass and stage of breast cancer at diagnosis. Int J Cancer. 2002;98(2):279-83.
Exclusion: wrong study design for key question.

Appendix A4. List of Excluded Studies

Cunningham JE, Walters CA, Hill EG, et al. Mind the gap: racial differences in breast cancer incidence and biologic phenotype, but not stage, among low-income women participating in a government-funded screening program. Breast Cancer Res Treat. 2013;137(2):589-98.
Exclusion: wrong intervention.

Cupples TE, Cunningham JE, Reynolds JC. Impact of computer-aided detection in a regional screening mammography program. AJR Am J Roentgenol. 2005;185(4):944-50.
Exclusion: wrong intervention.

Cust AE, Stocks T, Lukanova A, et al. The influence of overweight and insulin resistance on breast cancer risk and tumour stage at diagnosis: a prospective study. Breast Cancer Res Treat. 2009;113(3):567-76.
Exclusion: wrong outcomes.

Cuthbertson SA, Goyder EC, Poole J. Inequalities in breast cancer stage at diagnosis in the Trent region, and implications for the NHS Breast Screening Programme. J Public Health (Oxf). 2009;31(3):398-405.
Exclusion: wrong study design for key question.

Cutler WB, Burki RE, Kolter J, et al. Mammography for symptomless women--not so wise? Climacteric. 2013;16(3):313-5.
Exclusion: wrong publication type.

Cuzick J, Warwick J, Pinney E, et al. Tamoxifen and breast density in women at increased risk of breast cancer. J Natl Cancer Inst. 2004;96(8):621-8.
Exclusion: wrong intervention.

Dahlui M, Gan DEH, Taib NA, et al. Predictors of breast cancer screening uptake: a pre intervention community survey in Malaysia. Asian Pac J Cancer Prev. 2012;13(7):3443-9.
Exclusion: wrong outcomes.

Dai Q, Shu XO, Jin F, et al. Population-based case-control study of soyfood intake and breast cancer risk in Shanghai. Br J Cancer. 2001;85(3):372-8.
Exclusion: wrong outcomes.

Dale PS, Richards M, Mackie GC. Vascular calcifications on screening mammography identify women with increased risk of coronary artery disease and diabetes. Am J Surg. 2008;196(4):537-40.
Exclusion: wrong outcomes.

Danigelis NL, Worden JK, Flynn BS, et al. Increasing mammography screening among low-income African American women with limited access to health information. Prev Med. 2005;40(6):880-7.
Exclusion: wrong outcomes.

Das B, Feuer EJ, Mariotto A. Geographic association between mammography use and mortality reduction in the US. Cancer Causes Control. 2005;16(6):691-9.
Exclusion: wrong outcomes.

Davidson AS, Liao X, Magee BD. Attitudes of women in their forties toward the 2009 USPSTF mammogram guidelines: a randomized trial on the effects of media exposure. Am J Obstet Gynecol. 2011;205(1):30.e1-7.
Exclusion: wrong outcomes.

Davis TC, Arnold C, Berkel HJ, et al. Knowledge and attitude on screening mammography among low-literate, low-income women. Cancer. 1996;78(9):1912-20.
Exclusion: studies outside of search dates.

Day N, McCann J, Camilleri-Ferrante C, et al. Monitoring interval cancers in breast screening programmes: the east Anglian experience. Quality Assurance Management Group of the East Anglian Breast Screening Programme. J Med Screen. 1995;2(4):180-5.
Exclusion: wrong outcomes.

Day N, Warren R. Mammographic screening and mammographic patterns. Breast Cancer Res. 2000;2(4):247-51.
Exclusion: wrong publication type.

Day NE. Overdiagnosis and breast cancer screening. Breast Cancer Res. 2005;7(5):228-9.
Exclusion: wrong publication type.

de Gelder R, Bulliard J-L, de Wolf C, et al. Cost-effectiveness of opportunistic versus organised mammography screening in Switzerland. Eur J Cancer. 2009;45(1):127-38.
Exclusion: wrong outcomes.

de Gelder R, Draisma G, Heijnsdijk EAM, et al. Population-based mammography screening below age 50: balancing radiation-induced vs prevented breast cancer deaths. Br J Cancer. 2011;104(7):1214-20.
Exclusion: wrong outcomes.

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de Gelder R, van As E, Tilanus-Linthorst MMA, et al. Breast cancer screening: evidence for false reassurance? Int J Cancer. 2008;123(3):680-6.
Exclusion: studies outside of search dates.

de Glas NA, de Craen AJ, Bastiaannet E, et al. Effect of implementation of the mass breast cancer screening programme in older women in the Netherlands: population based study. BMJ. 2014;349:g5410.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

de Koning HJ. Mammographic screening: evidence from randomised controlled trials. Ann Oncol. 2003;14(8):1185-9.
Exclusion: review not meeting inclusion criteria.

de Koning HJ. Why improvement in survival of screen-detected cases is not necessarily equivalent to benefit? Breast. 2003;12(5):299-301.
Exclusion: wrong publication type.

De P, Neutel CI, Olivotto I, et al. Breast cancer incidence and hormone replacement therapy in Canada. J Natl Cancer Inst. 2010;102(19):1489-95.
Exclusion: wrong comparison.

Dean JC, Ilvento CC. Improved cancer detection using computer-aided detection with diagnostic and screening mammography: prospective study of 104 cancers. AJR Am J Roentgenol. 2006;187(1):20-8.
Exclusion: wrong intervention.

Dean PB. Comments and response on the USPSTF recommendation on screening for breast cancer. Ann Intern Med. 2010;152(8):539; author reply 43-4.
Exclusion: wrong publication type.

Dean PB. The rationale and current controversies of mammographic screening for breast cancer. Scand J Surg. 2002;91(3):288-92.
Exclusion: wrong publication type.

Dee KE, Sickles EA. Medical audit of diagnostic mammography examinations: comparison with screening outcomes obtained concurrently. AJR Am J Roentgenol. 2001;176(3):729-33.
Exclusion: wrong comparison.

DeFrank JT, Rimer BK, Bowling JM, et al. Influence of false-positive mammography results on subsequent screening: do physician recommendations buffer negative effects? J Med Screen. 2012;19(1):35-41.
Exclusion: wrong comparison.

Deglise C, Bouchardy C, Burri M, et al. Impact of obesity on diagnosis and treatment of breast cancer. Breast Cancer Res Treat. 2010;120(1):185-93.
Exclusion: wrong comparison.

del Carmen MG, Hughes KS, Halpern E, et al. Racial differences in mammographic breast density. Cancer. 2003;98(3):590-6.
Exclusion: wrong outcomes.

Del Maschio A, Bazzocchi M, Giuseppetti GM, et al. Breast MRI: report on a multicentric national trial by the Study Section of Magnetic Resonance and Breast Imaging. Radiol Med (Torino). 2002;104(4):262-72.
Exclusion: wrong publication type.

Del Turco MR. A critical review of screening for breast cancer. Recent Results Cancer Res. 1996;140:123-30.
Exclusion: wrong publication type.

Del Turco MR, Mantellini P, Ciatto S, et al. Full-field digital versus screen-film mammography: comparative accuracy in concurrent screening cohorts. AJR Am J Roentgenol. 2007;189(4):860-6.
Exclusion: wrong comparison.

Demicheli R, Bonadonna G, Hrushesky WJM, et al. Menopausal status dependence of early mortality reduction due to diagnosis of smaller breast cancers (T1 v T2-T3): relevance to screening. J Clin Oncol. 2004;22(1):102-7.
Exclusion: wrong population.

Demirci S, Nam J, Hubbs JL, et al. Radiation-induced cardiac toxicity after therapy for breast cancer: interaction between treatment era and follow-up duration. Int J Radiat Oncol Biol Phys. 2009;73(4):980-7.
Exclusion: wrong population.

den Heijer M, Seynaeve C, Vanheusden K, et al. Long-term psychological distress in women at risk for hereditary breast cancer adhering to regular surveillance: a risk profile. Psychooncology. 2013;22(3):598-604.
Exclusion: wrong population.

Dershaw DD. Status of mammography after the Digital Mammography Imaging Screening Trial: digital versus film. Breast J. 2006;12(2):99-102.
Exclusion: wrong publication type.

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Destounis S, Hanson S, Morgan R, et al. Computer-aided detection of breast carcinoma in standard mammographic projections with digital mammography. Int J Comput Assist Radiol Surg. 2009;4(4):331-6.
Exclusion: wrong outcomes.

Destounis SV, Arieno AL, Morgan RC, et al. Comparison of breast cancers diagnosed in screening patients in their 40s with and without family history of breast cancer in a community outpatient facility. AJR American Journal of Roentgenology. 2014;202(4):928-32.
Exclusion: wrong comparison.

Destounis SV, DiNitto P, Logan-Young W, et al. Can computer-aided detection with double reading of screening mammograms help decrease the false-negative rate? Initial experience. Radiology. 2004;232(2):578-84.
Exclusion: wrong intervention.

Deurloo EE, Muller SH, Peterse JL, et al. Clinically and mammographically occult breast lesions on MR images: potential effect of computerized assessment on clinical reading. Radiology. 2005;234(3):693-701.
Exclusion: wrong outcomes.

Devita VT, Jr. Breast cancer screening and mortality. Nat Rev Clin Oncol. 2010;7(2):65.
Exclusion: wrong publication type.

Dibble SL, Israel J, Nussey B, et al. Mammography with breast cushions. Womens Health Issues. 2005;15(2):55-63.
Exclusion: wrong intervention.

Dibble SL, Israel J, Nussey B, et al. Mammography with breast cushions. Women's Health Issues. 2005;15(2):55-63.
Exclusion: included in an included systematic review, not directly used.

Dietzel M, Baltzer PAT, Hopp T, et al. Co-registration of MR-mammography and X-ray mammography. Eur J Radiol. 2012;81 Suppl 1:S27-9.
Exclusion: wrong population.

Dietzel M, Baltzer PAT, Schon K, et al. MR-mammography: high sensitivity but low specificity? New thoughts and fresh data on an old mantra. Eur J Radiol. 2012;81 Suppl 1:S30-2.
Exclusion: wrong intervention.

Dinnes J, Moss S, Melia J, et al. Effectiveness and cost-effectiveness of double reading of mammograms in breast cancer screening: findings of a systematic review. Breast. 2001;10(6):455-63.
Exclusion: wrong outcomes.

Dinshaw K, Mishra G, Shastri S, et al. Determinants of compliance in a cluster randomised controlled trial on screening of breast and cervix cancer in Mumbai, India. 1. Compliance to screening. Oncology. 2007;73(3-4):145-53.
Exclusion: wrong outcomes.

Dinshaw K, Mishra G, Shastri S, et al. Determinants of compliance in a cluster randomised controlled trial on screening of breast and cervix cancer in mumbai, India. 2. Compliance to referral and treatment. Oncology. 2007;73(3-4):154-61.
Exclusion: wrong outcomes.

Diratzouian H, Freedman GM, Hanlon AL, et al. Importance of physical examination in the absence of a mammographic abnormality for the detection of early-stage breast cancer. Clin Breast Cancer. 2005;6(4):330-3.
Exclusion: wrong population.

Dissemination CfRa. Breast cancer diagnosis by scintimammography: a meta-analysis and review of the literature (Structured abstract). Database of Abstracts of Reviews of Effects. 2014(1)
Exclusion: wrong publication type.

Dissemination CfRa. Computer-aided detection (CAD) in mammography (Provisional abstract). Database of Abstracts of Reviews of Effects. 2014(1)
Exclusion: wrong intervention.

Dissemination CfRa. The early detection and diagnosis of breast cancer: a literature review. An update (Structured abstract). Database of Abstracts of Reviews of Effects. 2014(1)
Exclusion: wrong publication type.

Dissemination CfRa. Positron emission tomography: systematic review. PET as a diagnostic test in breast cancer (Structured abstract). Database of Abstracts of Reviews of Effects. 2014(1)
Exclusion: wrong publication type.

Dixon JM, Ravisekar O, Cunningham M, et al. Factors affecting outcome of patients with impalpable breast cancer detected by breast screening. Br J Surg. 1996;83(7):997-1001.
Exclusion: wrong population.

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Djulbegovic B, Hozo I, Lyman GH. Estimating net benefits and harms of screening mammography in women age 40 to 49 years. Ann Intern Med. 2007;147(12):882.
Exclusion: wrong publication type.

Dobson R. Advanced breast cancer more common in area with low uptake of screening. BMJ. 2003;327(7406):72.
Exclusion: wrong publication type.

Dogan L, Kalaylioglu Z, Karaman N, et al. Relationships between epidemiological features and tumor characteristics of breast cancer. Asian Pac J Cancer Prev. 2011;12(12):3375-80.
Exclusion: wrong intervention.

Domingo L, Jacobsen KK, von Euler-Chelpin M, et al. Seventeen-years overview of breast cancer inside and outside screening in Denmark. Acta Oncol. 2013;52(1):48-56.
Exclusion: wrong outcomes.

Domingo L, Romero A, Belvis F, et al. Differences in radiological patterns, tumour characteristics and diagnostic precision between digital mammography and screen-film mammography in four breast cancer screening programmes in Spain. Eur Radiol. 2011;21(9):2020-8.
Exclusion: wrong outcomes.

Domingo L, Romero A, Blanch J, et al. Clinical and radiological features of breast tumors according to history of false-positive results in mammography screening. Cancer epidemiol. 2013;37(5):660-5.
Exclusion: wrong outcomes.

Domingo L, Sala M, Servitja S, et al. Phenotypic characterization and risk factors for interval breast cancers in a population-based breast cancer screening program in Barcelona, Spain. Cancer Causes Control. 2010;21(8):1155-64.
Exclusion: wrong outcomes.

Donnelly J. Breast lump detection: who is more accurate, patients or their GPs? Int J Clin Pract. 2010;64(4):439-41.
Exclusion: wrong intervention.

Doorenbos AZ, Jacobsen C, Corpuz R, et al. A randomized controlled calendar mail-out to increase cancer screening among urban American Indian and Alaska Native patients. J Cancer Educ. 2011;26(3):549-54.
Exclusion: wrong intervention.

Dorrius MD, Jansen-van der Weide MC, van Ooijen PMA, et al. Computer-aided detection in breast MRI: a systematic review and meta-analysis. Eur Radiol. 2011;21(8):1600-8.
Exclusion: wrong outcomes.

Dorum A, Heimdal K, Lovslett K, et al. Prospectively detected cancer in familial breast/ovarian cancer screening. Acta Obstet Gynecol Scand. 1999;78(10):906-11.
Exclusion: wrong comparison.

Douek M, Davidson T, Taylor I. Breast cancer imaging--what are the optimal modalities? Eur J Surg Oncol. 1998;24(6):573-82.
Exclusion: review not meeting inclusion criteria.

Douek M, Tobias J. How reliable is MRI for predicting extent of residual breast cancer with different primary medical therapies? Nat Clin Pract Oncol. 2005;2(3):128-9.
Exclusion: wrong population.

Doyle TC, Elwood JM, Smale P, et al. Clinical outcomes of the Otago-Southland Breast Cancer Screening Programme 1991-1996. N Z Med J. 1998;111(1075):380-3.
Exclusion: wrong comparison.

Driul L, Bernardi S, Bertozzi S, et al. New surgical trends in breast cancer treatment: conservative interventions and oncoplastic breast surgery. Minerva Ginecol. 2013;65(3):289-96.
Exclusion: wrong outcomes.

Drossaert CHC, Boer H, Seydel ER. Does mammographic screening and a negative result affect attitudes towards future breast screening? J Med Screen. 2001;8(4):204-12.
Exclusion: studies outside of search dates.

Drossaert CHC, Boer H, Seydel ER. Does mammographic screening and a negative result affect attitudes towards future breast screening? J Med Screen. 2001;8(4):204-12.
Exclusion: included in an included systematic review, not directly used.

Drossaert CHC, Boer H, Seydel ER. Health education to improve repeat participation in the Dutch breast cancer screening programme: Evaluation of a leaflet tailored to previous participants. Patient Educ Couns. 1996;28(2):121-31.
Exclusion: included in an included systematic review, not directly used.

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Drossaert CHC, Boer H, Seydel ER. Monitoring women's experiences during three rounds of breast cancer screening: Results from a longitudinal study. J Med Screen. 2002;9(4):168-75.
Exclusion: included in an included systematic review, not directly used.

Drukker K, Giger ML, Horsch K, et al. Computerized lesion detection on breast ultrasound. Med Phys. 2002;29(7):1438-46.
Exclusion: wrong outcomes.

Drukker K, Giger ML, Mendelson EB. Computerized analysis of shadowing on breast ultrasound for improved lesion detection. Med Phys. 2003;30(7):1833-42.
Exclusion: wrong outcomes.

Drukker K, Gruszauskas NP, Sennett CA, et al. Breast US computer-aided diagnosis workstation: performance with a large clinical diagnostic population. Radiology. 2008;248(2):392-7.
Exclusion: wrong intervention.

Drukker K, Horsch KJ, Pesce LL, et al. Interreader scoring variability in an observer study using dual-modality imaging for breast cancer detection in women with dense breasts. Acad Radiol. 2013;20(7):847-53.
Exclusion: wrong outcomes.

Drukker K, Sennett CA, Giger ML. Computerized detection of breast cancer on automated breast ultrasound imaging of women with dense breasts. Med Phys. 2014;41(1):012901.
Exclusion: wrong outcomes.

Drukteinis JS, Mooney BP, Flowers CI, et al. Beyond mammography: new frontiers in breast cancer screening. Am J Med. 2013;126(6):472-9.
Exclusion: wrong publication type.

DuBard CA, Schmid D, Yow A, et al. Recommendation for and receipt of cancer screenings among medicaid recipients 50 years and older. Arch Intern Med. 2008;168(18):2014-21.
Exclusion: wrong outcomes.

Duffy S, Blamey RW. The UKCCCR trial of the frequency of breast cancer screening [abstract]. Eur J Cancer. 2003;1(46)
Exclusion: wrong publication type.

Duffy SW. Lymph node status in screen-detected cancers. Br J Cancer. 2005;92(1):3-4.
Exclusion: wrong publication type.

Duffy SW. Some current issues in breast cancer screening. J Med Screen. 2005;12(3):128-33.
Exclusion: wrong publication type.

Duffy SW, Chen HH, Tabár L, et al. Sojourn time, sensitivity and positive predictive value of mammography screening for breast cancer in women aged 40-49. Int J Epidemiol. 1996;25(6):1139-45.
Exclusion: wrong outcomes.

Duffy SW, Lynge E, Jonsson H, et al. Complexities in the estimation of overdiagnosis in breast cancer screening. Br J Cancer. 2008;99(7):1176-8.
Exclusion: wrong study design for key question.

Duffy SW, Mackay J, Thomas S, et al. Evaluation of mammographic surveillance services in women aged 40-49 years with a moderate family history of breast cancer: a single-arm cohort study. Health Technol Assess. 2013;17(11):vii-xiv, 1-95.
Exclusion: wrong intervention.

Duffy SW, Michalopoulos D, Sebuodegard S, et al. Trends in aggregate cancer incidence rates in relation to screening and possible overdiagnosis: a word of caution. J Med Screen. 2014;21(1):24-9.
Exclusion: wrong outcomes.

Duffy SW, Nagtegaal ID, Wallis M, et al. Correcting for lead time and length bias in estimating the effect of screen detection on cancer survival. Am J Epidemiol. 2008;168(1):98-104.
Exclusion: wrong study design for key question.

Duffy SW, Sasieni P, Olsen AH, et al. Modelling the likely effect of the increase of the upper age limit from 70 to 73 for breast screening in the UK National Programme. Stat Methods Med Res. 2010;19(5):547-55.
Exclusion: wrong study design for key question.

Duffy SW, Smith RA, Gabe R, et al. Screening for breast cancer. Surg Oncol Clin N Am. 2005;14(4):671-97.
Exclusion: review not meeting inclusion criteria.

Duffy SW, Smith RA, Tabár L. Re: Efficacy of breast cancer screening in the community according to risk level. J Natl Cancer Inst. 2005;97(22):1703; author reply -4.
Exclusion: wrong publication type.

Duffy SW, Tabár L, Chen H-H, et al. The impact of organized mammography service screening on breast carcinoma mortality in seven Swedish counties. Cancer. 2002;95(3):458-69.

Exclusion: wrong intervention.

Duffy SW, Tabár L, Vitak B, et al. The relative contributions of screen-detected in situ and invasive breast carcinomas in reducing mortality from the disease. Eur J Cancer. 2003;39(12):1755-60.
Exclusion: wrong study design for key question.

Duffy SW, Tabár L, Vitak B, et al. Tumor size and breast cancer detection: what might be the effect of a less sensitive screening tool than mammography? Breast J. 2006;12 Suppl 1:S91-5.
Exclusion: wrong study design for key question.

Duffy SW, Yen AM-F, Chen TH-H, et al. Long-term benefits of breast screening. Breast Cancer Management. 2012;1(1):31-8.
Exclusion: review not meeting inclusion criteria.

Duffy SW MJ, Thomas S, Anderson E, et al. Evaluation of mammographic surveillance services in women aged 40-49 years with a moderate family history of breast cancer: a single-arm cohort study. Health technology assessment (Winchester, England). 2013;17(11):vii-xiv.
Exclusion: wrong comparison.

Duijm LEM, Groenewoud JH, de Koning HJ, et al. Delayed diagnosis of breast cancer in women recalled for suspicious screening mammography. Eur J Cancer. 2009;45(5):774-81.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Duijm LEM, Groenewoud JH, Fracheboud J, et al. Introduction of additional double reading of mammograms by radiographers: effects on a biennial screening programme outcome. Eur J Cancer. 2008;44(9):1223-8.
Exclusion: wrong outcomes.

Duijm LEM, Groenewoud JH, Jansen FH, et al. Mammography screening in the Netherlands: delay in the diagnosis of breast cancer after breast cancer screening. Br J Cancer. 2004;91(10):1795-9.
Exclusion: wrong comparison.

Duijm LEM, Groenewoud JH, Roumen RMH, et al. A decade of breast cancer screening in The Netherlands: trends in the preoperative diagnosis of breast cancer. Breast Cancer Res Treat. 2007;106(1):113-9.
Exclusion: wrong outcomes.

Duijm LEM, Louwman MWJ, Groenewoud JH, et al. Inter-observer variability in mammography screening and effect of type and number of readers on screening outcome. Br J Cancer. 2009;100(6):901-7.
Exclusion: wrong outcomes.

Dullum JR, Lewis EC, Mayer JA. Rates and correlates of discomfort associated with mammography. Radiology. 2000;214(2):547-52.
Exclusion: included in an included systematic review, not directly used.

Dumane VA, Shankar PM, Piccoli CW, et al. Computer aided classification of masses in ultrasonic mammography. Med Phys. 2002;29(9):1968-73.
Exclusion: wrong outcomes.

Dummin LJ, Cox M, Plant L. Prediction of breast tumor size by mammography and sonography--A breast screen experience. Breast. 2007;16(1):38-46.
Exclusion: wrong outcomes.

Duncan AM. The role of nutrition in the prevention of breast cancer. AACN Clin Issues. 2004;15(1):119-35.
Exclusion: review not meeting inclusion criteria.

Dunn NAM. Effect of false-positive screening mammograms on rescreening in Western Australia. Med J Aust. 2012;197(9):490-1.
Exclusion: wrong publication type.

Duric N, Boyd N, Littrup P, et al. Breast density measurements with ultrasound tomography: a comparison with film and digital mammography. Med Phys. 2013;40(1):013501.
Exclusion: wrong intervention.

Eddy DM, Hasselblad V, McGivney W, et al. The value of mammography screening in women under age 50 years. JAMA. 1988;259(10):1512-9.
Exclusion: wrong study design for key question.

Edge SB. Advances in breast surgery, 2002-2012. J. 2013;11(1):53-9.
Exclusion: review not meeting inclusion criteria.

Ei Khouli RH, Jacobs MA, Mezban SD, et al. Diffusion-weighted imaging improves the diagnostic accuracy of conventional 3.0-T breast MR imaging. Radiology. 2010;256(1):64-73.
Exclusion: wrong outcomes.

Ekeberg Ø, Skjauff H, Kåresen R. Screening for breast cancer is associated with a low degree of psychological distress. Breast. 2001;10(1):20-4.

Exclusion: included in an included systematic review, not directly used.

Ekeh AP, Alleyne RS, Duncan AO. Role of mammography in diagnosis of breast cancer in an inner-city hospital. J Natl Med Assoc. 2000;92(8):372-4.
Exclusion: wrong comparison.

Ekwueme DU, Hall IJ, Richardson LC, et al. Estimating personal costs incurred by a woman participating in mammography screening in the National Breast and Cervical Cancer Early Detection Program. Cancer. 2008;113(3):592-601.
Exclusion: wrong outcomes.

Elena PM, Nehmat H, Ermes M, et al. Quality of mammography screening in the Milan programme: evidence of improved sensitivity based on interval cancer proportional incidence and radiological review. Breast. 2009;18(3):208-10.
Exclusion: wrong comparison.

Ellis RL, Meade AA, Mathiason MA, et al. Evaluation of computer-aided detection systems in the detection of small invasive breast carcinoma. Radiology. 2007;245(1):88-94.
Exclusion: wrong intervention.

Ellman R, Angeli N, Christians A, et al. Psychiatric morbidity associated with screening for breast cancer. Br J Cancer. 1989;60(5):781-4.
Exclusion: included in an included systematic review, not directly used.

Elmore JG, Carney PA. Does practice make perfect when interpreting mammography? J Natl Cancer Inst. 2002;94(5):321-3.
Exclusion: wrong publication type.

Elmore JG, Carney PA, Abraham LA, et al. The association between obesity and screening mammography accuracy. Arch Intern Med. 2004;164(10):1140-7.
Exclusion: studies outside of search dates.

Elmore JG, Fletcher SW. Overdiagnosis in breast cancer screening: time to tackle an underappreciated harm. Ann Intern Med. 2012;156(7):536-7.
Exclusion: wrong publication type.

Elmore JG, Fletcher SW. The risk of cancer risk prediction: "What is my risk of getting breast cancer"? J Natl Cancer Inst. 2006;98(23):1673-5.
Exclusion: wrong publication type.

Elmore JG, Jackson SL, Abraham L, et al. Variability in interpretive performance at screening mammography and radiologists' characteristics associated with accuracy. Radiology. 2009;253(3):641-51.
Exclusion: wrong comparison.

Elmore JG, Reisch LM, Barton MB, et al. Efficacy of breast cancer screening in the community according to risk level. J Natl Cancer Inst. 2005;97(14):1035-43.
Exclusion: wrong outcomes.

Elsamaloty H, Elzawawi MS, Mohammad S, et al. Increasing accuracy of detection of breast cancer with 3-T MRI. AJR Am J Roentgenol. 2009;192(4):1142-8.
Exclusion: wrong population.

Elting LS, Cooksley CD, Bekele BN, et al. Mammography capacity impact on screening rates and breast cancer stage at diagnosis. Am J Prev Med. 2009;37(2):102-8.
Exclusion: wrong outcomes.

Eltonsy NH, Tourassi GD, Fadeev A, et al. Significance of MPEG-7 textural features for improved mass detection in mammography. Conf Proc IEEE Eng Med Biol Soc. 2006;1:4779-82.
Exclusion: wrong study design for key question.

Emaus M VW, Bakker M, Monninkhof E, et al. Design of the DENSE trial: MRI as an additional screening modality to detect breast cancer in women aged 50-75 years with extremely dense breasts. Cancer Prev Res (Phila). 2012;5(11 SUPPL. 1):Oct 16 to Oct 19, 2012.
Exclusion: wrong publication type.

Engelken F, Bremme R, Bick U, et al. Factors affecting the rate of false positive marks in CAD in full-field digital mammography. Eur J Radiol. 2012;81(8):e844-8.
Exclusion: wrong study design for key question.

Engelman KK, Cupertino AP, Daley CM, et al. Engaging diverse underserved communities to bridge the mammography divide. BMC Public Health. 2011;11(47)
Exclusion: wrong publication type.

Erbas B, Amos A, Fletcher A, et al. Incidence of invasive breast cancer and ductal carcinoma in situ in a screening program by age: should older women continue screening? Cancer Epidemiol Biomarkers Prev. 2004;13(10):1569-73.

Exclusion: wrong study design for key question.

Erbas B, Provenzano E, Armes J, et al. The natural history of ductal carcinoma in situ of the breast: a review. Breast Cancer Res Treat. 2006;97(2):135-44.
Exclusion: wrong study design for key question.

Eriksson L, Czene K, Rosenberg L, et al. The influence of mammographic density on breast tumor characteristics. Breast Cancer Res Treat. 2012;134(2):859-66.
Exclusion: wrong comparison.

Ernst MF, Voogd AC, Coebergh JWW, et al. Breast carcinoma diagnosis, treatment, and prognosis before and after the introduction of mass mammographic screening. Cancer. 2004;100(7):1337-44.
Exclusion: wrong study design for key question.

Ernster VL. Screening mammography for women under 50: considerations for fully informed decision making. Womens Health. 1996;2(4):257-60; discussion 61-6.
Exclusion: wrong publication type.

Ernster VL, Ballard-Barbash R, Barlow WE, et al. Detection of ductal carcinoma in situ in women undergoing screening mammography. J Natl Cancer Inst. 2002;94(20):1546-54.
Exclusion: wrong intervention.

Erpeldinger S, Fayolle L, Boussageon R, et al. Is there excess mortality in women screened with mammography: a meta-analysis of non-breast cancer mortality. Trials. 2013;14:368.
Exclusion: wrong outcomes.

Escobedo LG, Zhong Z, Key C. Breast and cervical cancer screening and disease incidence and stage in New Mexico. Cancer Causes Control. 2002;13(2):137-45.
Exclusion: wrong outcomes.

Esserman L, Cowley H, Eberle C, et al. Improving the accuracy of mammography: volume and outcome relationships. J Natl Cancer Inst. 2002;94(5):369-75.
Exclusion: wrong outcomes.

Esserman LJ, Shieh Y, Rutgers EJT, et al. Impact of mammographic screening on the detection of good and poor prognosis breast cancers. Breast Cancer Res Treat. 2011;130(3):725-34.
Exclusion: wrong population.

Esserman LJ, Thompson IM, Jr., Reid B. Overdiagnosis and overtreatment in cancer: an opportunity for improvement. JAMA. 2013;310(8):797-8.
Exclusion: wrong publication type.

Esserman LJ, Thompson IM, Reid B, et al. Addressing overdiagnosis and overtreatment in cancer: a prescription for change. Lancet Oncol. 2014;15(6):e234-e42.
Exclusion: wrong publication type.

Esteve J, Seradour B, Jacquemier J, et al. Does a better grade of tumour occurring in women under hormone replacement therapy compensate for their lower probability of detection by screening mammography. J Med Screen. 2002;9(2):70-3.
Exclusion: wrong comparison.

Etim AE-EP, Schellhase KG, Sparapani R, et al. Effect of model of care delivery on mammography use among elderly breast cancer survivors. Breast Cancer Res Treat. 2006;96(3):293-9.
Exclusion: wrong population.

Etzioni R, Gulati R, Mallinger L, et al. Influence of study features and methods on overdiagnosis estimates in breast and prostate cancer screening. Ann Intern Med. 2013;158(11):831-8.
Exclusion: wrong outcomes.

Etzioni RD, Weiss NS. Analysis of case-control studies of screening: impact of misspecifying the duration of detectable preclinical pathologic changes. Am J Epidemiol. 1998;148(3):292-7.
Exclusion: wrong study design for key question.

Evans A. Hormone replacement therapy and mammographic screening. Clin Radiol. 2002;57(7):563-4.
Exclusion: review not meeting inclusion criteria.

Evans AJ, Kutt E, Record C, et al. Radiological and pathological findings of interval cancers in a multi-centre, randomized, controlled trial of mammographic screening in women from age 40-41 years. Clin Radiol. 2007;62(4):348-52.
Exclusion: wrong outcomes.

Evans AJ, Kutt E, Record C, et al. Radiological findings of screen-detected cancers in a multi-centre randomized, controlled trial of mammographic screening in women from age 40 to 48 years. Clin Radiol. 2006;61(9):784-8.
Exclusion: wrong outcomes.

Appendix A4. List of Excluded Studies

Evans WP. Breast cancer screening: successes and challenges. CA Cancer J Clin. 2012;62(1):5-9.
Exclusion: wrong publication type.

Everington D, Gilbert FJ, Tyack C, et al. The Scottish breast screening programme's experience of monitoring interval cancers. J Med Screen. 1999;6(1):21-7.
Exclusion: wrong outcomes.

Exbrayat C, Garnier A, Colonna M, et al. Analysis and classification of interval cancers in a French breast cancer screening programme (departement of Isere). Eur J Cancer Prev. 1999;8(3):255-60.
Exclusion: wrong comparison.

Fair AM, Monahan PO, Russell K, et al. The interaction of perceived risk and benefits and the relationship to predicting mammography adherence in African American women. Oncol Nurs Forum. 2012;39(1):53-60.
Exclusion: wrong comparison.

Falk RS, Hofvind S, Skaane P. Overdiagnosis of Invasive Breast Cancer due to Mammography Screening. Ann Intern Med. 2012;157(3):219; author reply 21-2.
Exclusion: wrong publication type.

Fantini S, Heffer EL, Pera VE, et al. Spatial and spectral information in optical mammography. Technol Cancer Res Treat. 2005;4(5):471-82.
Exclusion: wrong study design for key question.

Farham B. Screening--benefits or harms? S Afr Med J. 2013;Suid-Afrikaanse Tydskrif Vir Geneeskunde. 103(5):270-1.
Exclusion: wrong publication type.

Fasching PA, Heusinger K, Loehberg CR, et al. Influence of mammographic density on the diagnostic accuracy of tumor size assessment and association with breast cancer tumor characteristics. Eur J Radiol. 2006;60(3):398-404.
Exclusion: wrong outcomes.

Faulk RM, Sickles EA, Sollitto RA, et al. Clinical efficacy of mammographic screening in the elderly. Radiology. 1995;194(1):193-7.
Exclusion: studies outside of search dates.

Faulkner K, McCormack S, Bennison K. A retrospective analysis of digital stereotaxis in breast screening. Br J Radiol. 2007;80(955):563-8.
Exclusion: wrong intervention.

Fausto A, Casella D, Mantovani L, et al. Clinical value of second-look ultrasound: is there a way to make it objective? Eur J Radiol. 2012;81 Suppl 1:S36-40.
Exclusion: wrong intervention.

Feeley L, Kiernan D, Mooney T, et al. Digital mammography in a screening programme and its implications for pathology: a comparative study. J Clin Pathol. 2011;64(3):215-9.
Exclusion: wrong comparison.

Feig SA. Age-related accuracy of screening mammography: how should it be measured? Radiology. 2000;214(3):633-40.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Feig SA. Auditing and benchmarks in screening and diagnostic mammography. Radiol Clin North Am. 2007;45(5):791-800.
Exclusion: review not meeting inclusion criteria.

Feig SA. Current status of screening mammography. Obstet Gynecol Clin North Am. 2002;29(1):123-36.
Exclusion: wrong publication type.

Feig SA. Image quality of screening mammography: effect on clinical outcome. AJR Am J Roentgenol. 2002;178(4):805-7.
Exclusion: wrong publication type.

Feig SA. Increased benefit from shorter screening mammography intervals for women ages 40-49 years. Cancer. 1997;80(11):2035-9.
Exclusion: review not meeting inclusion criteria.

Feig SA. Methods to identify benefit from mammographic screening of women aged 40-49 years. Radiology. 1996;201(2):309-16.
Exclusion: wrong publication type.

Feig SA. Number needed to screen: appropriate use of this new basis for screening mammography guidelines. AJR Am J Roentgenol. 2012;198(5):1214-7.
Exclusion: wrong publication type.

Feig SA. Overdiagnosis of Invasive Breast Cancer and DCIS: Why Do Estimates Vary? Breast Diseases: A Year Book Quarterly. 2014;25(3):196-201.
Exclusion: wrong publication type.

Feig SA. Role and evaluation of mammography and other imaging methods for breast cancer detection, diagnosis, and staging. Semin Nucl Med. 1999;29(1):3-15.
Exclusion: review not meeting inclusion criteria.

Feig SA. Screening mammography controversies: resolved, partly resolved, and unresolved. Breast J. 2005;11 Suppl 1:S3-6.
Exclusion: wrong publication type.

Feig SA, Hendrick RE. Radiation risk from screening mammography of women aged 40-49 years. J Natl Cancer Inst. 1997;Monographs.(22):119-24.
Exclusion: wrong outcomes.

Feigelson HS, Henderson BE, Pike MC. Re: Recent trends in U.S. breast cancer incidence, survival, and mortality rates. J Natl Cancer Inst. 1997;89(23):1810-2.
Exclusion: wrong study design for key question.

Fenton A, Panay N. Breast cancer screening--when do we start and how often should it be done? Climacteric. 2011;14(5):513-4.
Exclusion: wrong publication type.

Fenton JJ, Abraham L, Taplin SH, et al. Effectiveness of computer-aided detection in community mammography practice. J Natl Cancer Inst. 2011;103(15):1152-61.
Exclusion: wrong intervention.

Fenton JJ, Barton MB, Geiger AM, et al. Screening clinical breast examination: how often does it miss lethal breast cancer? J Natl Cancer Inst. 2005;Monographs.(35):67-71.
Exclusion: wrong intervention.

Fenton JJ, Rolnick SJ, Harris EL, et al. Specificity of clinical breast examination in community practice. J Gen Intern Med. 2007;22(3):332-7.
Exclusion: wrong intervention.

Fenton JJ, Taplin SH, Carney PA, et al. Influence of computer-aided detection on performance of screening mammography. N Engl J Med. 2007;356(14):1399-409.
Exclusion: wrong outcomes.

Fenton JJ, Xing G, Elmore JG, et al. Short-term outcomes of screening mammography using computer-aided detection: a population-based study of medicare enrollees. Ann Intern Med. 2013;158(8):580-7.
Exclusion: wrong comparison.

Ferrante JM, Chen P-H, Kim S. The effect of patient navigation on time to diagnosis, anxiety, and satisfaction in urban minority women with abnormal mammograms: a randomized controlled trial. J Urban Health. 2008;85(1):114-24.
Exclusion: wrong population.

Ferrer S, Ramos M, Villaescusa JI, et al. Modelling of the mammographic exposure conditions for radiological detriment study in the Valencian Breast Cancer Screening Programme. Radiat Prot Dosimetry. 2005;116(1-4 Pt 2):396-400.
Exclusion: wrong study design for key question.

Fett MJ. Computer modelling of the Swedish two county trial of mammographic screening and trade offs between participation and screening interval. J Med Screen. 2001;8(1):39-45.
Exclusion: wrong study design for key question.

Feuer EJ. Modeling the impact of adjuvant therapy and screening mammography on U.S. breast cancer mortality between 1975 and 2000: introduction to the problem. J Natl Cancer Inst. 2006;Monographs.(36):2-6.
Exclusion: wrong study design for key question.

Feuer EJ, Etzioni R, Cronin KA, et al. The use of modeling to understand the impact of screening on U.S. mortality: examples from mammography and PSA testing. Stat Methods Med Res. 2004;13(6):421-42.
Exclusion: wrong study design for key question.

Field LR, Wilson TE, Strawderman M, et al. Mammographic screening in women more than 64 years old: a comparison of 1- and 2-year intervals. AJR Am J Roentgenol. 1998;170(4):961-5.
Exclusion: wrong comparison.

Fielder H, Rogers C, Gower-Thomas K, et al. Results from 10 years of breast screening in Wales. J Med Screen. 2001;8(1):21-3.
Exclusion: wrong comparison.

Fielder HM, Warwick J, Brook D, et al. A case-control study to estimate the impact on breast cancer death of the breast screening programme in Wales. J Med Screen. 2004;11(4):194-8.
Exclusion: included in an included systematic review, not directly used.

Filippini L, Braga M, Perna E, et al. Results of a mammographic and clinical screening in a health district (USSL) of Brescia, Italy. Tumori. 1996;82(5):430-6.

Appendix A4. List of Excluded Studies

Exclusion: wrong study design for key question.

Finucane TE. Cost-effectiveness of mammography for older women. Ann Intern Med. 2004;140(10):844; author reply
Exclusion: wrong publication type.

Fischer DR, Wurdinger S, Boettcher J, et al. Further signs in the evaluation of magnetic resonance mammography: a retrospective study. Invest Radiol. 2005;40(7):430-5.
Exclusion: wrong outcomes.

Fischmann A, Siegmann KC, Wersebe A, et al. Comparison of full-field digital mammography and film-screen mammography: image quality and lesion detection. Br J Radiol. 2005;78(928):312-5.
Exclusion: wrong study design for key question.

Fisher B, Costantino JP, Wickerham DL, et al. Tamoxifen for Prevention of Breast Cancer: Report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. J Natl Cancer Inst. 1998;90(18):1371-88.
Exclusion: wrong intervention.

Fisher TJ, Kirk J, Hopper JL, et al. A simple tool for identifying unaffected women at a moderately increased or potentially high risk of breast cancer based on their family history. Breast. 2003;12(2):120-7.
Exclusion: wrong outcomes.

Fitzgerald A, Berentson-Shaw J. Thermography as a screening and diagnostic tool: a systematic review. N Z Med J. 2012;125(1351):80-91.
Exclusion: wrong intervention.

Flamm CR, Ziegler KM, Aronson N. Technology Evaluation Center assessment synopsis: use of magnetic resonance imaging to avoid a biopsy in women with suspicious primary breast lesions. J Am Coll Radiol. 2005;2(6):485-7.
Exclusion: studies outside of search dates.

Flegg KM, Flaherty JJ, Bicknell AM, et al. Surgical outcomes of borderline breast lesions detected by needle biopsy in a breast screening program. World J Surg Oncol. 2010;8:78.
Exclusion: wrong outcomes.

Fleming RM, Dooley WC. Breast enhanced scintigraphy testing distinguishes between normal, inflammatory breast changes, and breast cancer: a prospective analysis and comparison with mammography. Integ Cancer Ther. 2002;1(3):238-45.
Exclusion: wrong intervention.

Fletcher SW. Breast cancer screening among women in their forties: an overview of the issues. J Natl Cancer Inst. 1997;Monographs.(22):5-9.
Exclusion: review not meeting inclusion criteria.

Fletcher SW. Breast cancer screening: a 35-year perspective. Epidemiol Rev. 2011;33(1):165-75.
Exclusion: review not meeting inclusion criteria.

Fletcher SW, Elmore JG. Clinical practice. Mammographic screening for breast cancer. N Engl J Med. 2003;348(17):1672-80.
Exclusion: review not meeting inclusion criteria.

Flobbe K, Bosch AM, Kessels AGH, et al. The additional diagnostic value of ultrasonography in the diagnosis of breast cancer. Arch Intern Med. 2003;163(10):1194-9.
Exclusion: wrong population.

Flobbe K, Nelemans PJ, Kessels AGH, et al. The role of ultrasonography as an adjunct to mammography in the detection of breast cancer. a systematic review. Eur J Cancer. 2002;38(8):1044-50.
Exclusion: wrong outcomes.

Flowers CI, O'Donoghue C, Moore D, et al. Reducing false-positive biopsies: a pilot study to reduce benign biopsy rates for BI-RADS 4A/B assessments through testing risk stratification and new thresholds for intervention. Breast Cancer Res Treat. 2013;139(3):769-77.
Exclusion: wrong intervention.

Foca F, Mancini S, Bucchi L, et al. Decreasing incidence of late-stage breast cancer after the introduction of organized mammography screening in Italy. Cancer. 2013;119(11):2022-8.
Exclusion: wrong outcomes.

Fontenoy A-M, Langlois A, Chang S-L, et al. Contribution and performance of mobile units in an organized mammography screening program. Can J Public Health. 2013;Revue Canadienne de Sante Publique. 104(3):e193-9.
Exclusion: wrong outcomes.

Appendix A4. List of Excluded Studies

Forastero C, Zamora LI, Guirado D, et al. A Monte Carlo tool to simulate breast cancer screening programmes. Phys Med Biol. 2010;55(17):5213-29.
Exclusion: wrong study design for key question.

Forbes LJ, Linsell L, Atkins L, et al. A promoting early presentation intervention increases breast cancer awareness in older women after 2 years: a randomised controlled trial. Br J Cancer. 2011;105(1):18-21.
Exclusion: wrong intervention.

Ford K, Marcus E, Lum B. Breast cancer screening, diagnosis, and treatment. Dis Mon. 1999;45(9):333-405.
Exclusion: review not meeting inclusion criteria.

Foster KR. Thermographic detection of breast cancer. IEEE Eng Med Biol Mag. 1998;17(6):10-4.
Exclusion: wrong publication type.

Foster RS, Jr. Primary breast cancer: opportunities and problems in detection and treatment. J Med Assoc Ga. 1997;86(3):197-200.
Exclusion: wrong publication type.

Fracheboud J, de Koning HJ, Beemsterboer PM, et al. Nation-wide breast cancer screening in The Netherlands: results of initial and subsequent screening 1990-1995. National Evaluation Team for Breast Cancer Screening. Int J Cancer. 1998;75(5):694-8.
Exclusion: wrong study design for key question.

Fracheboud J, de Koning HJ, Beemsterboer PM, et al. Interval cancers in the Dutch breast cancer screening programme. Br J Cancer. 1999;81(5):912-7.
Exclusion: wrong outcomes.

Fracheboud J, Groenewoud JH, Boer R, et al. Seventy-five years is an appropriate upper age limit for population-based mammography screening. Int J Cancer. 2006;118(8):2020-5.
Exclusion: wrong comparison.

Fracheboud J, Otto SJ, van Dijck JAAM, et al. Decreased rates of advanced breast cancer due to mammography screening in The Netherlands. Br J Cancer. 2004;91(5):861-7.
Exclusion: wrong outcomes.

Frede TE. Opportunistic breast cancer early detection in Tyrol, Austria 1996-2004. Is a mammography-screening program necessary? Eur J Radiol. 2005;55(1):130-8.
Exclusion: wrong comparison.

Freedman DA, Petitti DB, Robins JM. On the efficacy of screening for breast cancer. Int J Epidemiol. 2004;33(1):43-55.
Exclusion: wrong publication type.

Freedman GM, Anderson PR, Goldstein LJ, et al. Routine mammography is associated with earlier stage disease and greater eligibility for breast conservation in breast carcinoma patients age 40 years and older. Cancer. 2003;98(5):918-25.
Exclusion: wrong comparison.

Freeman JL, Goodwin JS, Zhang D, et al. Measuring the performance of screening mammography in community practice with Medicare claims data. Women Health. 2003;37(2):1-15.
Exclusion: wrong study design for key question.

Freer TW, Ulissey MJ. Screening mammography with computer-aided detection: prospective study of 12,860 patients in a community breast center. Radiology. 2001;220(3):781-6.
Exclusion: wrong study design for key question.

Friedenreich CM, Bryant HE, Courneya KS. Case-control study of lifetime physical activity and breast cancer risk. Am J Epidemiol. 2001;154(4):336-47.
Exclusion: wrong outcomes.

Frisell J, Eklund G, Hellström L, et al. The Stockholm breast cancer screening trial - 5-year results and stage at discovery. Breast Cancer Res Treat. 1989;13(1):79-87.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Frisell J, Glas U, Hellstrom L, et al. Randomized mammographic screening for breast cancer in Stockholm. Design, first round results and comparisons. Breast Cancer Res Treat. 1986;8(1):45-54.
Exclusion: studies outside of search dates.

Frost FJ, Tollestrup K, Trinkaus KM, et al. Mammography screening and breast cancer tumor size in female members of a managed care organization. Cancer Epidemiol Biomarkers Prev. 1998;7(7):585-9.
Exclusion: wrong comparison.

Fuglede N, Langballe O, Svendsen AL, et al. Development in incidence of breast cancer in non-screened Danish women, 1973-2002--a population-based study. Int J Cancer. 2006;118(9):2366-9.
Exclusion: wrong outcomes.

Fulton JP, Chiaverini L, Darcy DM. Progress in the control of female breast cancer in Rhode Island, 1987-2000. Med Health R I. 2002;85(6):192-3.
Exclusion: wrong outcomes.

Fulton JP, Darcy D. Progress in the early identification of breast cancer, Rhode Island, 1987-1998. Med Health R I. 2000;83(4):121-2.
Exclusion: wrong publication type.

Furman-Haran E, Eyal E, Shapiro-Feinberg M, et al. Advantages and drawbacks of breast DTI. Eur J Radiol. 2012;81 Suppl 1:S45-7.
Exclusion: wrong intervention.

Fyles AW, McCready DR, Manchul LA, et al. Tamoxifen with or without Breast Irradiation in Women 50 Years of Age or Older with Early Breast Cancer. N Engl J Med. 2004;351(10):963-70.
Exclusion: wrong intervention.

Gabe R, Duffy SW. Evaluation of service screening mammography in practice: the impact on breast cancer mortality. Ann Oncol. 2005;16 Suppl 2:ii153-62.
Exclusion: review not meeting inclusion criteria.

Gabe R, Tryggvadottir L, Sigfusson BF, et al. A case-control study to estimate the impact of the Icelandic population-based mammography screening program on breast cancer death. Acta Radiol. 2007;48(9):948-55.
Exclusion: included in an included systematic review, not directly used.

Gabram SGA, Lund MJB, Gardner J, et al. Effects of an outreach and internal navigation program on breast cancer diagnosis in an urban cancer center with a large African-American population. Cancer. 2008;113(3):602-7.
Exclusion: wrong intervention.

Galit W, Green MS, Lital K-B. Routine screening mammography in women older than 74 years: a review of the available data. Maturitas. 2007;57(2):109-19.
Exclusion: review not meeting inclusion criteria.

Gallagher TH, Cook AJ, Brenner RJ, et al. Disclosing harmful mammography errors to patients. Radiology. 2009;253(2):443-52.
Exclusion: wrong outcomes.

Ganry OF, Peng J, Raverdy NL, et al. Interval cancers in a French breast cancer-screening programme (Somme Department). Eur J Cancer Prev. 2001;10(3):269-74.
Exclusion: wrong outcomes.

Ganz PA, Land SR, Geyer CE, Jr., et al. Menstrual history and quality-of-life outcomes in women with node-positive breast cancer treated with adjuvant therapy on the NSABP B-30 trial. J Clin Oncol. 2011;29(9):1110-6.
Exclusion: wrong intervention.

Gao F, Chia K-S, Ng F-C, et al. Interval cancers following breast cancer screening in Singaporean women. Int J Cancer. 2002;101(5):475-9.
Exclusion: wrong outcomes.

Garcia-Manero M, Royo MP, Espinos J, et al. Pregnancy associated breast cancer. Eur J Surg Oncol. 2009;35(2):215-8.
Exclusion: wrong population.

Garcia-Manso A, Garcia-Orellana CJ, Gonzalez-Velasco HM, et al. Study of the effect of breast tissue density on detection of masses in mammograms. Comput Math Methods Med. 2013;2013:213794.
Exclusion: wrong study design for key question.

Garfinkel L, Boring CC, Heath CW, Jr. Changing trends. An overview of breast cancer incidence and mortality. Cancer. 1994;74(1 Suppl):222-7.
Exclusion: wrong publication type.

Garg AS, Rapelyea JA, Rechtman LR, et al. Full-field digital mammographic interpretation with prior analog versus prior digitized analog mammography: time for interpretation. AJR Am J Roentgenol. 2011;196(6):1436-8.
Exclusion: wrong outcomes.

Garne JP, Aspegren K, Balldin G, et al. Increasing incidence of and declining mortality from breast carcinoma. Trends in Malmö, Sweden, 1961-1992. Cancer. 1997;79(1):69-74.
Exclusion: wrong population.

Garnick MB. Screening and detection of breast cancer and prostate cancer. JAMA. 2010;303(11):1033; author reply -4.
Exclusion: wrong publication type.

Appendix A4. List of Excluded Studies

Gartlehner G, Thaler K, Chapman A, et al. Mammography in combination with breast ultrasonography versus mammography for breast cancer screening in women at average risk. Cochrane Database Syst Rev. 2013;4:CD009632.
Exclusion: wrong intervention.

Gartlehner G, Thaler KJ, Chapman A, et al. Adjunct ultrasonography for breast cancer screening in women at average risk: a systematic review. International Journal of Evidence-Based Healthcare. 2013;11(2):87-93.
Exclusion: wrong intervention.

Garvican L, Littlejohns P. Comparison of prognostic and socio-economic factors in screen-detected and symptomatic cases of breast cancer. Public Health. 1998;112(1):15-20.
Exclusion: wrong intervention.

Gaudette LA, Silberberger C, Altmayer CA, et al. Trends in breast cancer incidence and mortality. Health reports / Statistics Canada, Canadian Centre for Health Information = Rapports sur la santé / Statistique Canada, Centre canadien d'information sur la santé. 1996;8(2):29-37.
Exclusion: wrong study design for key question.

Gayde C, Goolam I, Bangash HK, et al. Outcome of mammography in women with large breasts. Breast. 2012;21(4):493-8.
Exclusion: wrong outcomes.

Ge J, Hadjiiski LM, Sahiner B, et al. Computer-aided detection system for clustered microcalcifications: comparison of performance on full-field digital mammograms and digitized screen-film mammograms. Phys Med Biol. 2007;52(4):981-1000.
Exclusion: wrong intervention.

Gelfand AE, Wang F. Modelling the cumulative risk for a false-positive under repeated screening events. Stat Med. 2000;19(14):1865-79.
Exclusion: wrong study design for key question.

Geller BM, Vacek PM, Skelly J, et al. The use of additional imaging increased specificity and decreased sensitivity in screening mammography. J Clin Epidemiol. 2005;58(9):942-50.
Exclusion: studies outside of search dates.

Gemignani ML. Breast cancer screening: why, when, and how many? Clin Obstet Gynecol. 2011;54(1):125-32.
Exclusion: review not meeting inclusion criteria.

Gemignani ML, Petrek JA, Borgen PI. Breast cancer and pregnancy. Surg Clin North Am. 1999;79(5):1157-69.
Exclusion: wrong population.

Gennaro G, Hendrick RE, Toledano A, et al. Combination of one-view digital breast tomosynthesis with one-view digital mammography versus standard two-view digital mammography: per lesion analysis. Eur Radiol. 2013;23(8):2087-94.
Exclusion: wrong intervention.

Georgian-Smith D, Moore RH, Halpern E, et al. Blinded comparison of computer-aided detection with human second reading in screening mammography. AJR Am J Roentgenol. 2007;189(5):1135-41.
Exclusion: wrong outcomes.

Gertig DM, Erbas B, Fletcher A, et al. Duration of hormone replacement therapy, breast tumour size and grade in a screening programme. Breast Cancer Res Treat. 2003;80(3):267-73.
Exclusion: wrong comparison.

Ghiasvand R, Bahmanyar S, Zendehdel K, et al. Postmenopausal breast cancer in Iran; risk factors and their population attributable fractions. BMC Cancer. 2012;12:414.
Exclusion: wrong outcomes.

GholamHosseini H, Alizad A, Fatemi M. Fusion of vibro-acoustography images and X-ray mammography. Conf Proc IEEE Eng Med Biol Soc. 2006;1:2803-6.
Exclusion: wrong study design for key question.

Ghosh K, Vachon CM, Pankratz VS, et al. Independent association of lobular involution and mammographic breast density with breast cancer risk. J Natl Cancer Inst. 2010;102(22):1716-23.
Exclusion: wrong outcomes.

Giannakopoulou G, Spyrou GM, Antaraki A, et al. Downgrading BIRADS 3 to BIRADS 2 category using a computer-aided microcalcification analysis and risk assessment system for early breast cancer. Comput Biol Med. 2010;40(11-12):853-9.
Exclusion: wrong intervention.

Gibis B, Busse R, Reese E, et al. Mammography screening as a method for the early detection of breast cancer (Structured abstract). Health Technology Assessment Database. 2014(1)
Exclusion: wrong publication type.

Appendix A4. List of Excluded Studies

Gibson LJ, Hery C, Mitton N, et al. Risk factors for breast cancer among Filipino women in Manila. Int J Cancer. 2010;126(2):515-21.
Exclusion: wrong outcomes.

Gierach GL, Brinton LA, Sherman ME. Lobular involution, mammographic density, and breast cancer risk: visualizing the future? J Natl Cancer Inst. 2010;102(22):1685-7.
Exclusion: wrong publication type.

Gifford D. Screening for breast cancer in women over the age of 70. Med Health R I. 2001;84(4):136-7.
Exclusion: wrong publication type.

Giger ML. Computerized analysis of images in the detection and diagnosis of breast cancer. Semin Ultrasound CT MR. 2004;25(5):411-8.
Exclusion: wrong study design for key question.

Gilbert FJ. New screening techniques for breast cancer (MRI). Dis Markers. 1999;15(1-3):115-6.
Exclusion: wrong publication type.

Gilbert FJ, Astley SM, Gillan MGC, et al. Single reading with computer-aided detection for screening mammography. N Engl J Med. 2008;359(16):1675-84.
Exclusion: wrong outcomes.

Gilbert FJ, Cordiner CM, Affleck IR, et al. Breast screening: The psychological sequelae of false-positive recall in women with and without a family history of breast cancer. Eur J Cancer. 1998;34(13):2010-4.
Exclusion: included in an included systematic review, not directly used.

Gill KS, Yankaskas BC. Screening mammography performance and cancer detection among black women and white women in community practice. Cancer. 2004;100(1):139-48.
Exclusion: wrong outcomes.

Gill PG, Farshid G, Luke CG, et al. Detection by screening mammography is a powerful independent predictor of survival in women diagnosed with breast cancer. Breast. 2004;13(1):15-22.
Exclusion: wrong comparison.

Gillett D, Kennedy C, Carmalt H. Breast cancer in young women. Aust N Z J Surg. 1997;67(11):761-4.
Exclusion: wrong comparison.

Giordano L, Cogo C, Patnick J, et al. Communicating the balance sheet in breast cancer screening. J Med Screen. 2012;19(suppl 1):67-71.
Exclusion: wrong outcomes.

Giordano L, Giorgi D, Piccini P, et al. Time trends of some indicators of mammography screening programmes in Italy, 1996-2003. Epidemiol Prev. 2006;30(1 Suppl 3):17-26.
Exclusion: wrong comparison.

Giordano L, Giorgi D, Piccini P, et al. Time trends of process and impact indicators in Italian breast screening programmes--1996-2005. Epidemiol Prev. 2008;32(2 Suppl 1):23-36.
Exclusion: wrong study design for key question.

Giordano L, von Karsa L, Tomatis M, et al. Mammographic screening programmes in Europe: organization, coverage and participation. J Med Screen. 2012;19(suppl 1):72-82.
Exclusion: wrong outcomes.

Giorgi D, Giordano L, Ventura L, et al. Mammography screening in Italy: 2003-2004 survey. Epidemiol Prev. 2006;30(1 Suppl 3):7-16.
Exclusion: wrong comparison.

Giorgi Rossi P, Camilloni L, Mantellini P, et al. Breast cancer diagnostic methods: screen-detected and clinical cases. An Italian survey of women's experiences. Tumori. 2007;93(5):452-60.
Exclusion: wrong outcomes.

Giorgi Rossi P, Federici A, Farchi S, et al. The effect of screening programmes on the treatment of benign breast neoplasms: observations from current practice in Italy. J Med Screen. 2006;13(3):123-8.
Exclusion: wrong outcomes.

Giuliano V, Giuliano C. Improved breast cancer detection in asymptomatic women using 3D-automated breast ultrasound in mammographically dense breasts. Clin Imaging. 2013;37(3):480-6.
Exclusion: wrong intervention.

Given-Wilson RM, Blanks RG. Incident screening cancers detected with a second mammographic view: pathological and radiological features. Clin Radiol. 1999;54(11):724-35.
Exclusion: wrong outcomes.

Appendix A4. List of Excluded Studies

Glass AG, Lacey JV, Jr., Carreon JD, et al. Breast cancer incidence, 1980-2006: combined roles of menopausal hormone therapy, screening mammography, and estrogen receptor status. J Natl Cancer Inst. 2007;99(15):1152-61.
Exclusion: wrong outcomes.

Glasziou P, Irwig L. The quality and interpretation of mammographic screening trials for women ages 40-49. J Natl Cancer Inst. 1997;Monographs.(22):73-7.
Exclusion: review not meeting inclusion criteria.

Glueck DH, Lamb MM, Lewin JM, et al. Two-modality mammography may confer an advantage over either full-field digital mammography or screen-film mammography. Acad Radiol. 2007;14(6):670-6.
Exclusion: wrong comparison.

Glynn CG, Farria DM, Monsees BS, et al. Effect of transition to digital mammography on clinical outcomes. Radiology. 2011;260(3):664-70.
Exclusion: wrong comparison.

Goel V, Cohen MM, Kaufert P, et al. Assessing the extent of contamination in the Canadian National Breast Screening Study. Am J Prev Med. 1998;15(3):206-11.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Gojnic M, Petkovic S, Pervulov M, et al. The utility of routine breast ultrasound screening in gynecology. Clin Exp Obstet Gynecol. 2003;30(4):265.
Exclusion: wrong publication type.

Golatta M, Franz D, Harcos A, et al. Interobserver reliability of automated breast volume scanner (ABVS) interpretation and agreement of ABVS findings with hand held breast ultrasound (HHUS), mammography and pathology results. Eur J Radiol. 2013;82(8):e332-6.
Exclusion: wrong intervention.

Goldman LE, Walker R, Miglioretti DL, et al. Facility characteristics do not explain higher false-positive rates in diagnostic mammography at facilities serving vulnerable women. Med Care. 2012;50(3):210-6.
Exclusion: wrong intervention.

Gordon PB. Ultrasound for breast cancer screening and staging. Radiol Clin North Am. 2002;40(3):431-41.
Exclusion: review not meeting inclusion criteria.

Gordon PB, Borugian MJ, Warren Burhenne LJ. A true screening environment for review of interval breast cancers: pilot study to reduce bias. Radiology. 2007;245(2):411-5.
Exclusion: wrong outcomes.

Gorey TF. Advances in breast cancer: clinical and biological lessons from screening. Ir J Med Sci. 1996;165(3):143-50.
Exclusion: wrong study design for key question.

Gorini G, Zappa M, Miccinesi G, et al. Breast cancer mortality trends in two areas of the province of Florence, Italy, where screening programmes started in the 1970s and 1990s. Br J Cancer. 2004;90(9):1780-3.
Exclusion: included in an included systematic review, not directly used.

Goscin CP, Berman CG, Clark RA. Magnetic resonance imaging of the breast. Cancer Control. 2001;8(5):399-406.
Exclusion: wrong publication type.

Goss PE, Ingle JN, Martino S, et al. A randomized trial of letrozole in postmenopausal women after five years of tamoxifen therapy for early-stage breast cancer. N Engl J Med. 2003;349(19):1793-802.
Exclusion: wrong intervention.

Goto M, Sakuma H, Kobayashi S, et al. Dynamic contrast-enhanced MR imaging of the entire breast with spectral-selective inversion fast three dimensional sequence. Magma. 1998;7(2):69-75.
Exclusion: wrong outcomes.

Gotzsche PC. Beyond randomized controlled trials: organized mammographic screening substantially reduces breast carcinoma mortality. Cancer. 2002;94(2):578; author reply 81-3.
Exclusion: wrong publication type.

Gotzsche PC. Increased incidence of invasive breast cancer after the introduction of service screening with mammography in Sweden. Int J Cancer. 2006;118(10):2648; author reply 9.
Exclusion: wrong publication type.

Gotzsche PC. Mortality reduction by breast-cancer screening. Lancet. 2003;362(9379):246.
Exclusion: wrong publication type.

Gotzsche PC. Relation between breast cancer mortality and screening effectiveness: systematic review of the mammography trials. Dan Med Bull. 2011;58(3):A4246.

Exclusion: review not meeting inclusion criteria.

Gotzsche PC. Screening for breast cancer. Ann Intern Med. 2003;138(9):769-70; author reply 70.
Exclusion: wrong publication type.

Gotzsche PC, Jorgensen KJ, Maehlen J, et al. Estimation of lead time and overdiagnosis in breast cancer screening. Br J Cancer. 2009;100(1):219; author reply 20.
Exclusion: wrong publication type.

Gotzsche PC, Jorgensen KJ, Zahl P-H, et al. Why mammography screening has not lived up to expectations from the randomised trials. Cancer Causes Control. 2012;23(1):15-21.
Exclusion: review not meeting inclusion criteria.

Gotzsche PC, Olsen O. Is screening for breast cancer with mammography justifiable? Lancet. 2000;355(9198):129-34.
Exclusion: wrong study design for key question.

Gower-Thomas K, Fielder HMP, Branston L, et al. Reviewing interval cancers: time well spent?.[Erratum appears in Clin Radiol 2002 Aug;57(8):770]. Clin Radiol. 2002;57(5):384-8.
Exclusion: wrong outcomes.

Gozzi G, Martinoli C, Conti GM, et al. Screening mammography interpretation test: more frequent mistakes. Radiol Med (Torino). 2005;109(3):268-79.
Exclusion: wrong publication type.

Grabler P, Dupuy D, Rai J, et al. Regular screening mammography before the diagnosis of breast cancer reduces black:white breast cancer differences and modifies negative biological prognostic factors. Breast Cancer Res Treat. 2012;135(2):549-53.
Exclusion: wrong comparison.

Gram IT, Lund E, Slenker SE. Quality of life following a false positive mammogram. Br J Cancer. 1990;62(6):1018-22.
Exclusion: studies outside of search dates.

Gram IT, Lund E, Slenker SE. Quality of life following a false positive mammogram. Br J Cancer. 1990;62(6):1018-22.
Exclusion: included in an included systematic review, not directly used.

Gray JAM, Patnick J, Blanks RG. Maximising benefit and minimising harm of screening. BMJ. 2008;336(7642):480-3.
Exclusion: wrong publication type.

Groenewoud JH, Otten JDM, Fracheboud J, et al. Cost-effectiveness of different reading and referral strategies in mammography screening in the Netherlands. Breast Cancer Res Treat. 2007;102(2):211-8.
Exclusion: wrong outcomes.

Gromet M. Comparison of computer-aided detection to double reading of screening mammograms: review of 231,221 mammograms. AJR Am J Roentgenol. 2008;190(4):854-9.
Exclusion: wrong outcomes.

Gross CP, Long JB, Ross JS, et al. The cost of breast cancer screening in the Medicare population. JAMA Intern Med. 2013;173(3):220-6.
Exclusion: wrong outcomes.

Group IW. Epidemiological changes in breast tumours in Italy: the IMPACT study on mammographic screening programmes. Pathologica. 2011;103(5):290-3.
Exclusion: wrong study design for key question.

Grube BJ. Barriers to diagnosis and treatment of breast cancer in the older woman. J Am Coll Surg. 2006;202(3):495-508.
Exclusion: review not meeting inclusion criteria.

Gruszauskas NP, Drukker K, Giger ML, et al. Breast US computer-aided diagnosis system: robustness across urban populations in South Korea and the United States. Radiology. 2009;253(3):661-71.
Exclusion: wrong intervention.

Gruszauskas NP, Drukker K, Giger ML, et al. Performance of breast ultrasound computer-aided diagnosis: dependence on image selection. Acad Radiol. 2008;15(10):1234-45.
Exclusion: wrong intervention.

Gui GP, Hogben RK, Walsh G, et al. The incidence of breast cancer from screening women according to predicted family history risk: Does annual clinical examination add to mammography? Eur J Cancer. 2001;37(13):1668-73.
Exclusion: wrong population.

Guliato D, Rangayyan RM, Daloia de Carvalho J, et al. Spiculation-preserving polygonal modeling of contours of breast tumors. Conf Proc IEEE Eng Med Biol Soc. 2006;1:2791-4.
Exclusion: wrong outcomes.

Appendix A4. List of Excluded Studies

Gullate M. The influence of spirituality and religiosity on breast cancer screening delay in African American women: application of the Theory of Reasoned Action and Planned Behavior (TRA/TPB). ABNF J. 2006;17(2):89-94.
Exclusion: wrong outcomes.

Gullatte MM, Phillips JM, Gibson LM. Factors associated with delays in screening of self-detected breast changes in African-American women. J Natl Black Nurses Assoc. 2006;17(1):45-50.
Exclusion: studies outside of search dates.

Guo Q, Shao J, Ruiz VF. Characterization and classification of tumor lesions using computerized fractal-based texture analysis and support vector machines in digital mammograms. Int J Comput Assist Radiol Surg. 2009;4(1):11-25.
Exclusion: wrong study design for key question.

Gur D, Abrams GS, Chough DM, et al. Digital breast tomosynthesis: observer performance study. AJR Am J Roentgenol. 2009;193(2):586-91.
Exclusion: wrong outcomes.

Gur D, Sumkin JH. Screening for early detection of breast cancer: overdiagnosis versus suboptimal patient management. Radiology. 2013;268(2):327-8.
Exclusion: wrong publication type.

Gur D, Sumkin JH, Hardesty LA, et al. Recall and detection rates in screening mammography. Cancer. 2004;100(8):1590-4.
Exclusion: wrong outcomes.

Gur D, Zuley ML, Anello MI, et al. Dose reduction in digital breast tomosynthesis (DBT) screening using synthetically reconstructed projection images: an observer performance study. Acad Radiol. 2012;19(2):166-71.
Exclusion: wrong outcomes.

Haakinson DJ, Leeds SG, Dueck AC, et al. The impact of obesity on breast cancer: a retrospective review. Ann Surg Oncol. 2012;19(9):3012-8.
Exclusion: wrong population.

Habbema JDF, Tan SYGL, Cronin KA. Impact of mammography on U.S. breast cancer mortality, 1975-2000: are intermediate outcome measures informative? J Natl Cancer Inst. 2006;Monographs.(36):105-11.
Exclusion: wrong study design for key question.

Habermann EB, Virnig BA, Riley GF, et al. The impact of a change in Medicare reimbursement policy and HEDIS measures on stage at diagnosis among Medicare HMO and fee-for-service female breast cancer patients. Med Care. 2007;45(8):761-6.
Exclusion: wrong comparison.

Habtes I, Friedman D, Raskind-Hood C, et al. Determining the impact of US mammography screening guidelines on patient survival in a predominantly African American population treated in a public hospital during 2008. Cancer. 2013;119(3):481-7.
Exclusion: wrong study design for key question.

Hackshaw A. The benefits and harms of mammographic screening for breast cancer: building the evidence base using service screening programmes. J Med Screen. 2012;19 Suppl 1:1-2.
Exclusion: wrong publication type.

Hackshaw AK, Wald NJ, Michell MJ, et al. An investigation into why two-view mammography is better than one-view in breast cancer screening. Clin Radiol. 2000;55(6):454-8.
Exclusion: wrong outcomes.

Hade EM, Murray DM, Pennell ML, et al. Intraclass correlation estimates for cancer screening outcomes: estimates and applications in the design of group-randomized cancer screening studies. J Natl Cancer Inst Monogr. 2010;2010(40):97-103.
Exclusion: wrong outcomes.

Hadi N, Sadeghi-Hassanabadi A, Talei AR, et al. Assessment of a breast cancer screening programme in Shiraz, Islamic Republic of Iran. East Mediterr Health J. 2002;8(2-3):386-92.
Exclusion: wrong outcomes.

Hahn KME, Bondy ML, Selvan M, et al. Factors associated with advanced disease stage at diagnosis in a population-based study of patients with newly diagnosed breast cancer. Am J Epidemiol. 2007;166(9):1035-44.
Exclusion: wrong study design for key question.

Haikel RL, Jr., Mauad EC, Silva TB, et al. Mammography-based screening program: preliminary results from a first 2-year round in a Brazilian region using mobile and fixed units. BMC Womens Health. 2012;12:32.
Exclusion: wrong outcomes.

Hakama M, Pukkala E, Heikkila M, et al. Effectiveness of the public health policy for breast cancer screening in Finland: population based cohort study. BMJ. 1997;314(7084):864-7.
Exclusion: included in an included systematic review, not directly used.

Hakim CM, Chough DM, Ganott MA, et al. Digital breast tomosynthesis in the diagnostic environment: A subjective side-by-side review. AJR Am J Roentgenol. 2010;195(2):W172-6.
Exclusion: wrong intervention.

Halapy EE, Chiarelli AM, Klar N, et al. Breast screening outcomes in women with and without a family history of breast and/or ovarian cancer. J Med Screen. 2004;11(1):32-8.
Exclusion: wrong outcomes.

Halbreich U, Shen J, Panaro V. Are chronic psychiatric patients at increased risk for developing breast cancer? Am J Psychiatry. 1996;153(4):559-60.
Exclusion: wrong comparison.

Hall AB, Wall M, Lancia N, et al. Air force breast cancer detection and treatment trends. Am Surg. 2013;79(5):E209-11.
Exclusion: wrong publication type.

Hall FM. Mammographically determined breast density and cancer risk. Radiology. 2008;248(3):1083; author reply
Exclusion: wrong publication type.

Hall FM. The rise and impending decline of screening mammography. Radiology. 2008;247(3):597-601.
Exclusion: wrong publication type.

Hall HI, Coates RJ, Uhler RJ, et al. Stage of breast cancer in relation to body mass index and bra cup size. Int J Cancer. 1999;82(1):23-7.
Exclusion: wrong outcomes.

Hall HI, Uhler RJ, Coughlin SS, et al. Breast and cervical cancer screening among Appalachian women. Cancer Epidemiol Biomarkers Prev. 2002;11(1):137-42.
Exclusion: wrong publication type.

Hall IJ, Newman B, Millikan RC, et al. Body size and breast cancer risk in black women and white women: the Carolina Breast Cancer Study. Am J Epidemiol. 2000;151(8):754-64.
Exclusion: wrong outcomes.

Halladay JR, Yankaskas BC, Bowling JM, et al. Positive predictive value of mammography: comparison of interpretations of screening and diagnostic images by the same radiologist and by different radiologists. AJR Am J Roentgenol. 2010;195(3):782-5.
Exclusion: wrong outcomes.

Hambly NM, McNicholas MM, Phelan N, et al. Comparison of digital mammography and screen-film mammography in breast cancer screening: a review in the Irish breast screening program. AJR Am J Roentgenol. 2009;193(4):1010-8.
Exclusion: wrong comparison.

Hampton T. Research findings point to advances in breast cancer screening and treatment. JAMA. 2007;298(4):389-90.
Exclusion: wrong publication type.

Han B-K, Choe YH, Ko Y-H, et al. Stereotactic core-needle biopsy of non-mass calcifications: outcome and accuracy at long-term follow-up. Korean J Radiol. 2003;4(4):217-23.
Exclusion: wrong population.

Han D, Nie J, Bonner MR, et al. Lifetime adult weight gain, central adiposity, and the risk of pre- and postmenopausal breast cancer in the Western New York exposures and breast cancer study. Int J Cancer. 2006;119(12):2931-7.
Exclusion: wrong study design for key question.

Han PK, Kobrin SC, Klein WM, et al. Perceived ambiguity about screening mammography recommendations: association with future mammography uptake and perceptions. Cancer Epidemiol Biomarkers Prev. 2007;16(3):458-66.
Exclusion: wrong outcomes.

Hanigan MH. Possible role of mammography in increased incidence of breast cancer not considered. Arch Intern Med. 2009;169(10):998-9.
Exclusion: wrong publication type.

Hanin L, Pavlova L. Optimal screening schedules for prevention of metastatic cancer. Stat Med. 2013;32(2):206-19.
Exclusion: wrong study design for key question.

Harding C, Knox WF, Faragher EB, et al. Hormone replacement therapy and tumour grade in breast cancer: prospective study in screening unit.[Erratum appears in BMJ 1996 Jul 27;313(7051):198]. BMJ. 1996;312(7047):1646-7.

Exclusion: wrong intervention.

Harmer C, Staples M, Kavanagh AM. Evaluation of breast cancer incidence: is the increase due entirely to mammographic screening? Cancer Causes Control. 1999;10(5):333-7.
Exclusion: wrong publication type.

Harms SE. Multicenter, double-blind, randomized, intraindividual crossover comparison of gadobenate dimeglumine and gadopentetate dimeglumine for breast MR imaging (DETECT trial). Breast Dis. 2012;23(1):37-8.
Exclusion: wrong publication type.

Harms SE, Flamig DP. Breast MRI. Clin Imaging. 2001;25(4):227-46.
Exclusion: wrong publication type.

Harris DH, Bates JH, Cress R, et al. Stage of breast cancer diagnosis among medically underserved women in California receiving mammography through a state screening program. Cancer Causes Control. 2004;15(7):721-9.
Exclusion: wrong comparison.

Harris R. Variation of benefits and harms of breast cancer screening with age. J Natl Cancer Inst. 1997;Monographs.(22):139-43.
Exclusion: wrong publication type.

Hartman AR, Daniel BL, Kurian AW, et al. Breast magnetic resonance image screening and ductal lavage in women at high genetic risk for breast carcinoma. Cancer. 2004;100(3):479-89.
Exclusion: wrong population.

Harvey JA, Pinkerton JV, Herman CR. Short-term cessation of hormone replacement therapy and improvement of mammographic specificity. J Natl Cancer Inst. 1997;89(21):1623-5.
Exclusion: wrong publication type.

Haukka J, Byrnes G, Boniol M, et al. Trends in breast cancer mortality in Sweden before and after implementation of mammography screening. PLoS ONE. 2011;6(9):e22422.
Exclusion: included in an included systematic review, not directly used.

Heimann R, Bradley J, Hellman S. The benefits of mammography are not limited to women of ages older than 50 years. Cancer. 1998;82(11):2221-6.
Exclusion: wrong comparison.

Heimann R, Munsell M, McBride R. Mammographically detected breast cancers and the risk of axillary lymph node involvement: is it just the tumor size? Cancer J. 2002;8(3):276-81.
Exclusion: wrong comparison.

Heinzen MT, Yankaskas BC, Kwok RK. Comparison of woman-specific versus breast-specific data for reporting screening mammography performance. Acad Radiol. 2000;7(4):232-6.
Exclusion: wrong outcomes.

Heleno BM, Lindberg L, Brodersen J. Alternative estimates for the likelihood that a woman with screen-detected breast cancer has had her "life saved" by that screening. Arch Intern Med. 2012;172(8):672.
Exclusion: wrong publication type.

Helmond FA. Breast cancer and hormone-replacement therapy: the Million Women Study. Lancet. 2003;362(9392):1330; author reply -1.
Exclusion: wrong publication type.

Helvie MA. Digital mammography imaging: breast tomosynthesis and advanced applications. Radiol Clin North Am. 2010;48(5):917-29.
Exclusion: review not meeting inclusion criteria.

Helvie MA, Chang JT, Hendrick RE, et al. Reduction in late-stage breast cancer incidence in the mammography era: Implications for overdiagnosis of invasive cancer. Cancer. 2014;120(17):2649-56.
Exclusion: wrong outcomes.

Helvie MA, Hadjiiski L, Makariou E, et al. Sensitivity of noncommercial computer-aided detection system for mammographic breast cancer detection: pilot clinical trial. Radiology. 2004;231(1):208-14.
Exclusion: wrong outcomes.

Hemminki K, Bermejo JL. Effects of screening for breast cancer on its age-incidence relationships and familial risk. Int J Cancer. 2005;117(1):145-9.
Exclusion: wrong outcomes.

Hendrick RE, Cole EB, Pisano ED, et al. Accuracy of soft-copy digital mammography versus that of screen-film mammography according to digital manufacturer: ACRIN DMIST retrospective multireader study. Radiology. 2008;247(1):38-48.
Exclusion: wrong comparison.

Hendrick RE, Cutter GR, Berns EA, et al. Community-based mammography practice: services, charges, and interpretation methods. AJR Am J Roentgenol. 2005;184(2):433-8.
Exclusion: wrong outcomes.

Hendrick RE, Pisano ED, Averbukh A, et al. Comparison of acquisition parameters and breast dose in digital mammography and screen-film mammography in the American College of Radiology Imaging Network digital mammographic imaging screening trial. AJR Am J Roentgenol. 2010;194(2):362-9.
Exclusion: wrong comparison.

Hendrick RE, Smith RA, Rutledge JH, 3rd, et al. Benefit of screening mammography in women aged 40-49: a new meta-analysis of randomized controlled trials. J Natl Cancer Inst. 1997;Monographs.(22):87-92.
Exclusion: review not meeting inclusion criteria.

Henry KA, Boscoe FP, Johnson CJ, et al. Breast cancer stage at diagnosis: is travel time important? J Community Health. 2011;36(6):933-42.
Exclusion: wrong outcomes.

Henry KA, Sherman R, Farber S, et al. The joint effects of census tract poverty and geographic access on late-stage breast cancer diagnosis in 10 US States. Health Place. 2013;21:110-21.
Exclusion: wrong outcomes.

Herrada J, Iyer RB, Atkinson EN, et al. Relative value of physical examination, mammography, and breast sonography in evaluating the size of the primary tumor and regional lymph node metastases in women receiving neoadjuvant chemotherapy for locally advanced breast carcinoma. Clin Cancer Res. 1997;3(9):1565-9.
Exclusion: wrong population.

Hersch J JJ, Barratt A, Irwig L, Houssami N, Jacklyn G, Thornton H, Dhillon H, McCaffery K. Overdetection in breast cancer screening: Development and preliminary evaluation of a decision aid. BMJ Open. 2014;4(9)
Exclusion: wrong outcomes.

Heyding RK, Cheung AM, Mocarski EJM, et al. A community-based intervention to increase screening mammography among disadvantaged women at an inner-city drop-in center. Women Health. 2005;41(1):21-31.
Exclusion: wrong outcomes.

Heyes GJ, Mill AJ, Charles MW. Enhanced biological effectiveness of low energy X-rays and implications for the UK breast screening programme. Br J Radiol. 2006;79(939):195-200.
Exclusion: wrong publication type.

Heyes GJ, Mill AJ, Charles MW. Mammography-oncogenecity at low doses. J Radiol Prot. 2009;29(2A):A123-32.
Exclusion: wrong population.

Heywang-Kobrunner SH, Viehweg P, Heinig A, et al. Contrast-enhanced MRI of the breast: accuracy, value, controversies, solutions. Eur J Radiol. 1997;24(2):94-108.
Exclusion: wrong study design for key question.

Hider P, Nicholas B. The early detection and diagnosis of breast cancer: a literature review – an update. NZHTA REPORT. 1999;2(2)
Exclusion: review not meeting inclusion criteria.

Highfield L. Spatial patterns of breast cancer incidence and uninsured women of mammography screening age. Breast J. 2013;19(3):293-301.
Exclusion: wrong outcomes.

Hill DA, Nibbe A, Royce ME, et al. Method of detection and breast cancer survival disparities in Hispanic women. Cancer Epidemiol Biomarkers Prev. 2010;19(10):2453-60.
Exclusion: wrong comparison.

Hillman BJ, Harms SE, Stevens G, et al. Diagnostic performance of a dedicated 1.5-T breast MR imaging system. Radiology. 2012;265(1):51-8.
Exclusion: wrong intervention.

Hirose K, Hamajima N, Takezaki T, et al. Physical exercise reduces risk of breast cancer in Japanese women. Cancer Sci. 2003;94(2):193-9.
Exclusion: wrong outcomes.

Hislop TG, Harris SR, Jackson J, et al. Satisfaction and anxiety for women during investigation of an abnormal screening mammogram. Breast Cancer Res Treat. 2002;76(3):245-54.
Exclusion: included in an included systematic review, not directly used.

Hislop TG, Worth AJ, Kan L, et al. Post screen-detected breast cancer within the Screening Mammography Program of British Columbia. Breast Cancer Res Treat. 1997;42(3):235-42.
Exclusion: wrong outcomes.

Ho WT, Lam PWT. Clinical performance of computer-assisted detection (CAD) system in detecting carcinoma in breasts of different densities. Clin Radiol. 2003;58(2):133-6.
Exclusion: wrong outcomes.

Hoerger TJ, Ekwueme DU, Miller JW, et al. Estimated effects of the National Breast and Cervical Cancer Early Detection Program on breast cancer mortality. Am J Prev Med. 2011;40(4):397-404.
Exclusion: wrong study design for key question.

Hoff SR, Abrahamsen A-L, Samset JH, et al. Breast cancer: missed interval and screening-detected cancer at full-field digital mammography and screen-film mammography-- results from a retrospective review.[Erratum appears in Radiology. 2013 Jan;266(1):367]. Radiology. 2012;264(2):378-86.
Exclusion: wrong comparison.

Hoff SR, Samset JH, Abrahamsen A-L, et al. Missed and true interval and screen-detected breast cancers in a population based screening program. Acad Radiol. 2011;18(4):454-60.
Exclusion: wrong outcomes.

Hoffman RM, Lewis CL, Pignone MP, et al. Decision-making processes for breast, colorectal, and prostate cancer screening: the DECISIONS survey. Med Decis Making. 2010;30(5 Suppl):53s-64s.
Exclusion: wrong outcomes.

Hofvind S. Organised mammographic screening--more benefits than harms. Tidsskr Nor Laegeforen. 2013;133(6):619-20.
Exclusion: wrong publication type.

Hofvind S, Geller B, Vacek PM, et al. Using the European guidelines to evaluate the Norwegian Breast Cancer Screening Program. Eur J Epidemiol. 2007;22(7):447-55.
Exclusion: wrong comparison.

Hofvind S, Geller BM, Rosenberg RD, et al. Screening-detected breast cancers: discordant independent double reading in a population-based screening program. Radiology. 2009;253(3):652-60.
Exclusion: wrong comparison.

Hofvind S, Geller BM, Skelly J, et al. Sensitivity and specificity of mammographic screening as practised in Vermont and Norway. Br J Radiol. 2012;85(1020):e1226-32.
Exclusion: wrong outcomes.

Hofvind S, Moller B, Thoresen S, et al. Use of hormone therapy and risk of breast cancer detected at screening and between mammographic screens. Int J Cancer. 2006;118(12):3112-7.
Exclusion: wrong comparison.

Hofvind S, Ponti A, Patnick J, et al. False-positive results in mammographic screening for breast cancer in Europe: a literature review and survey of service screening programmes. J Med Screen. 2012;19 Suppl 1:57-66.
Exclusion: review not meeting inclusion criteria.

Hofvind S, Sakshaug S, Ursin G, et al. Breast cancer incidence trends in Norway--explained by hormone therapy or mammographic screening? Int J Cancer. 2012;130(12):2930-8.
Exclusion: wrong study design for key question.

Hofvind S, Sorum R, Thoresen S. Incidence and tumor characteristics of breast cancer diagnosed before and after implementation of a population-based screening-program. Acta Oncol. 2008;47(2):225-31.
Exclusion: wrong outcomes.

Hofvind S, Thoresen S, Tretli S. The cumulative risk of a false-positive recall in the Norwegian Breast Cancer Screening Program. Cancer. 2004;101(7):1501-7.
Exclusion: wrong study design for key question.

Hofvind S, Vacek PM, Skelly J, et al. Comparing screening mammography for early breast cancer detection in Vermont and Norway. J Natl Cancer Inst. 2008;100(15):1082-91.
Exclusion: wrong comparison.

Holland DW, Boucher LD, Mortimer JE. Tubular breast cancer experience at Washington University: a review of the literature. Clin Breast Cancer. 2001;2(3):210-4.
Exclusion: review not meeting inclusion criteria.

Holowaty PH, Miller AB, Baines CJ, et al. Canadian National breast screening study: First screen results as predictors of future breast cancer risk. Cancer Epidemiol Biomarkers Prev. 1993;2(1):11-9.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Hooley RJ, Greenberg KL, Stackhouse RM, et al. Screening US in patients with mammographically dense breasts: initial experience with Connecticut Public Act 09-41. Radiology. 2012;265(1):59-69.

Appendix A4. List of Excluded Studies

Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Horn J, Åsvold BO, Opdahl S, et al. Reproductive factors and the risk of breast cancer in old age: a Norwegian cohort study. Breast Cancer Res Treat. 2013;139(1):237-43.
Exclusion: wrong comparison.

Horsch K, Giger ML, Metz CE. Potential effect of different radiologist reporting methods on studies showing benefit of CAD. Acad Radiol. 2008;15(2):139-52.
Exclusion: wrong outcomes.

Horsch K, Giger ML, Vyborny CJ, et al. Performance of computer-aided diagnosis in the interpretation of lesions on breast sonography. Acad Radiol. 2004;11(3):272-80.
Exclusion: wrong outcomes.

Hou M-F, Chuang H-Y, Ou-Yang F, et al. Comparison of breast mammography, sonography and physical examination for screening women at high risk of breast cancer in taiwan. Ultrasound Med Biol. 2002;28(4):415-20.
Exclusion: studies outside of search dates.

Hou S-I, Sealy D-A, Kabiru CW. Closing the disparity gap: cancer screening interventions among Asians--a systematic literature review. Asian Pac J Cancer Prev. 2011;12(11):3133-9.
Exclusion: review not meeting inclusion criteria.

Houssami N, Cuzick J, Dixon JM. The prevention, detection, and management of breast cancer. Med J Aust. 2006;184(5):230-4.
Exclusion: wrong publication type.

Houssami N, French J, Brennan M, et al. Breast cancer--new and emerging technologies for diagnosis and management. Aust Fam Physician. 2005;34(8):657-61.
Exclusion: review not meeting inclusion criteria.

Houssami N, Given-Wilson R. Incorporating new technologies into clinical practice without evidence of effectiveness in prospective studies: computer-aided detection (CAD) in breast screening reinforces the need for better initial evaluation. Breast. 2007;16(3):219-21.
Exclusion: wrong publication type.

Houssami N, Given-Wilson R, Ciatto S. Early detection of breast cancer: overview of the evidence on computer-aided detection in mammography screening. J Med Imaging Radiat Oncol. 2009;53(2):171-6.
Exclusion: review not meeting inclusion criteria.

Houssami N, Kerlikowske K. The impact of breast density on breast cancer risk and on breast screening. Current Breast Cancer Reports. 2012;4(2):161-8.
Exclusion: wrong outcomes.

Houssami N, Macaskill P, Bernardi D, et al. Breast screening using 2D-mammography or integrating digital breast tomosynthesis (3D-mammography) for single-reading or double-reading--evidence to guide future screening strategies. Eur J Cancer. 2014;50(10):1799-807.
Exclusion: wrong comparison.

Howard JM. Breast density changes associated with hormone replacement therapy in postmenopausal women. Effects on the specificity and sensitivity of mamographic screening. Eur J Gynaecol Oncol. 2006;27(1):104; author reply
Exclusion: wrong publication type.

Howarth D, Sillar R, Lan L, et al. Scintimammography: an adjunctive test for the detection of breast cancer. Med J Aust. 1999;170(12):588-91.
Exclusion: wrong intervention.

Howe GR. Radiation and screening. Radiat Res. 2005;163(6):693-4.
Exclusion: wrong publication type.

Hristova L, Hakama M. Effect of screening for cancer in the Nordic countries on deaths, cost and quality of life up to the year 2017. Acta Oncol. 1997;36 Suppl 9:1-60.
Exclusion: review not meeting inclusion criteria.

Huang Z, Willett WC, Colditz GA, et al. Waist circumference, waist:hip ratio, and risk of breast cancer in the Nurses' Health Study. Am J Epidemiol. 1999;150(12):1316-24.
Exclusion: wrong outcomes.

Hubbard RA, Miglioretti DL. A semiparametric censoring bias model for estimating the cumulative risk of a false-positive screening test under dependent censoring. Biometrics. 2013;69(1):245-53.
Exclusion: wrong study design for key question.

Hubbard RA, Miglioretti DL, Smith RA. Modelling the cumulative risk of a false-positive screening test. Stat Methods Med Res. 2010;19(5):429-49.
Exclusion: wrong study design for key question.

Hughes KS, Schnaper LA, Bellon JR, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. J Clin Oncol. 2013;31(19):2382-7.
Exclusion: wrong intervention.

Hughes KS, Schnaper LA, Berry D, et al. Lumpectomy plus tamoxifen with or without irradiation in women 70 years of age or older with early breast cancer. N Engl J Med. 2004;351(10):971-7.
Exclusion: wrong intervention.

Hunt KA, Sickles EA. Effect of obesity on screening mammography: outcomes analysis of 88,346 consecutive examinations. AJR Am J Roentgenol. 2000;174(5):1251-5.
Exclusion: wrong comparison.

Huo Z, Giger ML, Vyborny CJ, et al. Automated computerized classification of malignant and benign masses on digitized mammograms. Acad Radiol. 1998;5(3):155-68.
Exclusion: wrong intervention.

Hupse R, Samulski M, Lobbes MB, et al. Computer-aided detection of masses at mammography: interactive decision support versus prompts. Radiology. 2013;266(1):123-9.
Exclusion: wrong intervention.

Hutton J, Walker LG, Gilbert FJ, et al. Psychological impact and acceptability of magnetic resonance imaging and X-ray mammography: the MARIBS Study. Br J Cancer. 2011;104(4):578-86.
Exclusion: wrong population.

Hwang ES, Cody HS, 3rd. Does the proven benefit of mammography extend to breast cancer patients over age 70? South Med J. 1998;91(6):522-6.
Exclusion: wrong study design for key question.

Hylton NM. Evaluation of gadobenate dimeglumine for contrast-enhanced MRI of the breast. AJR Am J Roentgenol. 2003;181(3):677-8.
Exclusion: wrong publication type.

Iared W, Shigueoka DC, Torloni MR, et al. Comparative evaluation of digital mammography and film mammography: systematic review and meta-analysis. Sao Paulo Med J. 2011;129(4):250-60.
Exclusion: wrong comparison.

Ichikawa LE, Barlow WE, Anderson ML, et al. Time trends in radiologists' interpretive performance at screening mammography from the community-based Breast Cancer Surveillance Consortium, 1996-2004. Radiology. 2010;256(1):74-82.
Exclusion: wrong outcomes.

Ikeda DM, Birdwell RL, O'Shaughnessy KF, et al. Analysis of 172 subtle findings on prior normal mammograms in women with breast cancer detected at follow-up screening. Radiology. 2003;226(2):494-503.
Exclusion: wrong outcomes.

Ildefonso C, Vazquez J, Guinea O, et al. The mammographic appearance of breast carcinomas of invasive ductal type: relationship with clinicopathological parameters, biological features and prognosis. Eur J Obstet Gynecol Reprod Biol. 2008;136(2):224-31.
Exclusion: wrong population.

Institute for Clinical Systems I. Computer aided detection of breast cancer (Structured abstract). Health Technology Assessment Database. 2014(1)
Exclusion: wrong publication type.

Institute for Clinical Systems I. Magnetic resonance imaging (MRI) for the detection of breast abnormalities (Structured abstract). Health Technology Assessment Database. 2014(1)
Exclusion: wrong publication type.

Irvin VL, Kaplan RM. Screening Mammography & Breast Cancer Mortality: Meta-Analysis of Quasi-Experimental Studies. PLoS ONE. 2014;9(6):e98105.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Irwig L, Houssami N, van Vliet C. New technologies in screening for breast cancer: a systematic review of their accuracy. Br J Cancer. 2004;90(11):2118-22.
Exclusion: review not meeting inclusion criteria.

Irwin ML, Crumley D, McTiernan A, et al. Physical activity levels before and after a diagnosis of breast carcinoma: the Health, Eating, Activity, and Lifestyle (HEAL) study. Cancer. 2003;97(7):1746-57.
Exclusion: wrong outcomes.

Appendix A4. List of Excluded Studies

Ishida DN, Toomata-Mayer TF, Braginsky NS. Beliefs and attitudes of Samoan women toward early detection of breast cancer and mammography utilization. Cancer. 2001;91(1 Suppl):262-6.
Exclusion: wrong outcomes.

Ishida T, Suzuki A, Kawai M, et al. A randomized controlled trial to verify the efficacy of the use of ultrasonography in breast cancer screening aged 40-49 (J-START): 76 196 women registered. Jpn J Clin Oncol. 2014;44(2):134-40.
Exclusion: wrong publication type.

J H. Mammography screening among women aged 40-49 years shows no benefit. CMAJ : Canadian Medical Association journal. 2002;167(8):898.
Exclusion: wrong publication type.

Jacobellis J, Cutter G. Mammography screening and differences in stage of disease by race/ethnicity. Am J Public Health. 2002;92(7):1144-50.
Exclusion: wrong comparison.

Jafri NF, Ayyala RS, Ozonoff A, et al. Screening mammography: does ethnicity influence patient preferences for higher recall rates given the potential for earlier detection of breast cancer? Radiology. 2008;249(3):785-91.
Exclusion: wrong outcomes.

Jain MG, Miller AB, Rohan TE, et al. Body mass index and mortality in women: follow-up of the Canadian National Breast Screening Study cohort. Int J Obes (Lond). 2005;29(7):792-7.
Exclusion: wrong intervention.

Jalalian A, Mashohor SBT, Mahmud HR, et al. Computer-aided detection/diagnosis of breast cancer in mammography and ultrasound: a review. Clin Imaging. 2013;37(3):420-6.
Exclusion: review not meeting inclusion criteria.

Jamal N, Ng KH, Looi LM, et al. Quantitative assessment of breast density from digitized mammograms into Tabar's patterns. Phys Med Biol. 2006;51(22):5843-57.
Exclusion: wrong outcomes.

James JJ, Cornford EJ. Does computer-aided detection have a role in the arbitration of discordant double-reading opinions in a breast-screening programme? Clin Radiol. 2009;64(1):46-51.
Exclusion: wrong intervention.

Jamrozik K, Byrne MJ, Dewar JM, et al. The effect of mammographic screening on invasive breast cancer in Western Australia. Med J Aust. 2000;172(5):203-6.
Exclusion: wrong comparison.

Jansen JT, Zoetelief J. Assessment of lifetime gained as a result of mammographic breast cancer screening using a computer model. Br J Radiol. 1997;70(834):619-28.
Exclusion: wrong study design for key question.

Jansen JT, Zoetelief J. Optimisation of mammographic breast cancer screening using a computer simulation model. Eur J Radiol. 1997;24(2):137-44.
Exclusion: wrong intervention.

Jatoi I. The impact of advances in treatment on the efficacy of mammography screening. Prev Med. 2011;53(3):103-4.
Exclusion: wrong publication type.

Jatoi I. Screening clinical breast examination. Surg Clin North Am. 2003;83(4):789-801.
Exclusion: wrong intervention.

Jatoi I, Zhu K, Shah M, et al. Psychological distress in U.S. women who have experienced false-positive mammograms. Breast Cancer Res Treat. 2006;100(2):191-200.
Exclusion: studies outside of search dates.

Jensen A, Vejborg I, Severinsen N, et al. Performance of clinical mammography: a nationwide study from Denmark. Int J Cancer. 2006;119(1):183-91.
Exclusion: wrong intervention.

Jensen AR, Garne JP, Storm HH, et al. Does stage at diagnosis explain the difference in survival after breast cancer in Denmark and Sweden? Acta Oncol. 2004;43(8):719-26.
Exclusion: wrong comparison.

Jensen AR, Madsen AH, Overgaard J. Trends in breast cancer during three decades in Denmark: stage at diagnosis, surgical management and survival. Acta Oncol. 2008;47(4):537-44.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Jesneck JL, Lo JY, Baker JA. Breast mass lesions: computer-aided diagnosis models with mammographic and sonographic descriptors. Radiology. 2007;244(2):390-8.
Exclusion: wrong outcomes.

Jha MK, Avlonitis VS, Griffith CD, et al. Aggressive local treatment for screen-detected DCIS results in very low rates of recurrence. Eur J Surg Oncol. 2001;27(5):454-8.
Exclusion: wrong intervention.

Ji J, Hemminki K. Risk for contralateral breast cancers in a population covered by mammography: effects of family history, age at diagnosis and histology. Breast Cancer Res Treat. 2007;105(2):229-36.
Exclusion: wrong population.

Jiang Y, Metz CE. BI-RADS data should not be used to estimate ROC curves. Radiology. 2010;256(1):29-31.
Exclusion: wrong publication type.

Jiang Y, Miglioretti DL, Metz CE, et al. Breast cancer detection rate: designing imaging trials to demonstrate improvements. Radiology. 2007;243(2):360-7.
Exclusion: wrong outcomes.

Jiang Y, Nishikawa RM, Schmidt RA, et al. Improving breast cancer diagnosis with computer-aided diagnosis. Acad Radiol. 1999;6(1):22-33.
Exclusion: wrong intervention.

Jimenez-Lee R, Oslak SG, Hedberg K, et al. Surgical outcomes of a breast cancer-screening program for low-income women. Arch Surg. 2003;138(8):884-90.
Exclusion: wrong comparison.

Joensuu H, Asola R, Holli K, et al. Delayed diagnosis and large size of breast cancer after a false negative mammogram. Eur J Cancer. 1994;30A:1299-302.
Exclusion: wrong outcomes.

Joffe MM, Byrne C, Colditz GA. Postmenopausal hormone use, screening, and breast cancer: characterization and control of a bias. Epidemiology. 2001;12(4):429-38.
Exclusion: wrong study design for key question.

John EM, Phipps AI, Knight JA, et al. Medical radiation exposure and breast cancer risk: findings from the Breast Cancer Family Registry. Int J Cancer. 2007;121(2):386-94.
Exclusion: wrong intervention.

Johns LE, Moss SM, Age Trial Management G. False-positive results in the randomized controlled trial of mammographic screening from age 40 ("Age" trial). Cancer Epidemiol Biomarkers Prev. 2010;19(11):2758-64.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Johnson A. 'Overdiagnosis' and mortality in breast cancer screening. J R Soc Med. 2012;105(7):317-9.
Exclusion: wrong publication type.

Johnson A, Shekhdar J. Detection by screening mammography is a powerful independent predictor of survival in women diagnosed with breast cancer. Breast. 2005;14(1):79.
Exclusion: wrong publication type.

Johnson ET. Breast cancer racial differences before age 40--implications for screening. J Natl Med Assoc. 2002;94(3):149-56.
Exclusion: wrong population.

Johnson KS, Baker JA, Lee SS, et al. Suspicious breast lesions detected at 3.0 T magnetic resonance imaging: clinical and histological outcomes. Acad Radiol. 2012;19(6):667-74.
Exclusion: wrong outcomes.

Jonas CR, McCullough ML, Teras LR, et al. Dietary glycemic index, glycemic load, and risk of incident breast cancer in postmenopausal women. Cancer Epidemiol Biomarkers Prev. 2003;12(6):573-7.
Exclusion: wrong outcomes.

Jones BA, Kasi SV, Curnen MG, et al. Severe obesity as an explanatory factor for the black/white difference in stage at diagnosis of breast cancer. Am J Epidemiol. 1997;146(5):394-404.
Exclusion: wrong population.

Jones R, McLean L, Young J, et al. Proportion of cancers detected at the first incident screen which were false negative at the prevalent screen. Breast. 1996;5(5):339-43.
Exclusion: wrong comparison.

Jonsson H, Bordas P, Wallin H, et al. Service screening with mammography in Northern Sweden: effects on breast cancer mortality - an update. J Med Screen. 2007;14(2):87-93.
Exclusion: included in an included systematic review, not directly used.

Appendix A4. List of Excluded Studies

Jonsson H, Johansson R, Lenner P. Increased incidence of invasive breast cancer after the introduction of service screening with mammography in Sweden. Int J Cancer. 2005;117(5):842-7.
Exclusion: wrong outcomes.

Jonsson H, Larsson L-G, Lenner P. Detection of breast cancer with mammography in the first screening round in relation to expected incidence in different age groups. Acta Oncol. 2003;42(1):22-9.
Exclusion: wrong outcomes.

Jonsson H, Nyström L, Tornberg S, et al. Service screening with mammography of women aged 50-69 years in Sweden: effects on mortality from breast cancer. J Med Screen. 2001;8(3):152-60.
Exclusion: included in an included systematic review, not directly used.

Jonsson H, Nyström L, Tornberg S, et al. Service screening with mammography. Long-term effects on breast cancer mortality in the county of Gavleborg, Sweden.[Erratum appears in Breast. 2003 Aug;12(4):297]. Breast. 2003;12(3):183-93.
Exclusion: included in an included systematic review, not directly used.

Jonsson H, Tornberg S, Nyström L, et al. Service screening with mammography of women aged 70-74 years in Sweden. Effects on breast cancer mortality. Cancer Detect Prev. 2003;27(5):360-9.
Exclusion: wrong study design for key question.

Jordan S, Lim L, Vilainerun D, et al. Breast cancer in the Thai Cohort Study: an exploratory case-control analysis. Breast. 2009;18(5):299-303.
Exclusion: wrong study design for key question.

Jorgensen KJ. Mammography screening in Norway caused substantial overdiagnosis and did not reduce late-stage breast cancers. Evid Based Med. 2013;18(2):e17.
Exclusion: wrong publication type.

Jorgensen KJ. Mammography screening is not as good as we hoped. Maturitas. 2010;65(1):1-2.
Exclusion: wrong publication type.

Jorgensen KJ. Mammography screening. Benefits, harms, and informed choice. Dan Med J. 2013;60(4):B4614.
Exclusion: review not meeting inclusion criteria.

Jorgensen KJ, Gotzsche PC. Overdiagnosis in publicly organised mammography screening programmes: systematic review of incidence trends. BMJ. 2009;339:b2587.
Exclusion: review not meeting inclusion criteria.

Jorgensen KJ, Gotzsche PC. Who evaluates public health programmes? A review of the NHS Breast Screening Programme. J R Soc Med. 2010;103(1):14-20.
Exclusion: wrong publication type.

Jorgensen KJ, Keen JD, Gotzsche PC. Is mammographic screening justifiable considering its substantial overdiagnosis rate and minor effect on mortality? Radiology. 2011;260(3):621-7.
Exclusion: wrong publication type.

Jørgensen KJ, Zahl PH, Gøtzsche PC. Breast cancer mortality in organised mammography screening in Denmark: comparative study. BMJ. 2010;340:c1241.
Exclusion: included in an included systematic review, not directly used.

Judkins AF, Akins J. Breast cancer: initial diagnosis and current treatment options. Nurs Clin North Am. 2001;36(3):527-42.
Exclusion: wrong publication type.

Juel I-M, Skaane P, Hoff SR, et al. Screen-film mammography versus full-field digital mammography in a population-based screening program: The Sogn and Fjordane study. Acta Radiol. 2010;51(9):962-8.
Exclusion: wrong comparison.

Jung HJ, Hahn SY, Choi H-Y, et al. Breast sonographic elastography using an advanced breast tissue-specific imaging preset: initial clinical results. J Ultrasound Med. 2012;31(2):273-80.
Exclusion: wrong outcomes.

Junod B, Zahl P-H, Kaplan RM, et al. An investigation of the apparent breast cancer epidemic in France: screening and incidence trends in birth cohorts. BMC Cancer. 2011;11:401.
Exclusion: wrong outcomes.

Kaaks R, Van Noord PA, Den Tonkelaar I, et al. Breast-cancer incidence in relation to height, weight and body-fat distribution in the Dutch "DOM" cohort. Int J Cancer. 1998;76(5):647-51.
Exclusion: wrong outcomes.

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Kaas R, Muller SH, Hart AAM, et al. Stage of breast cancers found during the surveillance of women with a familial or hereditary risk. Eur J Surg Oncol. 2008;34(5):501-7.
Exclusion: wrong population.

Kabat GC, Heo M, Kamensky V, et al. Adult height in relation to risk of cancer in a cohort of Canadian women. Int J Cancer. 2013;132(5):1125-32.
Exclusion: wrong outcomes.

Kacl GM, Liu P, Debatin JF, et al. Detection of breast cancer with conventional mammography and contrast-enhanced MR imaging. Eur Radiol. 1998;8(2):194-200.
Exclusion: wrong intervention.

Kaida H, Ishibashi M, Fujii T, et al. Improved detection of breast cancer on FDG-PET cancer screening using breast positioning device. Ann Nucl Med. 2008;22(2):95-101.
Exclusion: wrong intervention.

Kaiser JS, Helvie MA, Blacklaw RL, et al. Palpable breast thickening: role of mammography and US in cancer detection. Radiology. 2002;223(3):839-44.
Exclusion: wrong population.

Kalager M, Haldorsen T, Bretthauer M, et al. Improved breast cancer survival following introduction of an organized mammography screening program among both screened and unscreened women: a population-based cohort study. Breast Cancer Res. 2009;11(4):R44.
Exclusion: wrong comparison.

Kalager M, Zelen M, Langmark F, et al. Effect of screening mammography on breast-cancer mortality in Norway. N Engl J Med. 2010;363(13):1203-10.
Exclusion: included in an included systematic review, not directly used.

Kalli S, Freer PE, Rafferty EA. Lesions of the skin and superficial tissue at breast MR imaging. Radiographics. 2010;30(7):1891-913.
Exclusion: wrong publication type.

Kamineni A, Anderson ML, White E, et al. Body mass index, tumor characteristics, and prognosis following diagnosis of early-stage breast cancer in a mammographically screened population. Cancer Causes Control. 2013;24(2):305-12.
Exclusion: wrong comparison.

Kandula NR, Wen M, Jacobs EA, et al. Low rates of colorectal, cervical, and breast cancer screening in Asian Americans compared with non-Hispanic whites: Cultural influences or access to care? Cancer. 2006;107(1):184-92.
Exclusion: wrong outcomes.

Kane KY, Lindbloom EJ, Stevermer JJ. Does mammography add any benefit to a thorough clinical breast examination (CBE)? Journal of Family Practice. 2000;49(12):1078.
Exclusion: wrong publication type.

Kann PE, Bradley C, Lane DS. Outcomes of recommendations for breast biopsies in women receiving mammograms from a county health van. Public Health Rep. 1998;113(1):71-4.
Exclusion: wrong intervention.

Karssemeijer N, Hendriks JH. Computer-assisted reading of mammograms. Eur Radiol. 1997;7(5):743-8.
Exclusion: wrong publication type.

Katalinic A, Bartel C, Raspe H, et al. Beyond mammography screening: quality assurance in breast cancer diagnosis (The QuaMaDi Project). Br J Cancer. 2007;96(1):157-61.
Exclusion: wrong comparison.

Katapodi MC, Dodd MJ, Lee KA, et al. Underestimation of breast cancer risk: influence on screening behavior. Oncol Nurs Forum. 2009;36(3):306-14.
Exclusion: studies outside of search dates.

Kauhava L, Immonen-Raiha P, Parvinen I, et al. Population-based mammography screening results in substantial savings in treatment costs for fatal breast cancer. Breast Cancer Res Treat. 2006;98(2):143-50.
Exclusion: wrong outcomes.

Kavanagh AM, Cawson J, Byrnes GB, et al. Hormone replacement therapy, percent mammographic density, and sensitivity of mammography. Cancer Epidemiol Biomarkers Prev. 2005;14(5):1060-4.
Exclusion: wrong outcomes.

Kavanagh AM, Giles GG, Mitchell H, et al. The sensitivity, specificity, and positive predictive value of screening mammography and symptomatic status. J Med Screen. 2000;7(2):105-10.
Exclusion: wrong population.

Appendix A4. List of Excluded Studies

Kavanagh AM, Mitchell H, Giles GG. Hormone replacement therapy and accuracy of mammographic screening. Lancet. 2000;355(9200):270-4.
Exclusion: studies outside of search dates.

Kawai M, Kuriyama S, Suzuki A, et al. Effect of screening mammography on breast cancer survival in comparison to other detection methods: a retrospective cohort study. Cancer Sci. 2009;100(8):1479-84.
Exclusion: wrong population.

Keating NL, Kouri EM, He Y, et al. Effect of Massachusetts health insurance reform on mammography use and breast cancer stage at diagnosis. Cancer. 2013;119(2):250-8.
Exclusion: wrong outcomes.

Keavey E, Phelan N, O'Connell AM, et al. Comparison of the clinical performance of three digital mammography systems in a breast cancer screening programme. Br J Radiol. 2012;85(1016):1123-7.
Exclusion: wrong outcomes.

Keen JD. Promoting screening mammography: insight or uptake? J Am Board Fam Med. 2010;23(6):775-82.
Exclusion: wrong publication type.

Keen JD. Where is the evidence: does computer-aided overdiagnosis save lives? Radiology. 2010;254(3):989.
Exclusion: wrong publication type.

Keen JD, Keen JE. How does age affect baseline screening mammography performance measures? A decision model. BMC Med Inform Decis Mak. 2008;8:40.
Exclusion: wrong study design for key question.

Keen JD, Keen JE. What is the point: will screening mammography save my life? BMC Med Inform Decis Mak. 2009;9:18.
Exclusion: wrong study design for key question.

Kelly KM, Dean J, Comulada WS, et al. Breast cancer detection using automated whole breast ultrasound and mammography in radiographically dense breasts. Eur Radiol. 2010;20(3):734-42.
Exclusion: wrong comparison.

Kennedy DA, Lee T, Seely D. A comparative review of thermography as a breast cancer screening technique. Integ Cancer Ther. 2009;8(1):9-16.
Exclusion: review not meeting inclusion criteria.

Kennedy G, Markert M, Alexander JR, et al. Predictive value of BI-RADS classification for breast imaging in women under age 50. Breast Cancer Res Treat. 2011;130(3):819-23.
Exclusion: wrong outcomes.

Kenney PJ, Ellison MC. Ductal lavage in the screening of high-risk women. Curr Womens Health Rep. 2003;3(2):151-5.
Exclusion: wrong publication type.

Kerlikowske K. Efficacy of screening mammography among women aged 40 to 49 years and 50 to 69 years: comparison of relative and absolute benefit. J Natl Cancer Inst. 1997;Monographs.(22):79-86.
Exclusion: review not meeting inclusion criteria.

Kerlikowske K. How do personal characteristics affect sensitivity and specificity of mammography? Nat Clin Pract Oncol. 2005;2(1):16-7.
Exclusion: wrong publication type.

Kerlikowske K. Screening mammography in women less than age 50 years. Curr Opin Obstet Gynecol. 2012;24(1):38-43.
Exclusion: review not meeting inclusion criteria.

Kerlikowske K, Barclay J. Outcomes of modern screening mammography. J Natl Cancer Inst. 1997;Monographs.(22):105-11.
Exclusion: review not meeting inclusion criteria.

Kerlikowske K, Creasman J, Leung JWT, et al. Differences in screening mammography outcomes among White, Chinese, and Filipino women. Arch Intern Med. 2005;165(16):1862-8.
Exclusion: wrong comparison.

Kerlikowske K, Grady D, Barclay J, et al. Effect of age, breast density, and family history on the sensitivity of first screening mammography. JAMA. 1996;276(1):33-8.
Exclusion: wrong comparison.

Kerlikowske K, Grady D, Barclay J, et al. Likelihood ratios for modern screening mammography. Risk of breast cancer based on age and mammographic interpretation. JAMA. 1996;276(1):39-43.
Exclusion: wrong outcomes.

Kerlikowske K, Grady D, Rubin SM, et al. Efficacy of screening mammography. A meta-analysis. JAMA. 1995;273(2):149-54.
Exclusion: review not meeting inclusion criteria.

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Exclusion: wrong comparison.

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Exclusion: wrong outcomes.

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Exclusion: wrong study design for key question.

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Exclusion: wrong intervention.

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Exclusion: wrong comparison.

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Exclusion: wrong outcomes.

Khanna R, Bhanegaonkar A, Colsher P, et al. Breast cancer screening, incidence, and mortality in West Virginia. W V Med J. 2009;105 Spec No:24-32.
Exclusion: wrong intervention.

Khoo LAL, Taylor P, Given-Wilson RM. Computer-aided detection in the United Kingdom National Breast Screening Programme: prospective study. Radiology. 2005;237(2):444-9.
Exclusion: wrong intervention.

Kiely BE, Hossack LK, Shadbolt CL, et al. Practicalities of developing a breast magnetic resonance imaging screening service for women at high risk for breast cancer. ANZ J Surg. 2011;81(10):688-93.
Exclusion: wrong population.

Kim EK, Ko KH, Oh KK, et al. Clinical application of the BI-RADS final assessment to breast sonography in conjunction with mammography. AJR Am J Roentgenol. 2008;190(5):1209-15.
Exclusion: wrong intervention.

Kim SH, Kang BJ, Choi BG, et al. Radiologists' performance for detecting lesions and the interobserver variability of automated whole breast ultrasound. Korean J Radiol. 2013;14(2):154-63.
Exclusion: wrong outcomes.

Kim SJ, Chang JM, Cho N, et al. Outcome of breast lesions detected at screening ultrasonography. Eur J Radiol. 2012;81(11):3229-33.
Exclusion: wrong comparison.

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Exclusion: wrong intervention.

Kim SJ, Moon WK, Cho N, et al. Computer-aided detection in full-field digital mammography: sensitivity and reproducibility in serial examinations. Radiology. 2008;246(1):71-80.
Exclusion: wrong intervention.

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Exclusion: wrong outcomes.

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Exclusion: wrong outcomes.

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Exclusion: review not meeting inclusion criteria.

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Exclusion: wrong outcomes.

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Exclusion: wrong study design for key question.

Kitchen PR, Cawson JN, Winch KL, et al. Characteristics and treatment of breast cancers 10 mm or less detected by a mammographic screening programme. Aust N Z J Surg. 1998;68(1):45-9.
Exclusion: wrong study design for key question.

Kitchen PRB, Cawson JN, Moore SE, et al. Margins and outcome of screen-detected breast cancer with extensive in situ component. ANZ J Surg. 2006;76(7):591-5.
Exclusion: wrong comparison.

Kleit AN, Ruiz JF. False positive mammograms and detection controlled estimation. Health Serv Res. 2003;38(4):1207-28.
Exclusion: wrong study design for key question.

Klemi PJ, Parvinen I, Pylkkanen L, et al. Significant improvement in breast cancer survival through population-based mammography screening. Breast. 2003;12(5):308-13.
Exclusion: wrong comparison.

Klemi PJ, Toikkanen S, Rasanen O, et al. Mammography screening interval and the frequency of interval cancers in a population-based screening. Br J Cancer. 1997;75(5):762-6.
Exclusion: wrong outcomes.

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Kmietowicz Z. Mammography reduces risk of breast cancer death by 28%, study finds. BMJ. 2014;348:g4062.
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Exclusion: wrong comparison.

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Exclusion: wrong outcomes.

Kobetz E, Mendoza AD, Barton B, et al. Mammography use among Haitian women in Miami, Florida: an opportunity for intervention. J Immigr Minor Health. 2010;12(3):418-21.
Exclusion: wrong outcomes.

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Exclusion: wrong outcomes.

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Exclusion: wrong outcomes.

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Exclusion: wrong comparison.

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Exclusion: wrong study design for key question.

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Exclusion: wrong outcomes.

Kontos D, Bakic PR, Carton A-K, et al. Parenchymal texture analysis in digital breast tomosynthesis for breast cancer risk estimation: a preliminary study. Acad Radiol. 2009;16(3):283-98.
Exclusion: wrong outcomes.

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Exclusion: wrong publication type.

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Exclusion: wrong publication type.

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Exclusion: wrong publication type.

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Exclusion: wrong publication type.

Kopans DB. The most recent breast cancer screening controversy about whether mammographic screening benefits women at any age: nonsense and nonscience. AJR Am J Roentgenol. 2003;180(1):21-6.
Exclusion: wrong publication type.

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Exclusion: wrong publication type.

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Exclusion: wrong publication type.

Kopans DB. Updated results of the trials of screening mammography. Surg Oncol Clin N Am. 1997;6(2):233-63.
Exclusion: review not meeting inclusion criteria.

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Exclusion: wrong publication type.

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Exclusion: wrong publication type.

Kopans DB, Moore RH, McCarthy KA, et al. Biasing the Interpretation of Mammography Screening Data by Age Grouping: Nothing Changes Abruptly at Age 50. Breast J. 1998;4(3):139-45.
Exclusion: wrong outcomes.

Kopans DB, Smith RA, Duffy SW. Mammographic screening and "overdiagnosis". Radiology. 2011;260(3):616-20.
Exclusion: wrong publication type.

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Exclusion: wrong publication type.

Korn JE, Bar-Cohen A. Breast cancer screening in Minnesota. The role of physicians. Minn Med. 1996;79(10):26-9.
Exclusion: wrong outcomes.

Kornguth PJ, Rimer BK, Conaway MR, et al. Impact of patient-controlled compression on the mammography experience. Radiology. 1993;186(1):99-102.
Exclusion: included in an included systematic review, not directly used.

Kosters JP, Gotzsche PC. Regular self-examination or clinical examination for early detection of breast cancer. Cochrane Database Syst Rev. 2008;1
Exclusion: wrong outcomes.

Kosters PJ, Gotzsche PC. Regular self-examination or clinical examination for early detection of breast cancer. Cochrane Database Syst Rev. 2009(4)
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Kotsianos-Hermle D, Hiltawsky KM, Wirth S, et al. Analysis of 107 breast lesions with automated 3D ultrasound and comparison with mammography and manual ultrasound. Eur J Radiol. 2009;71(1):109-15.
Exclusion: wrong intervention.

Kotsianos-Hermle D, Wirth S, Fischer T, et al. First clinical use of a standardized three-dimensional ultrasound for breast imaging. Eur J Radiol. 2009;71(1):102-8.
Exclusion: wrong intervention.

Kriege M, Brekelmans CTM, Boetes C, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. N Engl J Med. 2004;351(5):427-37.
Exclusion: wrong population.

Kriege M, Brekelmans CTM, Boetes C, et al. Differences between first and subsequent rounds of the MRISC breast cancer screening program for women with a familial or genetic predisposition. Cancer. 2006;106(11):2318-26.
Exclusion: wrong population.

Krishnaiah PB, Nunes NL, Safranek S. FPIN's clinical inquiries. Screening mammography for reducing breast cancer mortality. Am Fam Physician. 2012;85(2):176-83.
Exclusion: wrong publication type.

Kritz-Silverstein D, Schneider DL, Sandwell J. Breast cancer and bone mass in older women: is bone density prescreening for mammography useful? Osteoporos Int. 2006;17(8):1196-201.
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Exclusion: wrong publication type.

Krupinski EA. Computer-aided detection in clinical environment: benefits and challenges for radiologists. Radiology. 2004;231(1):7-9.
Exclusion: wrong publication type.

Kuhl CK, Schild HH. Dynamic image interpretation of MRI of the breast. J Magn Reson Imaging. 2000;12(6):965-74.
Exclusion: review not meeting inclusion criteria.

Kuhl CK, Schmutzler RK, Leutner CC, et al. Breast MR imaging screening in 192 women proved or suspected to be carriers of a breast cancer susceptibility gene: preliminary results. Radiology. 2000;215(1):267-79.
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Exclusion: wrong population.

Kuo S-J, Chen TH-H, Yen AM-F, et al. Optimal two-stage breast cancer screening for countries with intermediate or low incidence of breast cancer. J Eval Clin Pract. 2010;16(6):1345-52.
Exclusion: wrong study design for key question.

Kuroki Y, Nasu K, Kuroki S, et al. Diffusion-weighted imaging of breast cancer with the sensitivity encoding technique: analysis of the apparent diffusion coefficient value. Magn Reson Med Sci. 2004;3(2):79-85.
Exclusion: wrong intervention.

Kurz KD, Steinhaus D, Klar V, et al. Assessment of three different software systems in the evaluation of dynamic MRI of the breast. Eur J Radiol. 2009;69(2):300-7.
Exclusion: wrong outcomes.

Kusano AS, Trichopoulos D, Terry KL, et al. A prospective study of breast size and premenopausal breast cancer incidence. Int J Cancer. 2006;118(8):2031-4.
Exclusion: wrong outcomes.

Kwek BH, Lau TN, Ng FC, et al. Non-consensual double reading in the Singapore Breast Screening Project: benefits and limitations. Ann Acad Med Singapore. 2003;32(4):438-41.
Exclusion: wrong outcomes.

Kwong A, Cheung PSY, Wong AYW, et al. The acceptance and feasibility of breast cancer screening in the East. Breast. 2008;17(1):42-50.
Exclusion: wrong comparison.

La Guardia M, Giammanco M. Breast cancer and obesity. Panminerva Med. 2001;43(2):123-33.
Exclusion: review not meeting inclusion criteria.

LaCroix AZ, Chlebowski RT, Manson JE, et al. Health outcomes after stopping conjugated equine estrogens among postmenopausal women with prior hysterectomy: a randomized controlled trial. JAMA. 2011;305(13):1305-14.
Exclusion: wrong intervention.

Lagerlund M, Sontrop JM, Zackrisson S. Psychosocial factors and attendance at a population-based mammography screening program in a cohort of Swedish women. BMC Womens Health. 2014;14(1):33.
Exclusion: wrong outcomes.

Lahmann PH, Hoffmann K, Allen N, et al. Body size and breast cancer risk: findings from the European Prospective Investigation into Cancer And Nutrition (EPIC). Int J Cancer. 2004;111(5):762-71.
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Lahmann PH, Lissner L, Berglund G. Breast cancer risk in overweight postmenopausal women. Cancer Epidemiol Biomarkers Prev. 2004;13(8):1414.
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Exclusion: wrong outcomes.

Lai MS, Yen MF, Kuo HS, et al. Efficacy of breast-cancer screening for female relatives of breast-cancer-index cases: Taiwan multicentre cancer screening (TAMCAS). Int J Cancer. 1998;78(1):21-6.
Exclusion: wrong population.

Lai Y-C, Huang Y-S, Wang D-W, et al. Computer-aided diagnosis for 3-d power Doppler breast ultrasound. Ultrasound Med Biol. 2013;39(4):555-67.
Exclusion: wrong outcomes.

Lajous M, Lazcano-Ponce E, Hernandez-Avila M, et al. Folate, vitamin B(6), and vitamin B(12) intake and the risk of breast cancer among Mexican women. Cancer Epidemiol Biomarkers Prev. 2006;15(3):443-8.
Exclusion: wrong outcomes.

Lambah A, Dixon J. Breast cancer: detection and management. Practitioner. 2000;244(1615):884-6.
Exclusion: wrong publication type.

Lambertz CK. Pre-medication with Acetaminophen for Screening Mammography: Gonzaga University; 1998.Book
Exclusion: included in an included systematic review, not directly used.

Lambertz CK, Johnson CJ, Montgomery PG, et al. Premedication to reduce discomfort during screening mammography. Radiology. 2008;248(3):765-72.
Exclusion: studies outside of search dates.

Lampic C, Thurfjell E, Bergh J, et al. Short- and long-term anxiety and depression in women recalled after breast cancer screening. Eur J Cancer. 2001;1990) 37(4):463-9.
Exclusion: studies outside of search dates.

Lampic C, Thurfjell E, Bergh J, et al. Short- and long-term anxiety and depression in women recalled after breast cancer screening. Eur J Cancer. 2001;37(4):463-9.
Exclusion: included in an included systematic review, not directly used.

Lampic C, Thurfjell E, Sjödén PO. The influence of a false-positive mammogram on a woman's subsequent behaviour for detecting breast cancer. Eur J Cancer. 2003;39(12):1730-7.
Exclusion: included in an included systematic review, not directly used.

Lane DS, Messina CR. Current perspectives on physician barriers to breast cancer screening. J Am Board Fam Pract. 1999;12(1):8-15.
Exclusion: wrong outcomes.

Lansdorp-Vogelaar I, Gulati R, Mariotto AB, et al. Personalizing age of cancer screening cessation based on comorbid conditions: model estimates of harms and benefits.[Summary for patients in Ann Intern Med. 2014 Jul 15;161(2). doi: 10.7326/P14-9023; PMID: 25023262]. Ann Intern Med. 2014;161(2):104-12.
Exclusion: wrong study design for key question.

Lantz PM, Ubel PA. The use of life expectancy in cancer screening guidelines. Moving with caution from model-based evidence to evidence-based guidelines. J Gen Intern Med. 2005;20(6):552-3.
Exclusion: wrong publication type.

Larsson SC, Bergkvist L, Wolk A. Glycemic load, glycemic index and breast cancer risk in a prospective cohort of Swedish women. Int J Cancer. 2009;125(1):153-7.
Exclusion: wrong outcomes.

Larsson SC, Mantzoros CS, Wolk A. Diabetes mellitus and risk of breast cancer: a meta-analysis. Int J Cancer. 2007;121(4):856-62.
Exclusion: wrong population.

Law J, Faulkner K. Concerning the relationship between benefit and radiation risk, and cancers detected and induced, in a breast screening programme. Br J Radiol. 2002;75(896):678-84.
Exclusion: wrong study design for key question.

Law J, Faulkner K. Radiation benefit and risk at the assessment stage of the UK breast screening programme. Br J Radiol. 2006;79:479-82.
Exclusion: wrong study design for key question.

Lazarus E, Mainiero MB, Gareen IF. Effect of referring physician specialty and practice type on referral for image-guided breast biopsy. J Am Coll Radiol. 2005;2(6):488-93.
Exclusion: wrong intervention.

Leconte I, Feger C, Galant C, et al. Mammography and subsequent whole-breast sonography of nonpalpable breast cancers: the importance of radiologic breast density. AJR Am J Roentgenol. 2003;180(6):1675-9.
Exclusion: wrong intervention.

Lee A, Chang J, Lim W, et al. Effectiveness of breast-specific gamma imaging (BSGI) for breast cancer in Korea: a comparative study. Breast J. 2012;18(5):453-8.
Exclusion: wrong intervention.

Lee CH. Problem solving MR imaging of the breast. Radiol Clin North Am. 2004;42(5):919-34.
Exclusion: wrong publication type.

Lee CH, Weinreb JC. The use of magnetic resonance imaging in breast cancer screening. J Am Coll Radiol. 2004;1(3):176-82.
Exclusion: wrong publication type.

Lee H-J, Kim E-K, Kim MJ, et al. Observer variability of Breast Imaging Reporting and Data System (BI-RADS) for breast ultrasound. Eur J Radiol. 2008;65(2):293-8.
Exclusion: wrong outcomes.

Lee S, Zelen M. A stochastic model for predicting the mortality of breast cancer. J Natl Cancer Inst. 2006;Monographs.(36):79-86.
Exclusion: wrong study design for key question.

Lee SJ, Boscardin WJ, Stijacic-Cenzer I, et al. Time lag to benefit after screening for breast and colorectal cancer: meta-analysis of survival data from the United States, Sweden, United Kingdom, and Denmark. BMJ. 2013;346:e8441.
Exclusion: wrong outcomes.

Lee SY, Jeong SH, Kim YN, et al. Cost-effective mammography screening in Korea: high incidence of breast cancer in young women. Cancer Sci. 2009;100(6):1105-11.
Exclusion: wrong outcomes.

Lees A, Gabos A, Jenkins H. Investigations for staging and follow-up of breast cancer patients. Cancer Prev Control. 1997;1(2):157-60.
Exclusion: wrong population.

Leff DR, Warren OJ, Enfield LC, et al. Diffuse optical imaging of the healthy and diseased breast: a systematic review. Breast Cancer Res Treat. 2008;108(1):9-22.
Exclusion: review not meeting inclusion criteria.

Legler J, Meissner HI, Coyne C, et al. The effectiveness of interventions to promote mammography among women with historically lower rates of screening. Cancer Epidemiol Biomarkers Prev. 2002;11(1):59-71.
Exclusion: wrong outcomes.

Legorreta AP, Brooks RJ, Leibowitz AN, et al. Cost of breast cancer treatment. A 4-year longitudinal study. Arch Intern Med. 1996;156(19):2197-201.
Exclusion: wrong outcomes.

Legorreta AP, Chernicoff HO, Trinh JB, et al. Diagnosis, clinical staging, and treatment of breast cancer: a retrospective multiyear study of a large controlled population. Am J Clin Oncol. 2004;27(2):185-90.
Exclusion: wrong population.

Lehman C, Holt S, Peacock S, et al. Use of the American College of Radiology BI-RADS guidelines by community radiologists: concordance of assessments and recommendations assigned to screening mammograms. AJR Am J Roentgenol. 2002;179(1):15-20.
Exclusion: wrong outcomes.

Lehman CD. Clinical indications: what is the evidence? Eur J Radiol. 2012;81 Suppl 1:S82-4.
Exclusion: review not meeting inclusion criteria.

Lehman CD. Role of MRI in screening women at high risk for breast cancer. J Magn Reson Imaging. 2006;24(5):964-70.
Exclusion: review not meeting inclusion criteria.

Lehman CD. Screening MRI for women at high risk for breast cancer. Semin Ultrasound CT MR. 2006;27(4):333-8.
Exclusion: review not meeting inclusion criteria.

Lehman CD, Blume JD, DeMartini WB, et al. Accuracy and interpretation time of computer-aided detection among novice and experienced breast MRI readers. AJR Am J Roentgenol. 2013;200(6):W683-9.
Exclusion: wrong outcomes.

Lehman CD, Isaacs C, Schnall MD, et al. Cancer yield of mammography, MR, and US in high-risk women: prospective multi-institution breast cancer screening study. Radiology. 2007;244(2):381-8.
Exclusion: wrong population.

Lehtimaki T, Lundin M, Linder N, et al. Long-term prognosis of breast cancer detected by mammography screening or other methods. Breast Cancer Res. 2011;13(6):R134.
Exclusion: wrong comparison.

Leinsinger GL, Friedl L, Tiling R, et al. Comparison of dynamic MR imaging of the breast and sestamibi scintimammography for evaluation of indeterminate mammographic lesions. Eur Radiol. 2001;11(10):2050-7.
Exclusion: wrong intervention.

Leitch AM. Breast cancer: screening and early detection. Tex Med. 2001;97(2):74-8.
Exclusion: review not meeting inclusion criteria.

Leivo T, Sintonen H, Tuominen R, et al. The cost-effectiveness of nationwide breast carcinoma screening in Finland, 1987-1992. Cancer. 1999;86(4):638-46.
Exclusion: wrong outcomes.

Lemon SC, Zapka JG, Clemow L, et al. Mammography screening after breast cancer diagnosis in a first degree female relative: age group differences (United States). Cancer Causes Control. 2006;17(8):1053-65.
Exclusion: wrong population.

Lenner P, Jonsson H. Excess mortality from breast cancer in relation to mammography screening in northern Sweden. J Med Screen. 1997;4(1):6-9.
Exclusion: wrong outcomes.

Lenz S. Breast ultrasound in office gynecology--ten years of experience. Ultraschall Med. 2011;32 Suppl 1:S3-7.
Exclusion: wrong outcomes.

Leonard BE, Leonard VF. Mammogram and diagnostic X-rays--evidence of protective Bystander, Adaptive Response (AR) radio-protection and AR retention at high dose levels. Int J Radiat Biol. 2008;84(11):885-99.
Exclusion: wrong outcomes.

Le-Petross CH, Bidaut L, Yang WT. Evolving role of imaging modalities in inflammatory breast cancer. Semin Oncol. 2008;35(1):51-63.
Exclusion: wrong publication type.

Lerman C, Trock B, Rimer BK, et al. Psychological and behavioral implications of abnormal mammograms. Ann Intern Med. 1991;114(8):657-61.
Exclusion: studies outside of search dates.

Lerman C, Trock B, Rimer BK, et al. Psychological and behavioral implications of abnormal mammograms. Ann Intern Med. 1991;114(8):657-61.
Exclusion: included in an included systematic review, not directly used.

Lerman C, Trock B, Rimer BK, et al. Psychological side effects of breast cancer screening. Health Psychol. 1991;10(4):259-67.
Exclusion: studies outside of search dates.

Lester J. Breast cancer in 2007: incidence, risk assessment, and risk reduction strategies. Clin J Oncol Nurs. 2007;11(5):619-22.
Exclusion: wrong publication type.

Letton AH, Mason EM, Ramshaw B. Twenty-year follow-up breast screening project. J Med Assoc Ga. 1996;85(1):31-2.
Exclusion: wrong study design for key question.

Letton AH, Mason EM, Ramshaw BJ. Twenty-year review of a breast cancer screening project. Ninety-five percent survival of patients with nonpalpable cancers. Cancer. 1996;77(1):104-6.
Exclusion: studies outside of search dates.

Leung GM, Lam TH, Hedley AJ. Screening mammography re-evaluated. Lancet. 2000;355(9205):750-1; author reply 2.
Exclusion: wrong publication type.

Leung GM, Lam T-H, Thach TQ, et al. Will screening mammography in the East do more harm than good? Am J Public Health. 2002;92(11):1841-6.
Exclusion: review not meeting inclusion criteria.

Leung JWT. Screening mammography reduces morbidity of breast cancer treatment. AJR Am J Roentgenol. 2005;184(5):1508-9.
Exclusion: wrong publication type.

Leung JWT, Margolin FR, Dee KE, et al. Performance parameters for screening and diagnostic mammography in a community practice: are there differences between specialists and general radiologists? AJR Am J Roentgenol. 2007;188(1):236-41.
Exclusion: wrong outcomes.

Levman JED, Causer P, Warner E, et al. Effect of the enhancement threshold on the computer-aided detection of breast cancer using MRI. Acad Radiol. 2009;16(9):1064-9.
Exclusion: wrong outcomes.

Appendix A4. List of Excluded Studies

Levman JED, Martel AL. A margin sharpness measurement for the diagnosis of breast cancer from magnetic resonance imaging examinations. Acad Radiol. 2011;18(12):1577-81.
Exclusion: wrong intervention.

Lewin JM, D'Orsi CJ, Hendrick RE, et al. Clinical comparison of full-field digital mammography and screen-film mammography for detection of breast cancer. AJR Am J Roentgenol. 2002;179(3):671-7.
Exclusion: wrong comparison.

Lewin JM, Hendrick RE, D'Orsi CJ, et al. Comparison of full-field digital mammography with screen-film mammography for cancer detection: results of 4,945 paired examinations. Radiology. 2001;218(3):873-80.
Exclusion: wrong comparison.

Li CI, Littman AJ, White E. Relationship between age maximum height is attained, age at menarche, and age at first full-term birth and breast cancer risk. Cancer Epidemiol Biomarkers Prev. 2007;16(10):2144-9.
Exclusion: wrong outcomes.

Li CI, Stanford JL, Daling JR. Anthropometric variables in relation to risk of breast cancer in middle-aged women. Int J Epidemiol. 2000;29(2):208-13.
Exclusion: wrong intervention.

Li H, Giger ML, Huo Z, et al. Computerized analysis of mammographic parenchymal patterns for assessing breast cancer risk: effect of ROI size and location. Med Phys. 2004;31(3):549-55.
Exclusion: wrong outcomes.

Lian M, Jeffe DB, Schootman M. Racial and geographic differences in mammography screening in St. Louis City: a multilevel study. J Urban Health. 2008;85(5):677-92.
Exclusion: wrong outcomes.

Liberman L, Freeman HP, Chandra S, et al. Carcinoma detection at the breast examination center of Harlem. Cancer. 2002;95(1):8-14.
Exclusion: wrong comparison.

Liberman L, Mason G, Morris EA, et al. Does size matter? Positive predictive value of MRI-detected breast lesions as a function of lesion size. AJR Am J Roentgenol. 2006;186(2):426-30.
Exclusion: wrong intervention.

Liberman M, Sampalis F, Mulder DS, et al. Breast cancer diagnosis by scintimammography: A meta-analysis and review of the literature. Breast Cancer Res Treat. 2003;80(1):115-26.
Exclusion: wrong intervention.

Libstug AR, Moravan V, Aitken SE. Results from the Ontario breast screening program, 1990-1995. J Med Screen. 1998;5(2):73-80.
Exclusion: wrong comparison.

Lickley HL. Primary breast cancer in the elderly. Can J Surg. 1997;40(5):341-51.
Exclusion: wrong publication type.

Lidbrink E, Elfving J, Frisell J, et al. Neglected aspects of false positive findings of mammography in breast cancer screening: Analysis of false positive cases from the Stockholm trial. Br Med J. 1996;312(7026):273-6.
Exclusion: wrong outcomes.

Lidbrink E, Elfwing J, Frisell J, et al. Neglected aspects of false positive findings of mammography in breast cancer screening: analysis of false positive cases from the Stockholm trial [see comments]. Br Med J. 1996;312:273-6.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Lidbrink E, Frisell J, Brandberg Y, et al. Nonattendance in the Stockholm mammography screening trial: Relative Mortality and reasons for nonattendance. Breast Cancer Res Treat. 1995;35(3):267-75.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Lidbrink E, Levi L, Pettersson I, et al. Single-view screening mammography: psychological, endocrine and immunological effects of recalling for a complete three-view examination. Eur J Cancer. 1995;31(6):932-3.
Exclusion: included in an included systematic review, not directly used.

Lind DS. Breast cancer testing: what is appropriate? J Surg Oncol. 2002;81(3):111-2.
Exclusion: wrong publication type.

Appendix A4. List of Excluded Studies

Linda A, Zuiani C, Londero V, et al. Outcome of initially only magnetic resonance mammography-detected findings with and without correlate at second-look sonography: distribution according to patient history of breast cancer and lesion size. Breast. 2008;17(1):51-7.
Exclusion: wrong intervention.

Lindfors KK, McGahan MC, Rosenquist CJ, et al. Computer-aided detection of breast cancer: a cost-effectiveness study.[Erratum appears in Radiology. 2007 Jan;242(1):320]. Radiology. 2006;239(3):710-7.
Exclusion: wrong outcomes.

Lindgren A, Pukkala E, Tuomilehto J, et al. Incidence of breast cancer among postmenopausal, hypertensive women. Int J Cancer. 2007;121(3):641-4.
Exclusion: wrong comparison.

Linver MN, Paster SB. Mammography outcomes in a practice setting by age: prognostic factors, sensitivity, and positive biopsy rate. J Natl Cancer Inst. 1997;Monographs.(22):113-7.
Exclusion: wrong outcomes.

Lipasti S, Anttila A, Pamilo M. Mammographic findings of women recalled for diagnostic work-up in digital versus screen-film mammography in a population-based screening program. Acta Radiol. 2010;51(5):491-7.
Exclusion: wrong comparison.

Lipkus IM, Halabi S, Strigo TS, et al. The impact of abnormal mammograms on psychosocial outcomes and subsequent screening. Psychooncology. 2000;9(5):402-10.
Exclusion: studies outside of search dates.

Lisby MD. Screening mammography in women 40 to 49 years of age. Am Fam Physician. 2004;70(9):1750-2.
Exclusion: wrong publication type.
Litherland JC, Evans AJ, Wilson AR. The effect of hormone replacement therapy on recall rate in the National Health Service Breast Screening Programme. Clin Radiol. 1997;52(4):276-9.
Exclusion: wrong outcomes.

Litherland JC, Stallard S, Hole D, et al. The effect of hormone replacement therapy on the sensitivity of screening mammograms. Clin Radiol. 1999;54(5):285-8.
Exclusion: wrong outcomes.

Liu MJ, Hawk H, Gershman ST, et al. The effects of a National Breast and Cervical Cancer Early Detection Program on social disparities in breast cancer diagnosis and treatment in Massachusetts. Cancer Causes Control. 2005;16(1):27-33.
Exclusion: wrong comparison.

Ljubicic N, Ivanda T, Strnad M, et al. The Croatian national breast cancer screening program--"mamma". Breast J. 2011;17(1):106-8.
Exclusion: wrong publication type.

Lo G, Cheung PSY. Use of magnetic resonance imaging for detecting clinically and mammographically occult ductal carcinoma in situ. Hong Kong Med J. 2008;14(3):229-32.
Exclusion: wrong study design for key question.

Lobb R, Ayanian JZ, Allen JD, et al. Stage of breast cancer at diagnosis among low-income women with access to mammography. Cancer. 2010;116(23):5487-96.
Exclusion: wrong comparison.

Localio AR, Zhou L, Norman SA. Measuring screening intensity in case-control studies of the efficacy of mammography. Am J Epidemiol. 2006;164(3):272-81.
Exclusion: wrong study design for key question.

Lochner DM, Brubaker KL. Incidence of malignancy in hormone therapy users with indeterminate calcifications on mammogram. Am J Obstet Gynecol. 2006;194(1):82-5.
Exclusion: wrong comparison.

Louwman WJ, van de Poll-Franse LV, Fracheboud J, et al. Impact of a programme of mass mammography screening for breast cancer on socio-economic variation in survival: a population-based study. Breast Cancer Res Treat. 2007;105(3):369-75.
Exclusion: wrong population.

Louwman WJ, van Diest PJ, van Beek MWPM, et al. Trends in breast cancer aggressiveness before the introduction of mass screening in southeastern Netherlands 1975-1989. Breast Cancer Res Treat. 2002;73(3):199-206.
Exclusion: wrong comparison.

Lowe JB, Balanda KP, Del Mar C, et al. Psychologic distress in women with abnormal findings in mass mammography screening. Cancer. 1999;85(5):1114-8.
Exclusion: included in an included systematic review, not directly used.

Lowe JB, Balanda KP, Del Mar C, et al. Psychologic distress in women with abnormal findings in mass mammography screening. Cancer. 1999;85(5):1114-8.
Exclusion: included in an included systematic review, not directly used.

Lowery JT, Byers T, Hokanson JE, et al. Complementary approaches to assessing risk factors for interval breast cancer. Cancer Causes Control. 2011;22(1):23-31.
Exclusion: wrong outcomes.

Lui CY, Lam HS, Chan LK, et al. Opportunistic breast cancer screening in Hong Kong; a revisit of the Kwong Wah Hospital experience. Hong Kong Med J. 2007;13(2):106-13.
Exclusion: wrong study design for key question.

Luke C, Priest K, Roder D. Changes in incidence of in situ and invasive breast cancer by histology type following mammography screening. Asian Pac J Cancer Prev. 2006;7(1):69-74.
Exclusion: wrong population.

Lumachi F, Ermani M, Marzola MC, et al. Relationship between prognostic factors of breast cancer and 99mTc-sestamibi uptake in patients who underwent scintimammography: Multivariate analysis of causes of false-negative results. Breast. 2006;15(1):130-4.
Exclusion: wrong comparison.

Lund E, Dumeaux V, Braaten T, et al. Cohort profile: The Norwegian Women and Cancer Study--NOWAC--Kvinner og kreft. Int J Epidemiol. 2008;37(1):36-41.
Exclusion: wrong publication type.

Lund E, Mode N, Waaseth M, et al. Overdiagnosis of breast cancer in the Norwegian Breast Cancer Screening Program estimated by the Norwegian Women and Cancer cohort study. BMC Cancer. 2013;13:614.
Exclusion: wrong outcomes.

Lynge E. Mammography screening for breast cancer in Copenhagen April 1991-March 1997. Mammography Screening Evaluation Group. APMIS Suppl. 1998;83:1-44.
Exclusion: studies outside of search dates.

Lynge E, Braaten T, Njor SH, et al. Mammography activity in Norway 1983 to 2008. Acta Oncol. 2011;50(7):1062-7.
Exclusion: studies outside of search dates.

Ma I, Dueck A, Gray R, et al. Clinical and self breast examination remain important in the era of modern screening. Ann Surg Oncol. 2012;19(5):1484-90.
Exclusion: wrong publication type.

Madjar H, Sauerbrei W, Hansen L. Multivariate analysis of flow data in breast lesions and validation in a normal clinical setting. Ultraschall Med. 2011;32(5):511-7.
Exclusion: wrong intervention.

Maes RM, Dronkers DJ, Hendriks JH, et al. Do non-specific minimal signs in a biennial mammographic breast cancer screening programme need further diagnostic assessment? Br J Radiol. 1997;70:34-8.
Exclusion: wrong comparison.

Magnus MC, Ping M, Shen MM, et al. Effectiveness of mammography screening in reducing breast cancer mortality in women aged 39-49 years: a meta-analysis. J Womens Health (Larchmt). 2011;20(6):845-52.
Exclusion: review not meeting inclusion criteria.

Mahnken JD, Chan W, Freeman DH, Jr., et al. Reducing the effects of lead-time bias, length bias and over-detection in evaluating screening mammography: a censored bivariate data approach. Stat Methods Med Res. 2008;17(6):643-63.
Exclusion: wrong study design for key question.

Mahoney MC, Meganathan K. False positive marks on unsuspicious screening mammography with computer-aided detection. J Digit Imaging. 2011;24(5):772-7.
Exclusion: wrong comparison.

Maidment AD. Digital mammography. Semin Roentgenol. 2003;38(3):216-30.
Exclusion: review not meeting inclusion criteria.

Majek O, Danes J, Skovajsova M, et al. Breast cancer screening in the Czech Republic: time trends in performance indicators during the first seven years of the organised programme. BMC Public Health. 2011;11:288.
Exclusion: wrong comparison.

Makela M, Saalasti-Koskinen U, Saarenmaa I, et al. The impact of an extension of breast cancer screening: update of Finohta's report 16/2000 (Structured abstract). Health Technology Assessment Database. 2014(1)
Exclusion: wrong publication type.

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Makretsov NA, Carter BA, Hayes MM. Mammography screening and indeterminate core biopsy diagnoses. Maturitas. 2012;73(3):177-9.
Exclusion: wrong publication type.

Malich A, Fischer DR, Facius M, et al. Effect of breast density on computer aided detection. J Digit Imaging. 2005;18(3):227-33.
Exclusion: wrong intervention.

Malich A, Marx C, Facius M, et al. Tumour detection rate of a new commercially available computer-aided detection system. Eur Radiol. 2001;11(12):2454-9.
Exclusion: wrong outcomes.

Malmgren J, Atwood M, Kaplan H. Breast cancer detection method among 20- to 49-year-old patients at a community based cancer center: 1990-2008. Breast J. 2012;18(3):257-60.
Exclusion: wrong population.

Malmgren JA, Atwood MK, Kaplan HG. Increase in mammography detected breast cancer over time at a community based regional cancer center: a longitudinal cohort study 1990-2005. BMC Cancer. 2008;8:131.
Exclusion: wrong study design for key question.

Malmgren JA, Parikh J, Atwood MK, et al. Impact of mammography detection on the course of breast cancer in women aged 40-49 years. Radiology. 2012;262(3):797-806.
Exclusion: wrong comparison.

Malmgren JA, Parikh J, Atwood MK, et al. Improved Prognosis of Women Aged 75 and Older with Mammography-detected Breast Cancer. Radiology. 2014
Exclusion: wrong comparison.

Mandelblatt J, Schechter CB, Lawrence W, et al. The SPECTRUM population model of the impact of screening and treatment on U.S. breast cancer trends from 1975 to 2000: principles and practice of the model methods. J Natl Cancer Inst. 2006;Monographs.(36):47-55.
Exclusion: wrong study design for key question.

Mandelblatt J, van Ravesteyn N, Schechter C, et al. Which strategies reduce breast cancer mortality most? Collaborative modeling of optimal screening, treatment, and obesity prevention. Cancer. 2013;119(14):2541-8.
Exclusion: wrong study design for key question.

Mandelblatt JS, Cronin KA, Bailey S, et al. Effects of mammography screening under different screening schedules: model estimates of potential benefits and harms.[Erratum appears in Ann Intern Med. 2010 Jan 19;152(2):136]. Ann Intern Med. 2009;151(10):738-47.
Exclusion: wrong study design for key question.

Mandelblatt JS, Cronin KA, Berry DA, et al. Modeling the impact of population screening on breast cancer mortality in the United States. Breast. 2011;20 Suppl 3:S75-81.
Exclusion: wrong study design for key question.

Mandelblatt JS, Schechter CB, Yabroff KR, et al. Toward optimal screening strategies for older women. Costs, benefits, and harms of breast cancer screening by age, biology, and health status. J Gen Intern Med. 2005;20(6):487-96.
Exclusion: wrong outcomes.

Mandelblatt JS, Schechter CB, Yabroff KR, et al. Benefits and costs of interventions to improve breast cancer outcomes in African American women. J Clin Oncol. 2004;22(13):2554-66.
Exclusion: wrong outcomes.

Mandelson MT, Oestreicher N, Porter PL, et al. Breast density as a predictor of mammographic detection: comparison of interval- and screen-detected cancers. J Natl Cancer Inst. 2000;92(13):1081-7.
Exclusion: wrong comparison.

Manfrin E, Mariotto R, Remo A, et al. Is there still a role for fine-needle aspiration cytology in breast cancer screening? Experience of the Verona Mammographic Breast Cancer Screening Program with real-time integrated radiopathologic activity (1999-2004). Cancer. 2008;114(2):74-82.
Exclusion: wrong outcomes.

Mann RM, Hoogeveen YL, Blickman JG, et al. MRI compared to conventional diagnostic work-up in the detection and evaluation of invasive lobular carcinoma of the breast: a review of existing literature. Breast Cancer Res Treat. 2008;107(1):1-14.
Exclusion: wrong intervention.

Marchick J, Henson DE. Correlations between access to mammography and breast cancer stage at diagnosis. Cancer. 2005;103(8):1571-80.
Exclusion: wrong outcomes.

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Mariotto R, Brancato B, Bonetti F, et al. Real-time reading in mammography breast screening. Radiol Med (Torino). 2007;112(2):287-303.
Exclusion: wrong outcomes.

Marquez Cruz MD, Marquez Calderon S. Diagnostic performance of digital mammography in breast cancer screening (Structured abstract). Health Technology Assessment Database. 2014(1)
Exclusion: wrong comparison.

Marshall T. Informed consent for mammography screening: modelling the risks and benefits for American women. Health Expect. 2005;8(4):295-305.
Exclusion: wrong intervention.

Marshall T, Adab P. Informed consent for breast screening: what should we tell women? J Med Screen. 2003;10(1):22-6.
Exclusion: studies outside of search dates.

Martincich L, Faivre-Pierret M, Zechmann CM, et al. Multicenter, double-blind, randomized, intraindividual crossover comparison of gadobenate dimeglumine and gadopentetate dimeglumine for Breast MR imaging (DETECT Trial). Radiology. 2011;258(2):396-408.
Exclusion: wrong intervention.

Marx C, Malich A, Facius M, et al. Are unnecessary follow-up procedures induced by computer-aided diagnosis (CAD) in mammography? Comparison of mammographic diagnosis with and without use of CAD. Eur J Radiol. 2004;51(1):66-72.
Exclusion: wrong outcomes.

Maskarinec G, Nagata C, Shimizu H, et al. Comparison of mammographic densities and their determinants in women from Japan and Hawaii.[Erratum appears in Int J Cancer. 2003 May 10;104(6):800]. Int J Cancer. 2002;102(1):29-33.
Exclusion: wrong study design for key question.

Maskarinec G, Pagano I, Chen Z, et al. Ethnic and geographic differences in mammographic density and their association with breast cancer incidence. Breast Cancer Res Treat. 2007;104(1):47-56.
Exclusion: wrong study design for key question.

Maskarinec G, Pagano I, Lurie G, et al. A longitudinal investigation of mammographic density: the multiethnic cohort. Cancer Epidemiol Biomarkers Prev. 2006;15(4):732-9.
Exclusion: wrong outcomes.

Maskarinec G, Wilkens L, Meng L. Mammography screening and the increase in breast cancer incidence in Hawaii. Cancer Epidemiol Biomarkers Prev. 1997;6(3):201-8.
Exclusion: wrong study design for key question.

Maskarinec G, Williams AE, Carlin L. Mammographic densities in a one-year isoflavone intervention. Eur J Cancer Prev. 2003;12(2):165-9.
Exclusion: wrong outcomes.

Masroor I. Prediction of benignity or malignancy of a lesion using BI-RADS. J Coll Physicians Surg Pak. 2005;15(11):686-8.
Exclusion: wrong outcomes.

Massat NJ, Sasieni PD, Parmar D, et al. An ongoing case-control study to evaluate the NHS breast screening programme. BMC Cancer. 2013;13:596.
Exclusion: wrong publication type.

Matcham NJ, Ridley NTF, Taylor SJ, et al. Breast screening: the use of consensus opinion for all recalls. Breast. 2004;13(3):184-7.
Exclusion: wrong study design for key question.

Mathijssen IMJ, Strijdhorst H, Kiestra SK, et al. Added value of ultrasound in screening the clinically negative axilla in breast cancer. J Surg Oncol. 2006;94(5):364-7.
Exclusion: wrong population.

Mattsson A, Leitz W, Rutqvist LE. Radiation risk and mammographic screening of women from 40 to 49 years of age: effect on breast cancer rates and years of life. Br J Cancer. 2000;82(1):220-6.
Exclusion: wrong outcomes.

Mattsson P. Mammography-related breast pain is associated with migraine. Cephalalgia. 2009;29(6):616-23.
Exclusion: wrong outcomes.

Maurice A, Evans DG, Affen J, et al. Surveillance of women at increased risk of breast cancer using mammography and clinical breast examination: further evidence of benefit. Int J Cancer. 2012;131(2):417-25.
Exclusion: wrong population.

Mayor S. Five year survival rate of women whose cancer is detected by screening has risen to 96.4%. BMJ. 2008;336(7658):1398-9.
Exclusion: wrong publication type.

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Mayor S. Mammography screening has little or no effect on breast cancer deaths, Swedish data indicate. BMJ. 2012;345:e4847.
Exclusion: wrong publication type.

Mayor S. Number of breast cancer cases detected by screening has doubled in a decade in England. BMJ. 2009;338:b414.
Exclusion: wrong outcomes.

McBean AM, Yu X, Virnig BA. Screening mammography rate and predictors following treatment for colorectal cancer. J Cancer Surviv. 2009;3(1):12-20.
Exclusion: wrong population.

McCann J, Duffy S, Day N, et al. Predicted long-term mortality reduction associated with the second round of breast screening in East Anglia. Br J Cancer. 2001;84(3):423-8.
Exclusion: wrong study design for key question.

McCann J, Stockton D, Day N. Breast cancer in East Anglia: the impact of the breast screening programme on stage at diagnosis. J Med Screen. 1998;5(1):42-8.
Exclusion: wrong outcomes.

McCann J, Stockton D, Godward S. Impact of false-positive mammography on subsequent screening attendance and risk of cancer. Breast Cancer Res. 2002;4(5):R11.
Exclusion: included in an included systematic review, not directly used.

McCann J, Treasure P, Duffy S. Modelling the impact of detecting and treating ductal carcinoma in situ in a breast screening programme. J Med Screen. 2004;11(3):117-25.
Exclusion: wrong study design for key question.

McCann J, Wait S, Seradour B, et al. A comparison of the performance and impact of breast cancer screening programmes in East Anglia, U.K. and Bouches du Rhone, France. Eur J Cancer. 1997;33(3):429-35.
Exclusion: wrong outcomes.

McCarthy EP, Burns RB, Coughlin SS, et al. Mammography use helps to explain differences in breast cancer stage at diagnosis between older black and white women. Ann Intern Med. 1998;128(9):729-36.
Exclusion: wrong outcomes.

McCarthy EP, Burns RB, Freund KM, et al. Mammography use, breast cancer stage at diagnosis, and survival among older women. J Am Geriatr Soc. 2000;48(10):1226-33.
Exclusion: wrong population.

McCarty CA, Reding DJ, Commins J, et al. Alcohol, genetics and risk of breast cancer in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial. Breast Cancer Res Treat. 2012;133(2):785-92.
Exclusion: wrong outcomes.

McCormack VA, dos Santos Silva I, De Stavola BL, et al. Fetal growth and subsequent risk of breast cancer: results from long term follow up of Swedish cohort. BMJ. 2003;326(7383):248.
Exclusion: wrong outcomes.

McCormack VA, Perry N, Vinnicombe SJ, et al. Ethnic variations in mammographic density: a British multiethnic longitudinal study. Am J Epidemiol. 2008;168(4):412-21.
Exclusion: wrong outcomes.

McCoy CB, Pereyra M, Metsch LR, et al. A community-based breast cancer screening program for medically underserved women: its effect on disease stage at diagnosis and on hazard of death. Rev Panam Salud Publica. 2004;15(3):160-7.
Exclusion: wrong outcomes.

McDonald S, Saslow D, Alciati MH. Performance and reporting of clinical breast examination: a review of the literature. CA Cancer J Clin. 2004;54(6):345-61.
Exclusion: wrong intervention.

McDougall JA, Li CI. Trends in distant-stage breast, colorectal, and prostate cancer incidence rates from 1992 to 2004: potential influences of screening and hormonal factors. Horm Cancer. 2010;1(1):55-62.
Exclusion: wrong outcomes.

McElroy JA, Remington PL, Gangnon RE, et al. Identifying geographic disparities in the early detection of breast cancer using a geographic information system. Prev Chronic Dis. 2006;3(1):A10.
Exclusion: wrong outcomes.

McGreevy JM, Loftus TJ. Outcomes evaluation for operative and nonoperative management of the abnormal mammogram. Am J Surg. 1998;175(1):69-72.
Exclusion: wrong population.

McKenzie F, Ives A, Jeffreys M. Socio-economic inequalities in survival from screen-detected breast cancer in South West England: population-based cohort study. Eur J Public Health. 2012;22(3):418-22.
Exclusion: wrong comparison.

McLaren CE, Chen W-P, Nie K, et al. Prediction of malignant breast lesions from MRI features: a comparison of artificial neural network and logistic regression techniques. Acad Radiol. 2009;16(7):842-51.
Exclusion: wrong intervention.

McLaughlin JM, Anderson RT, Ferketich AK, et al. Effect on survival of longer intervals between confirmed diagnosis and treatment initiation among low-income women with breast cancer. J Clin Oncol. 2012;30(36):4493-500.
Exclusion: wrong outcomes.

McPherson CP, Swenson KK, Jolitz G, et al. Survival of women ages 40-49 years with breast carcinoma according to method of detection. Cancer. 1997;79(10):1923-32.
Exclusion: wrong comparison.

McPherson CP, Swenson KK, Lee MW. The effects of mammographic detection and comorbidity on the survival of older women with breast cancer. J Am Geriatr Soc. 2002;50(6):1061-8.
Exclusion: wrong comparison.

McRae S. Screening mammography. Can J Rural Med. 2010;15(4):167; author reply 8.
Exclusion: wrong publication type.

McTiernan A. Exercise and breast cancer--time to get moving? N Engl J Med. 1997;336(18):1311-2.
Exclusion: wrong publication type.

McTiernan A, Irwin M, Vongruenigen V. Weight, physical activity, diet, and prognosis in breast and gynecologic cancers. J Clin Oncol. 2010;28(26):4074-80.
Exclusion: wrong population.

Medical Advisory S. Screening mammography for women aged 40 to 49 years at average risk for breast cancer: an evidence-based analysis (Structured abstract). Health Technology Assessment Database. 2014(1)
Exclusion: review not meeting inclusion criteria.

Medved M, Newstead GM, Abe H, et al. Clinical implementation of a multislice high spectral and spatial resolution-based MRI sequence to achieve unilateral full-breast coverage. Magn Reson Imaging. 2010;28(1):16-21.
Exclusion: wrong intervention.

Meersman SC, Breen N, Pickle LW, et al. Access to mammography screening in a large urban population: a multi-level analysis. Cancer Causes Control. 2009;20(8):1469-82.
Exclusion: wrong outcomes.

Meijnen P, Gilhuijs KG, Rutgers EJT. The effect of margins on the clinical management of ductal carcinoma in situ of the breast. J Surg Oncol. 2008;98(8):579-84.
Exclusion: wrong publication type.

Meissner HI, Smith RA, Rimer BK, et al. Promoting cancer screening: Learning from experience. Cancer. 2004;101(5 Suppl):1107-17.
Exclusion: wrong publication type.

Meldrum P, Turnbull D, Dobson HM, et al. Tailored written invitations for second round breast cancer screening: a randomised controlled trial. J Med Screen. 1994;1(4):245-8.
Exclusion: included in an included systematic review, not directly used.

Mellemkjaer L, Bigaard J, Tjonneland A, et al. Body composition and breast cancer in postmenopausal women: a Danish prospective cohort study. Obesity (Silver Spring). 2006;14(10):1854-62.
Exclusion: wrong outcomes.

Menashe I, Anderson WF, Jatoi I, et al. Underlying causes of the black-white racial disparity in breast cancer mortality: a population-based analysis. J Natl Cancer Inst. 2009;101(14):993-1000.
Exclusion: wrong outcomes.

Mendez A, Cabanillas F, Echenique M, et al. Evaluation of Breast Imaging Reporting and Data System Category 3 mammograms and the use of stereotactic vacuum-assisted breast biopsy in a nonacademic community practice. Cancer. 2004;100(4):710-4.
Exclusion: wrong outcomes.

Menes TS, Rosenberg R, Balch S, et al. Upgrade of high-risk breast lesions detected on mammography in the Breast Cancer Surveillance Consortium. Am J Surg. 2014;207(1):24-31.

Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Menna S, Di Virgilio MR, Burke P, et al. Diagnostic accuracy of commercial system for computer-assisted detection (CADx) as an adjunct to interpretation of mammograms. Radiol Med (Torino). 2005;110(4):334-40.
Exclusion: wrong intervention.

Menvielle G, Kunst AE, van Gils CH, et al. The contribution of risk factors to the higher incidence of invasive and in situ breast cancers in women with higher levels of education in the European prospective investigation into cancer and nutrition. Am J Epidemiol. 2011;173(1):26-37.
Exclusion: wrong outcomes.

Messecar DC. Mammography screening for older women with and without cognitive impairment. J Gerontol Nurs. 2000;26(4):14-24; quiz 52-3.
Exclusion: wrong study design for key question.

Meystre-Agustoni G, Paccaud F, Jeannin A, et al. Anxiety in a cohort of Swiss women participating in a mammographic screening programme. J Med Screen. 2001;8(4):213-9.
Exclusion: studies outside of search dates.

Michael M, Garzoli E, Reiner CS. Mammography, sonography and MRI for detection and characterization of invasive lobular carcinoma of the breast. Breast Dis. 2008;30:21-30.
Exclusion: wrong intervention.

Michaelsen K, Krishnaswamy V, Pogue BW, et al. Near-infrared spectral tomography integrated with digital breast tomosynthesis: effects of tissue scattering on optical data acquisition design. Med Phys. 2012;39(7):4579-87.
Exclusion: wrong outcomes.

Michaelson JS, Halpern E, Kopans DB. Breast cancer: computer simulation method for estimating optimal intervals for screening. Radiology. 1999;212(2):551-60.
Exclusion: wrong study design for key question.

Michaelson JS, Satija S, Kopans D, et al. Gauging the impact of breast carcinoma screening in terms of tumor size and death rate. Cancer. 2003;98(10):2114-24.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Michell MJ. Breast cancer screening. Int J Clin Pract. 2001;55(8):531-5.
Exclusion: wrong publication type.

Michell MJ, Iqbal A, Wasan RK, et al. A comparison of the accuracy of film-screen mammography, full-field digital mammography, and digital breast tomosynthesis. Clin Radiol. 2012;67(10):976-81.
Exclusion: wrong comparison.

Michels KB, Terry KL, Eliassen AH, et al. Adult weight change and incidence of premenopausal breast cancer. Int J Cancer. 2012;130(4):902-9.
Exclusion: wrong outcomes.

Michels KB, Terry KL, Willett WC. Longitudinal study on the role of body size in premenopausal breast cancer. Arch Intern Med. 2006;166(21):2395-402.
Exclusion: wrong outcomes.

Michels KB, Xue F, Terry KL, et al. Longitudinal study of birthweight and the incidence of breast cancer in adulthood. Carcinogenesis. 2006;27(12):2464-8.
Exclusion: wrong comparison.

Miglioretti DL, Gard CC, Carney PA, et al. When radiologists perform best: the learning curve in screening mammogram interpretation. Radiology. 2009;253(3):632-40.
Exclusion: wrong outcomes.

Miglioretti DL, Rutter CM, Geller BM, et al. Effect of breast augmentation on the accuracy of mammography and cancer characteristics. JAMA. 2004;291(4):442-50.
Exclusion: wrong comparison.

Miglioretti DL, Smith-Bindman R, Abraham L, et al. Radiologist characteristics associated with interpretive performance of diagnostic mammography. J Natl Cancer Inst. 2007;99(24):1854-63.
Exclusion: wrong intervention.

Miglioretti DL, Walker R, Weaver DL, et al. Accuracy of screening mammography varies by week of menstrual cycle. Radiology. 2011;258(2):372-9.
Exclusion: wrong outcomes.

Miller AB. Is mammography screening for breast cancer really not justifiable? Recent Results Cancer Res. 2003;163:115-28; discussion 264-6.
Exclusion: wrong publication type.

Appendix A4. List of Excluded Studies

Miller AB. Organized breast cancer screening programs in Canada. CMAJ. 2000;163(9):1150-1.
Exclusion: wrong publication type.

Miller AB. Overdiagnosis of breast cancer. Int J Cancer. 2013;133(11):2511.
Exclusion: wrong publication type.

Miller AB, Baines CJ, Sickles EA. Canadian National Breast Screening Study. AJR Am J Roentgenol. 1990;155(5):1133-4.
Exclusion: studies outside of search dates.

Miller AB, Baines CJ, To T. The Gothenburg breast screening trial: first results on mortality, incidence, and mode of detection for women ages 39-49 years at randomization. Cancer. 1998;83(1):186-90.
Exclusion: wrong publication type.

Miller AB, Fletcher SW. Annual mammography screening did not reduce long-term breast cancer mortality in women 40 to 59 years of age. Ann Intern Med. 2014;160(10):JC7.
Exclusion: wrong publication type.

Miller D, Livingstone V, Herbison P. Interventions for relieving the pain and discomfort of screening mammography. Cochrane Database Syst Rev. 2008(1):CD002942.
Exclusion: studies outside of search dates.

Miller D, Livingstone V, Herbison PG. Interventions for relieving the pain and discomfort of screening mammography. Cochrane Database Syst Rev. 2009(1)
Exclusion: review not meeting inclusion criteria.

Miller JC, Rafferty EA, Specht MC, et al. When is breast magnetic resonance imaging recommended for cancer detection? J Am Coll Radiol. 2008;5(3):224-6.
Exclusion: wrong publication type.

Miller JW, King JB, Ryerson AB, et al. Mammography use from 2000 to 2006: state-level trends with corresponding breast cancer incidence rates. AJR Am J Roentgenol. 2009;192(2):352-60.
Exclusion: wrong study design for key question.

Miller M. Cancer incidence trends differ between Europe, United States. J Natl Cancer Inst. 2001;93(19):1444-5.
Exclusion: wrong publication type.

Millet I, Pages E, Hoa D, et al. Pearls and pitfalls in breast MRI. Br J Radiol. 2012;85(1011):197-207.
Exclusion: review not meeting inclusion criteria.

Milne ENC, Krupinski EA, Helvie MA, et al. Computer-aided detection of breast cancer. Radiology. 2004;233(2):615-6; author reply 6-7.
Exclusion: wrong publication type.

Miltenburg GA, Peeters PH, Fracheboud J, et al. Seventeen-year evaluation of breast cancer screening: the DOM project, The Netherlands. Diagnostisch Onderzoek (investigation) Mammacarcinoom. Br J Cancer. 1998;78(7):962-5.
Exclusion: wrong study design for key question.

Mincey BA, Perez EA. Advances in screening, diagnosis, and treatment of breast cancer. Mayo Clin Proc. 2004;79(6):810-6.
Exclusion: review not meeting inclusion criteria.

Mink PJ, Shahar E, Rosamond WD, et al. Serum insulin and glucose levels and breast cancer incidence: the atherosclerosis risk in communities study. Am J Epidemiol. 2002;156(4):349-52.
Exclusion: wrong outcomes.

Mitchell J, Lannin DR, Mathews HF, et al. Religious beliefs and breast cancer screening. J Womens Health (Larchmt). 2002;11(10):907-15.
Exclusion: wrong outcomes.

Mittra I, Baum M, Thornton H, et al. Is clinical breast examination an acceptable alternative to mammographic screening? BMJ. 2000;321(7268):1071-3.
Exclusion: wrong publication type.

Mittra I, Mishra GA, Singh S, et al. A cluster randomized, controlled trial of breast and cervix cancer screening in Mumbai, India: methodology and interim results after three rounds of screening. Int J Cancer. 2010;126(4):976-84.
Exclusion: wrong intervention.

Miyake K, Hayakawa K, Nishino M, et al. Benign or malignant?: differentiating breast lesions with computed tomography attenuation values on dynamic computed tomography mammography. J Comput Assist Tomogr. 2005;29(6):772-9.
Exclusion: wrong intervention.

Miyake T, Shimazu K, Ohashi H, et al. Indication for sentinel lymph node biopsy for breast cancer when core biopsy shows ductal carcinoma in situ. Am J Surg. 2011;202(1):59-65.
Exclusion: wrong intervention.

Appendix A4. List of Excluded Studies

Mobley LR, Kuo T-MM, Watson L, et al. Geographic disparities in late-stage cancer diagnosis: multilevel factors and spatial interactions. Health Place. 2012;18(5):978-90.
Exclusion: wrong outcomes.

Moin P, Deshpande R, Sayre J, et al. An observer study for a computer-aided reading protocol (CARP) in the screening environment for digital mammography. Acad Radiol. 2011;18(11):1420-9.
Exclusion: wrong outcomes.

Moller B, Weedon-Fekjaer H, Hakulinen T, et al. The influence of mammographic screening on national trends in breast cancer incidence. Eur J Cancer Prev. 2005;14(2):117-28.
Exclusion: wrong outcomes.

Monnin P, Bochud FO, Verdun FR. Using a NPWE model observer to assess suitable image quality for a digital mammography quality assurance programme. Radiat Prot Dosimetry. 2010;139(1-3):459-62.
Exclusion: wrong outcomes.

Montella M, Buonanno M, Biondi E, et al. Changing patterns of breast cancer stage at diagnosis in southern italy: hospital data as indicators of progressive changes. Prev Med. 2000;30(2):174-7.
Exclusion: wrong comparison.

Montella M, Schittulli F. Reduction in the number of women with advanced breast cancer stage at diagnosis in Italy. Eur J Cancer Prev. 2005;14(1):79-80.
Exclusion: wrong publication type.

Montgomery M, McCrone SH. Psychological distress associated with the diagnostic phase for suspected breast cancer: systematic review. J Adv Nurs. 2010;66(11):2372-90.
Exclusion: review not meeting inclusion criteria.

Monticciolo DL, Caplan LS. The American College of Radiology's BI-RADS 3 Classification in a Nationwide Screening Program: current assessment and comparison with earlier use. Breast J. 2004;10(2):106-10.
Exclusion: wrong outcomes.

Moon JH, Kim HH, Shin HJ, et al. Supplemental use of optical diffusion breast imaging for differentiation between benign and malignant breast lesions. AJR Am J Roentgenol. 2011;197(3):732-9.
Exclusion: wrong population.

Moon WK, Choi JW, Cho N, et al. Computer-aided analysis of ultrasound elasticity images for classification of benign and malignant breast masses. AJR Am J Roentgenol. 2010;195(6):1460-5.
Exclusion: wrong intervention.

Moon WK, Shen Y-W, Huang C-S, et al. Comparative study of density analysis using automated whole breast ultrasound and MRI. Med Phys. 2011;38(1):382-9.
Exclusion: wrong population.

Moore SG, Shenoy PJ, Fanucchi L, et al. Cost-effectiveness of MRI compared to mammography for breast cancer screening in a high risk population. BMC Health Serv Res. 2009;9:9.
Exclusion: wrong outcomes.

Moorman PG, Jones BA, Millikan RC, et al. Race, anthropometric factors, and stage at diagnosis of breast cancer. Am J Epidemiol. 2001;153(3):284-91.
Exclusion: wrong study design for key question.

Moraes PdC, Chala LF, Chang YS, et al. Observer variability in the application of morphologic and dynamic criteria according to the BI-RADS for MRI. Breast J. 2010;16(5):558-60.
Exclusion: wrong publication type.

Moran CJ, Saranathan M, Nnewihe AN, et al. High resolution images of the breast. Eur J Radiol. 2012;81 Suppl 1:S101-3.
Exclusion: wrong study design for key question.

Morimoto T, Okazaki M, Endo T. Current status and goals of mammographic screening for breast cancer in Japan. Breast Cancer. 2004;11(1):73-81.
Exclusion: review not meeting inclusion criteria.

Morimoto T, Sasa M, Yamaguchi T, et al. Breast cancer screening by mammography in women aged under 50 years in Japan. Anticancer Res. 2000;20(5C):3689-94.
Exclusion: wrong population.

Morimoto T, Sasa M, Yamaguchi T, et al. Effectiveness of mammographic screening for breast cancer in women aged over 50 years in Japan. Jpn J Cancer Res. 1997;88(8):778-84.
Exclusion: wrong outcomes.

Morin RL, Maidment ADA. Digital mammography: coming of age. J Am Coll Radiol. 2005;2(9):798-801.
Exclusion: wrong publication type.

Appendix A4. List of Excluded Studies

Morland B, Lund Haheim L, Linnestad K. Mammography screening (Structured abstract). Health Technology Assessment Database. 2014(1)
Exclusion: review not meeting inclusion criteria.

Morrell S, Taylor R, Roder D, et al. Mammography screening and breast cancer mortality in Australia: an aggregate cohort study. J Med Screen. 2012;19(1):26-34.
Exclusion: wrong study design for key question.

Morrow M. The certainties and the uncertainties of ductal carcinoma in situ. J Natl Cancer Inst. 2004;96(6):424-5.
Exclusion: wrong publication type.

Morrow M. Magnetic resonance imaging in breast cancer: is seeing always believing? Eur J Cancer. 2005;41(10):1368-9.
Exclusion: wrong publication type.

Morrow M, Harris JR. More mastectomies: is this what patients really want? J Clin Oncol. 2009;27(25):4038-40.
Exclusion: wrong publication type.

Mortensen PB. Breast cancer risk in psychiatric patients. Am J Psychiatry. 1997;154(4):589; author reply -90.
Exclusion: wrong publication type.

Moskowitz M. Guidelines for screening for breast cancer: Is a revision in order? Radiol Clin North Am. 1992;30(1):221-33.
Exclusion: wrong publication type.

Moss S. Screening women aged 40-49 years. Prev Med. 2011;53(3):105-7.
Exclusion: wrong publication type.

Moss S. A trial to study the effect on breast cancer mortality of annual mammographic screening in women starting at age 40. J Med Screen. 1999;6(3):144-8.
Exclusion: wrong publication type.

Moss S, Thomas I, Evans A, et al. Randomised controlled trial of mammographic screening in women from age 40: results of screening in the first 10 years. Br J Cancer. 2005;92(5):949-54.
Exclusion: studies outside of search dates.

Moss SM. Advances in screening for breast cancer. Cancer Treat Res. 1996;86:77-91.
Exclusion: review not meeting inclusion criteria.

Moss SM, Blanks RG, Bennett RL. Is radiologists' volume of mammography reading related to accuracy? A critical review of the literature. Clin Radiol. 2005;60(6):623-6.
Exclusion: review not meeting inclusion criteria.

Moss SM, Brown J, Garvican L, et al. Routine breast screening for women aged 65-69: results from evaluation of the demonstration sites. Br J Cancer. 2001;85(9):1289-94.
Exclusion: wrong study design for key question.

Moss SM, Nyström L, Jonsson H, et al. The impact of mammographic screening on breast cancer mortality in Europe: a review of trend studies. J Med Screen. 2012;19 Suppl 1:26-32.
Exclusion: review not meeting inclusion criteria.

Mou X, Chen X, Sun L, et al. The impact of calibration phantom errors on dual-energy digital mammography. Phys Med Biol. 2008;53(22):6321-36.
Exclusion: wrong outcomes.

Mouchawar J, Taplin S, Ichikawa L, et al. Late-stage breast cancer among women with recent negative screening mammography: do clinical encounters offer opportunity for earlier detection? J Natl Cancer Inst. 2005;Monographs.(35):39-46.
Exclusion: wrong comparison.

Mountford CE, Stanwell P, Ramadan S. Breast MR imaging at 3.0 T. Radiology. 2008;248(1):319-20; author reply 20.
Exclusion: wrong publication type.

Mousa NA, Crystal P, Wolfman WL, et al. Aromatase inhibitors and mammographic breast density in postmenopausal women receiving hormone therapy. Menopause. 2008;15(5):875-84.
Exclusion: wrong outcomes.

Moy L, Elias K, Patel V, et al. Is breast MRI helpful in the evaluation of inconclusive mammographic findings? AJR Am J Roentgenol. 2009;193(4):986-93.
Exclusion: wrong intervention.

Moy L, Noz ME, Maguire GQ, Jr., et al. Role of fusion of prone FDG-PET and magnetic resonance imaging of the breasts in the evaluation of breast cancer. Breast J. 2010;16(4):369-76.
Exclusion: wrong outcomes.

Moy L, Ponzo F, Noz ME, et al. Improving specificity of breast MRI using prone PET and fused MRI and PET 3D volume datasets. J Nucl Med. 2007;48(4):528-37.
Exclusion: wrong intervention.

Moyle P, Warren R. Screening women at moderate risk of breast cancer. Br J Hosp Med (Lond). 2007;68(11):584-8.
Exclusion: review not meeting inclusion criteria.

Muir TM, Tresham J, Fritschi L, et al. Screening for breast cancer post reduction mammoplasty.[Erratum appears in Clin Radiol. 2010 Jun;65(6):498]. Clin Radiol. 2010;65(3):198-205.
Exclusion: wrong outcomes.

Mukhtar TK, Yeates DR, Goldacre MJ. Breast cancer mortality trends in England and the assessment of the effectiveness of mammography screening: population-based study. J R Soc Med. 2013;106(6):234-42.
Exclusion: wrong comparison.

Muller-Schimpfle M, Ohmenhauser K, Sand J, et al. Dynamic 3D-MR mammography: is there a benefit of sophisticated evaluation of enhancement curves for clinical routine? J Magn Reson Imaging. 1997;7(1):236-40.
Exclusion: wrong outcomes.

Mundy L, Braunack-Mayer A, Merlin T. The role of scintimammography in the diagnosis of breast cancer (Structured abstract). Health Technology Assessment Database. 2014(1)
Exclusion: wrong intervention.

Murad M, Bari V. Ultrasound differentiation of benign versus malignant solid breast masses. J Coll Physicians Surg Pak. 2004;14(3):166-9.
Exclusion: wrong outcomes.

Muramatsu C, Li Q, Schmidt RA, et al. Determination of similarity measures for pairs of mass lesions on mammograms by use of BI-RADS lesion descriptors and image features. Acad Radiol. 2009;16(4):443-9.
Exclusion: wrong outcomes.

Murday V, Pears R, Ball J, et al. An audit of screening for familial breast cancer before 50 years in the South Thames Region - have we got it right? Fam Cancer. 2004;3(1):29-34.
Exclusion: wrong study design for key question.

Murthy NS, Agarwal UK, Chaudhry K, et al. A study on time trends in incidence of breast cancer - Indian scenario. Eur J Cancer Care (Engl). 2007;16(2):185-6.
Exclusion: wrong study design for key question.

Mushlin AI, Kouides RW, Shapiro DE. Estimating the accuracy of screening mammography: a meta-analysis. Am J Prev Med. 1998;14(2):143-53.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Mussurakis S, Buckley DL, Coady AM, et al. Observer variability in the interpretation of contrast enhanced MRI of the breast. Br J Radiol. 1996;69(827):1009-16.
Exclusion: wrong outcomes.

Muti P. Re: "Serum insulin and glucose levels and breast cancer incidence: the Atherosclerosis Risk in Communities Study". Am J Epidemiol. 2003;158(6):607; author reply 8.
Exclusion: wrong publication type.

Muti P, Quattrin T, Grant BJB, et al. Fasting glucose is a risk factor for breast cancer: a prospective study. Cancer Epidemiol Biomarkers Prev. 2002;11(11):1361-8.
Exclusion: wrong outcomes.

Muttalib M, Sinnett HD. Re: Power et al. Needle-localised biopsy of impalpable breast lesions: a novel adjunct to surgical technique and specimen mammography. Surg J R Coll Surg Edinb Irel 2004; 2(6): 343-45. Surgeon. 2006;4(1):60.
Exclusion: wrong publication type.

Myles JP, Nixon RM, Duffy SW, et al. Bayesian evaluation of breast cancer screening using data from two studies. Stat Med. 2003;22(10):1661-74.
Exclusion: wrong outcomes.

Myles JP, Salmininen T, Duffy SW, et al. Prospective estimation of rates of change in mammographic parenchymal patterns: influence of age and of hormone replacement therapy. Breast. 2004;13(1):56-60.
Exclusion: wrong outcomes.

Naderi T, Bahrampoor A. Determination of sensitivity and specificity of breast tumor diagnosis by primary health care providers (Behvarz) using clinical examination by obstetrician as a gold standard. J Obstet Gynaecol Res. 2003;29(2):59-62.
Exclusion: wrong intervention.

Nakagawa T, Hara T, Fujita H, et al. Radial-searching contour extraction method based on a modified active contour model for mammographic masses. Radiol Phys Technol. 2008;1(2):151-61.
Exclusion: wrong intervention.

Nakano S, Ohtsuka M, Mibu A, et al. Diagnostic imaging strategy for MDCT- or MRI-detected breast lesions: use of targeted sonography. BMC Medical Imaging. 2012;12:13.
Exclusion: wrong intervention.

Nakano S, Yoshida M, Fujii K, et al. Real-time virtual sonography, a coordinated sonography and MRI system that uses magnetic navigation, improves the sonographic identification of enhancing lesions on breast MRI. Ultrasound Med Biol. 2012;38(1):42-9.
Exclusion: wrong outcomes.

Narayanan D, Madsen KS, Kalinyak JE, et al. Interpretation of positron emission mammography and MRI by experienced breast imaging radiologists: performance and observer reproducibility. AJR Am J Roentgenol. 2011;196(4):971-81.
Exclusion: wrong outcomes.

Narod SA. Age of diagnosis, tumor size, and survival after breast cancer: implications for mammographic screening. Breast Cancer Res Treat. 2011;128(1):259-66.
Exclusion: wrong comparison.

Narod SA. Re: Canadian national breast screening study-2: 13-year results of a randomized trial in women aged 50-59 years. J Natl Cancer Inst. 2001;93(5):396-7.
Exclusion: wrong publication type.

Nasseri K. Secular trends in the incidence of female breast cancer in the United States, 1973-1998.[Erratum appears in Breast J. 2004 Jul-Aug;10(4):380]. Breast J. 2004;10(2):129-35.
Exclusion: wrong comparison.

National Cancer Institute. Cancer control research. U.S. National Institutes of Health. Available at: http://cancercontrol.cancer.gov/grants/abstract.asp?applid=6965060. Accessed.
Exclusion: wrong publication type.

Nattinger AB. Older women, mammography, and mortality from breast cancer. Am J Med. 2000;108(2):174-5.
Exclusion: wrong publication type.

Navarro AM, Senn KL, McNicholas LJ, et al. Por La Vida model intervention enhances use of cancer screening tests among Latinas. Am J Prev Med. 1998;15(1):32-41.
Exclusion: wrong outcomes.

Nederend J, Duijm LE, Louwman MW, et al. Trends in surgery for screen-detected and interval breast cancers in a national screening programme. Br J Surg. 2014;101(8):949-58.
Exclusion: wrong outcomes.

Nederend J, Duijm LE, Voogd AC, et al. Trends in incidence and detection of advanced breast cancer at biennial screening mammography in The Netherlands: a population based study. Breast Cancer Res. 2012;14(1):R10.
Exclusion: wrong comparison.

Nederend J, Duijm LEM, Louwman MWJ, et al. Impact of transition from analog screening mammography to digital screening mammography on screening outcome in The Netherlands: a population-based study. Ann Oncol. 2012;23(12):3098-103.
Exclusion: wrong comparison.

Neeser K, Szucs T, Bulliard J-L, et al. Cost-effectiveness analysis of a quality-controlled mammography screening program from the Swiss statutory health-care perspective: quantitative assessment of the most influential factors. Value Health. 2007;10(1):42-53.
Exclusion: wrong comparison.

Nekhlyudov L, Li R, Fletcher SW. Informed decision making before initiating screening mammography: does it occur and does it make a difference? Health Expect. 2008;11(4):366-75.
Exclusion: studies outside of search dates.

Nelson R. MRI better than mammography for detection of breast cancer? Lancet Oncol. 2004;5(9):520.
Exclusion: wrong publication type.

Newman LA, Sabel M. Advances in breast cancer detection and management. Med Clin North Am. 2003;87(5):997-1028.
Exclusion: review not meeting inclusion criteria.

Ng EH, Ng FC, Tan PH, et al. Results of intermediate measures from a population-based, randomized trial of mammographic screening prevalence and detection of breast carcinoma among Asian women: the Singapore Breast Screening Project. Cancer. 1998;82(8):1521-8.

Exclusion: wrong population.

Ng EH, Ng FC, Tan PH, et al. Results of intermediate measures from a population-based, randomized trial of mammographic screening prevalence and detection of breast carcinoma among Asian women: the Singapore Breast Screening Project.[Erratum appears in Cancer 1998 Jul 1;83(1):191]. Cancer. 1998;82(8):1521-8.
Exclusion: wrong outcomes.

Nickson C, Kavanagh AM. Tumour size at detection according to different measures of mammographic breast density. J Med Screen. 2009;16(3):140-6.
Exclusion: wrong comparison.

Nickson C, Mason KE, English DR, et al. Mammographic screening and breast cancer mortality: a case-control study and meta-analysis. Cancer Epidemiol Biomarkers Prev. 2012;21(9):1479-88.
Exclusion: wrong study design for key question.

Nickson C, Mason KE, Kavanagh AM. Breast cancer screening of women aged 70-74 years: results from a natural experiment across Australia. Breast Cancer Res Treat. 2014;143(2):367-72.
Exclusion: wrong outcomes.

Nie K, Chen J-H, Yu HJ, et al. Quantitative analysis of lesion morphology and texture features for diagnostic prediction in breast MRI. Acad Radiol. 2008;15(12):1513-25.
Exclusion: wrong population.

Nilsen TI, Vatten LJ. Adult height and risk of breast cancer: a possible effect of early nutrition. Br J Cancer. 2001;85(7):959-61.
Exclusion: wrong outcomes.

Nishikawa RM, Acharyya S, Gatsonis C, et al. Comparison of soft-copy and hard-copy reading for full-field digital mammography. Radiology. 2009;251(1):41-9.
Exclusion: wrong intervention.

Nishikawa RM, Schmidt RA, Linver MN, et al. Clinically missed cancer: how effectively can radiologists use computer-aided detection?.[Erratum appears in AJR Am J Roentgenol. 2012 May;198(5):1232]. AJR Am J Roentgenol. 2012;198(3):708-16.
Exclusion: wrong intervention.

Nixon R, Prevost TC, Duffy SW, et al. Some random-effects models for the analysis of matched-cluster randomised trials: application to the Swedish two-county trial of breast-cancer screening. J Epidemiol Biostat. 2000;5(6):349-58.
Exclusion: wrong study design for key question.

Nixon RM, Pharoah P, Tabár L, et al. Mammographic screening in women with a family history of breast cancer: some results from the Swedish two-county trial. Rev Epidemiol Sante Publique. 2000;48(4):325-31.
Exclusion: wrong comparison.

Njor S, Nyström L, Moss S, et al. Breast cancer mortality in mammographic screening in Europe: a review of incidence-based mortality studies. J Med Screen. 2012;19 Suppl 1:33-41.
Exclusion: review not meeting inclusion criteria.

Njor SH, Hallas J, Schwartz W, et al. Type of hormone therapy and risk of misclassification at mammography screening. Menopause. 2011;18(2):171-7.
Exclusion: wrong comparison.

Njor SH, Olsen AH, Schwartz W, et al. Tumour size distribution in mammography screening. Breast. 2005;14(4):329-32.
Exclusion: wrong comparison.

Njor SH, Pedersen AT, Schwartz W, et al. Minimizing misclassification of hormone users at mammography screening. Int J Cancer. 2009;124(9):2159-65.
Exclusion: wrong comparison.

Noble M, Bruening W, Uhl S, et al. Computer-aided detection mammography for breast cancer screening: systematic review and meta-analysis. Arch Gynecol Obstet. 2009;279(6):881-90.
Exclusion: wrong outcomes.

Norden T, Thurfjell E, Hasselgren M, et al. Mammographic screening for breast cancer. What cancers do we find? Eur J Cancer. 1997;33(4):624-8.
Exclusion: wrong comparison.

Norman SA, Daly MB, McCorkle R, et al. Breast cancer and mammography: an American Cancer Society profile of Philadelphia and Montgomery Counties. Cancer Pract. 1996;4(2):68-75.
Exclusion: wrong publication type.

Appendix A4. List of Excluded Studies

Norman SA, Localio AR, Zhou L, et al. Benefit of screening mammography in reducing the rate of late-stage breast cancer diagnoses (United States). Cancer Causes Control. 2006;17(7):921-9.
Exclusion: wrong study design for key question.

Norman SA, Russell Localio A, Weber AL, et al. Protection of mammography screening against death from breast cancer in women aged 40-64 years. Cancer Causes Control. 2007;18(9):909-18.
Exclusion: wrong study design for key question.

Northington L, Martin T, Walker JT, et al. Integrated community education model: breast health awareness to impact late-stage breast cancer. Clin J Oncol Nurs. 2011;15(4):387-92.
Exclusion: wrong publication type.

Nuno T, Martinez ME, Harris R, et al. A Promotora-administered group education intervention to promote breast and cervical cancer screening in a rural community along the U.S.-Mexico border: A randomized controlled trial. Cancer Causes Control. 2011;22(3):367-74.
Exclusion: wrong intervention.

Nusbaum NJ. Role of the clinical breast examination in breast cancer screening does this patient have breast cancer? Does this patient have breast cancer? Barton MB, Harris R, Fletcher SW JAMA 1999;282:1270-1280. J Am Geriatr Soc. 2001;49(7):991-2.
Exclusion: wrong publication type.

Nyante SJ, Dallal CM, Gierach GL, et al. Risk factors for specific histopathological types of postmenopausal breast cancer in the NIH-AARP Diet and Health Study. Am J Epidemiol. 2013;178(3):359-71.
Exclusion: wrong outcomes.

Nyström L, Larsson LG, Wall S, et al. An overview of the Swedish randomised mammography trials: total mortality pattern and the representivity of the study cohorts. J Med Screen. 1996;3(2):85-7.
Exclusion: review not meeting inclusion criteria.

Obenauer S, Sohns C, Werner C, et al. Computer-aided detection in full-field digital mammography: detection in dependence of the BI-RADS categories. Breast J. 2006;12(1):16-9.
Exclusion: wrong intervention.

Obenauer S, Sohns C, Werner C, et al. Impact of breast density on computer-aided detection in full-field digital mammography. J Digit Imaging. 2006;19(3):258-63.
Exclusion: wrong intervention.

Oberaigner W, Buchberger W, Frede T, et al. Breast cancer incidence and mortality in Tyrol/Austria after fifteen years of opportunistic mammography screening. BMC Public Health. 2010;10:86.
Exclusion: wrong study design for key question.

Obuchowski NA, Lieber ML, Powell KA. Data analysis for detection and localization of multiple abnormalities with application to mammography. Acad Radiol. 2000;7(7):516-25.
Exclusion: wrong outcomes.

O'Connor MK, Li H, Rhodes DJ, et al. Comparison of radiation exposure and associated radiation-induced cancer risks from mammography and molecular imaging of the breast. Med Phys. 2010;37(12):6187-98.
Exclusion: wrong comparison.

Oestreicher N, Lehman CD, Seger DJ, et al. The incremental contribution of clinical breast examination to invasive cancer detection in a mammography screening program. AJR Am J Roentgenol. 2005;184(2):428-32.
Exclusion: wrong outcomes.

Oestreicher N, White E, Lehman CD, et al. Predictors of sensitivity of clinical breast examination (CBE). Breast Cancer Res Treat. 2002;76(1):73-81.
Exclusion: studies outside of search dates.

Ohlinger R, Heyer H, Thomas A, et al. Non-palpable breast lesions in asymptomatic women: diagnostic value of initial ultrasonography and comparison with mammography. Anticancer Res. 2006;26(5B):3943-55.
Exclusion: studies outside of search dates.

Ohnuki K. Mammographic screening for non-palpable breast cancer in Japan. Breast Cancer. 2005;12(4):258-66.
Exclusion: wrong publication type.

Ohta T, Okamoto K, Kanemaki Y, et al. Use of ultrasonography as an alternative modality for first-line examination in detecting breast cancer in selected patients. Clin Breast Cancer. 2007;7(8):624-6.

Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Ohuchi N, Ishida T, Kawai M, et al. Randomized controlled trial on effectiveness of ultrasonography screening for breast cancer in women aged 40-49 (J-START): research design. Jpn J Clin Oncol. 2011;41(2):275-7.
Exclusion: wrong publication type.

Okamoto H, Ogawara T, Arihara F, et al. Usefulness of ultrasonography combined with conventional physical examination in mass screening for breast cancer: a retrospective study of Yamanashi Health Care Center results from 1989 to 1994. Jpn J Cancer Res. 1996;87(3):317-23.
Exclusion: studies outside of search dates.

Okunade AA, Karakus MC. Mortality from breast carcinoma among US women: the role and implications of socio-economics, heterogeneous insurance, screening mammography, and geography. Health Care Manag Sci. 2003;6(4):237-48.
Exclusion: wrong study design for key question.

Oleske DM, Galvez A, Cobleigh MA, et al. Are tri-ethnic low-income women with breast cancer effective teachers of the importance of breast cancer screening to their first-degree relatives? Results from a randomized clinical trial. Breast J. 2007;13(1):19-27.
Exclusion: wrong outcomes.

Olivotto IA, Gomi A, Bancej C, et al. Influence of delay to diagnosis on prognostic indicators of screen-detected breast carcinoma. Cancer. 2002;94(8):2143-50.
Exclusion: studies outside of search dates.

Olivotto IA, Kan L, Coldman AJ. False positive rate of screening mammography. N Engl J Med. 1998;339:560.
Exclusion: wrong publication type.

Olivotto IA, Kan L, d'Yachkova Y, et al. Ten years of breast screening in the Screening Mammography Program of British Columbia, 1988-97. J Med Screen. 2000;7(3):152-9.
Exclusion: wrong comparison.

Olsen AH, Jensen A, Njor SH, et al. Breast cancer incidence after the start of mammography screening in Denmark. Br J Cancer. 2003;88(3):362-5.
Exclusion: wrong study design for key question.

Olsen AH, Njor SH, Lynge E. Estimating the benefits of mammography screening: the impact of study design. Epidemiology. 2007;18(4):487-92.
Exclusion: wrong study design for key question.

Olsen AH, Njor SH, Vejborg I, et al. Breast cancer mortality in Copenhagen after introduction of mammography screening: cohort study. BMJ. 2005;330(7485):220.
Exclusion: included in an included systematic review, not directly used.

Olsen AH, Njor SH, Vejborg I, et al. A model for determining the effect of mammography service screening. Acta Oncol. 2005;44(2):120-8.
Exclusion: wrong study design for key question.

Olsen O. Beyond randomized controlled trials: organized mammographic screening substantially reduces breast carcinoma mortality. Cancer. 2002;94(2):578-9; author reply 81-3.
Exclusion: wrong publication type.

Olsen O, Gotzsche PC. Cochrane review on screening for breast cancer with mammography.[Erratum appears in Lancet. 2006 Feb 11;367(9509):474]. Lancet. 2001;358(9290):1340-2.
Exclusion: wrong publication type.

Olson RA, Nichol A, Caron NR, et al. Effect of community population size on breast cancer screening, stage distribution, treatment use and outcomes. Can J Public Health. 2012;Revue Canadienne de Sante Publique. 103(1):46-52.
Exclusion: wrong outcomes.

Olsson A, Borgquist S, Butt S, et al. Tumour-related factors and prognosis in breast cancer detected by screening. Br J Surg. 2012;99(1):78-87.
Exclusion: wrong population.

Olsson A, Garne JP, Tengrup I, et al. Body mass index and breast cancer survival in relation to the introduction of mammographic screening. Eur J Surg Oncol. 2009;35(12):1261-7.
Exclusion: wrong comparison.

Olsson P, Armelius K, Nordahl G, et al. Women with false positive screening mammograms: how do they cope? J Med Screen. 1999;6(2):89-93.
Exclusion: studies outside of search dates.

Oluwole SF, Ali AO, Adu A, et al. Impact of a cancer screening program on breast cancer stage at diagnosis in a medically underserved urban community. J Am Coll Surg. 2003;196(2):180-8.

Exclusion: wrong comparison.

O'Meara ES, Zhu W, Hubbard RA, et al. Mammographic screening interval in relation to tumor characteristics and false-positive risk by race/ethnicity and age. Cancer. 2013;119(22):3959-67.
Exclusion: wrong outcomes.

Omer Z, Hwang E, Esserman L, et al. P5-15-01: Words Matter: Influence of DCIS Diagnosis Terminology on Patient Treatment Decisions. Cancer Res. 2011;71(24 Supplement):P5-15-01.
Exclusion: wrong outcomes.

Ondrusova M, Muzik J, Durdik S, et al. Long-term trends in the development of the epidemiology of breast cancer in the Slovak and Czech Republic with reference to applied screening and international comparisons. Neoplasma. 2012;59(1):70-8.
Exclusion: wrong comparison.

Onega T, Cook A, Kirlin B, et al. The influence of travel time on breast cancer characteristics, receipt of primary therapy, and surveillance mammography. Breast Cancer Res Treat. 2011;129(1):269-75.
Exclusion: wrong comparison.

Onesti JK, Mangus BE, Helmer SD, et al. Breast cancer tumor size: correlation between magnetic resonance imaging and pathology measurements. Am J Surg. 2008;196(6):844-48; discussion 9-50.
Exclusion: wrong population.

Ong G, Austoker J, Brett J. Breast screening: adverse psychological consequences one month after placing women on early recall because of a diagnostic uncertainty. A multicentre study. J Med Screen. 1997;4(3):158-68.
Exclusion: included in an included systematic review, not directly used.

Onishi H, Masuda N, Takechi K, et al. Computed radiography-based mammography with 50-microm pixel size: intra-individual comparison with film-screen mammography for diagnosis of breast cancers. Acad Radiol. 2009;16(7):836-41.
Exclusion: wrong intervention.

Onitilo AA, Engel JM, Liang H, et al. Mammography utilization: patient characteristics and breast cancer stage at diagnosis. AJR Am J Roentgenol. 2013;201(5):1057-63.
Exclusion: wrong comparison.

Ooi CWL, Campbell ID, Kollias J, et al. National Breast Cancer Audit: overview of invasive breast cancer in New Zealand. N Z Med J. 2012;125(1359):7-16.
Exclusion: wrong comparison.

O'Regan RM. Do tumors detected by mammography screening have a favorable prognosis? JAMA. 2004;292(9):1062-3.
Exclusion: wrong publication type.
Orel SG. High-resolution MR imaging for the detection, diagnosis, and staging of breast cancer. Radiographics. 1998;18(4):903-12.
Exclusion: review not meeting inclusion criteria.

Orel SG. MR imaging of the breast. Radiol Clin North Am. 2000;38(4):899-913.
Exclusion: review not meeting inclusion criteria.

Orel SG, Hochman MG, Schnall MD, et al. High-resolution MR imaging of the breast: clinical context. Radiographics. 1996;16(6):1385-401.
Exclusion: review not meeting inclusion criteria.

Orguc S, Basara I, Coskun T. Diffusion-weighted MR imaging of the breast: comparison of apparent diffusion coefficient values of normal breast tissue with benign and malignant breast lesions. Singapore Med J. 2012;53(11):737-43.
Exclusion: wrong outcomes.

Orlacchio A, Bolacchi F, Rotili A, et al. MR breast imaging: a comparative analysis of conventional and parallel imaging acquisition. Radiol Med (Torino). 2008;113(4):465-76.
Exclusion: wrong comparison.

Orton M, Fitzpatrick R, Fuller A, et al. Factors affecting women's response to an invitation to attend for a second breast cancer screening examination. Br J Gen Pract. 1991;41(349):320-2.
Exclusion: included in an included systematic review, not directly used.

Osako T, Iwase T, Takahashi K, et al. Diagnostic mammography and ultrasonography for palpable and nonpalpable breast cancer in women aged 30 to 39 years. Breast Cancer. 2007;14(3):255-9.
Exclusion: wrong population.

Osako T, Takahashi K, Iwase T, et al. Diagnostic ultrasonography and mammography for invasive and noninvasive breast cancer in women aged 30 to 39 years. Breast Cancer. 2007;14(2):229-33.
Exclusion: wrong population.

Osmun WE, Copeland J, Boisvert L. Mammography screening: how far is too far? Rural Remote Health. 2013;13(1):2149.
Exclusion: wrong outcomes.

Ostbye T, Greenberg GN, Taylor DH, Jr., et al. Screening mammography and Pap tests among older American women 1996-2000: results from the Health and Retirement Study (HRS) and Asset and Health Dynamics Among the Oldest Old (AHEAD). Ann Fam Med. 2003;1(4):209-17.
Exclusion: wrong outcomes.

O'Sullivan I, Sutton S, Dixon S, et al. False positive results do not have a negative effect on reattendance for subsequent breast screening. J Med Screen. 2001;8(3):145-8.
Exclusion: included in an included systematic review, not directly used.

Otten JD, Fracheboud J, den Heeten GJ, et al. Likelihood of early detection of breast cancer in relation to false-positive risk in life-time mammographic screening: population-based cohort study. Ann Oncol. 2013;24(10):2501-6.
Exclusion: wrong population.

Otten JDM, Broeders MJM, Fracheboud J, et al. Impressive time-related influence of the Dutch screening programme on breast cancer incidence and mortality, 1975-2006. Int J Cancer. 2008;123(8):1929-34.
Exclusion: included in an included systematic review, not directly used.

Otto SJ, Fracheboud J, Looman CWN, et al. Initiation of population-based mammography screening in Dutch municipalities and effect on breast-cancer mortality: a systematic review. Lancet. 2003;361(9367):1411-7.
Exclusion: included in an included systematic review, not directly used.

Otto SJ, Fracheboud J, Verbeek ALM, et al. Mammography screening and risk of breast cancer death: a population-based case-control study. Cancer Epidemiol Biomarkers Prev. 2012;21(1):66-73.
Exclusion: included in an included systematic review, not directly used.

Ouedraogo S, Dabakuyo TS, Gentil J, et al. Attending breast cancer screening alone does not explain the detection of tumours at an early stage. Eur J Cancer Prev. 2013;22(2):103-11.
Exclusion: wrong study design for key question.

Ouedraogo S, Dabakuyo TS, Gentil J, et al. Population-based study of breast cancer screening in Cote d'Or (France): clinical implications and factors affecting screening round adequacy.[Erratum appears in Eur J Cancer Prev. 2012 Jan;21(1):109]. Eur J Cancer Prev. 2011;20(6):462-74.
Exclusion: wrong outcomes.

Ozanne EM, Shieh Y, Barnes J, et al. Characterizing the impact of 25 years of DCIS treatment. Breast Cancer Res Treat. 2011;129(1):165-73.
Exclusion: wrong intervention.

Paajanen H, Kyhala L, Varjo R, et al. Effect of screening mammography on the surgery of breast cancer in Finland: a population-based analysis during the years 1985-2004. Am Surg. 2006;72(2):167-71.
Exclusion: wrong comparison.

Paakko E, Reinikainen H, Lindholm E-L, et al. Low-field versus high-field MRI in diagnosing breast disorders. Eur Radiol. 2005;15(7):1361-8.
Exclusion: wrong intervention.

Paap E, Holland R, den Heeten GJ, et al. A remarkable reduction of breast cancer deaths in screened versus unscreened women: a case-referent study. Cancer Causes Control. 2010;21(10):1569-73.
Exclusion: wrong study design for key question.

Paap E, Verbeek ALM, Puliti D, et al. Breast cancer screening case-control study design: impact on breast cancer mortality. Ann Oncol. 2011;22(4):863-9.
Exclusion: wrong study design for key question.

Pace LE, Keating NL. A systematic assessment of benefits and risks to guide breast cancer screening decisions. JAMA. 2014;311(13):1327-35.
Exclusion: review not meeting inclusion criteria.

Paci E, Alexander FE. Study design of randomized controlled clinical trials of breast cancer screening. J Natl Cancer Inst. 1997;Monographs.(22):21-5.
Exclusion: wrong publication type.

Paci E, Broeders M, Hofvind S, et al. European breast cancer service screening outcomes: a first balance sheet of the benefits and harms. Cancer Epidemiol Biomarkers Prev. 2014;23(7):1159-63.
Exclusion: review not meeting inclusion criteria.

Paci E, Coviello E, Miccinesi G, et al. Evaluation of service mammography screening impact in Italy. The contribution of hazard analysis. Eur J Cancer. 2008;44(6):858-65.
Exclusion: wrong study design for key question.

Paci E, Duffy S. Overdiagnosis and overtreatment of breast cancer: overdiagnosis and overtreatment in service screening. Breast Cancer Res. 2005;7(6):266-70.
Exclusion: studies outside of search dates.

Paci E, Duffy SW, Giorgi D, et al. Are breast cancer screening programmes increasing rates of mastectomy? Observational study. BMJ. 2002;325(7361):418.
Exclusion: wrong outcomes.

Paci E, Duffy SW, Giorgi D, et al. Quantification of the effect of mammographic screening on fatal breast cancers: The Florence Programme 1990-96. Br J Cancer. 2002;87(1):65-9.
Exclusion: wrong comparison.

Paci E, Giorgi D, Bianchi S, et al. Assessment of the early impact of the population-based breast cancer screening programme in Florence (Italy) using mortality and surrogate measures. Eur J Cancer. 2002;38(4):568-73.
Exclusion: included in an included systematic review, not directly used.

Paci E, Group EW. Summary of the evidence of breast cancer service screening outcomes in Europe and first estimate of the benefit and harm balance sheet. J Med Screen. 2012;19 Suppl 1:5-13.
Exclusion: review not meeting inclusion criteria.

Paci E, Pannelli F. Female breast cancer. Epidemiol Prev. 2004;28(2 Suppl):64-7.
Exclusion: wrong publication type.

Paci E, Ponti A, Crocetti E, et al. Re: Role of detection method in predicting breast cancer survival: analysis of randomized screening trials. J Natl Cancer Inst. 2005;97(24):1853-4; author reply 4.
Exclusion: wrong publication type.

Paci E, Zappa M. Re: Efficacy of breast cancer screening in the community according to risk level. J Natl Cancer Inst. 2005;97(22):1704; author reply -5.
Exclusion: wrong publication type.

Paesmans M, Ameye L, Moreau M, et al. Breast cancer screening in the older woman: an effective way to reduce mortality? Maturitas. 2010;66(3):263-7.
Exclusion: review not meeting inclusion criteria.

Pagan JA, Brown CJ, Asch DA, et al. Health literacy and breast cancer screening among Mexican American women in South Texas. J Cancer Educ. 2012;27(1):132-7.
Exclusion: wrong outcomes.

Page DL, Gray GF, Jr. Pathology of mammographically discovered breast cancer. Clinical implications of size and histologic differentiation. Surg Oncol Clin N Am. 1997;6(2):335-42.
Exclusion: review not meeting inclusion criteria.

Pai VR, Gregory NE, Swinford AE, et al. Ductal carcinoma in situ: computer-aided detection in screening mammography. Radiology. 2006;241(3):689-94.
Exclusion: wrong intervention.

Paik S, Shak S, Tang G, et al. A Multigene Assay to Predict Recurrence of Tamoxifen-Treated, Node-Negative Breast Cancer. N Engl J Med. 2004;351(27):2817-26.
Exclusion: wrong intervention.

Paik S, Tang G, Shak S, et al. Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer. J Clin Oncol. 2006;24(23):3726-34.
Exclusion: wrong population.

Palka I, Kelemen G, Ormandi K, et al. Tumor characteristics in screen-detected and symptomatic breast cancers. Pathol Oncol Res. 2008;14(2):161-7.
Exclusion: wrong outcomes.

Pande AR, Lohani B, Sayami P, et al. Predictive value of ultrasonography in the diagnosis of palpable breast lump. Kathmandu Univ Med J. 2003;1(2):78-84.
Exclusion: wrong intervention.

Panetta K, Zhou Y, Agaian S, et al. Nonlinear unsharp masking for mammogram enhancement. IEEE Trans Inf Technol Biomed. 2011;15(6):918-28.
Exclusion: wrong intervention.

Panizza P, Vigano S, Bonelli L, et al. Screening women at intermediate risk: harm or charm? Eur J Radiol. 2012;81 Suppl 1:S116-7.
Exclusion: wrong publication type.

Papadopoulos A, Fotiadis DI, Costaridou L. Improvement of microcalcification cluster detection in mammography utilizing image enhancement techniques. Comput Biol Med. 2008;38(10):1045-55.
Exclusion: wrong study design for key question.

Appendix A4. List of Excluded Studies

Papas MA, Klassen AC. Pain and discomfort associated with mammography among urban low-income African-American women. J Community Health. 2005;30(4):253-67.
Exclusion: included in an included systematic review, not directly used.

Paquerault S, Samuelson FW, Petrick N, et al. Investigation of reading mode and relative sensitivity as factors that influence reader performance when using computer-aided detection software. Acad Radiol. 2009;16(9):1095-107.
Exclusion: wrong intervention.

Paquette D, Snider J, Bouchard F, et al. Performance of screening mammography in organized programs in Canada in 1996. The Database Management Subcommittee to the National Committee for the Canadian Breast Cancer Screening Initiative. CMAJ. 2000;163(9):1133-8.
Exclusion: wrong comparison.

Parikh JR. Breast imaging flow models. J Am Coll Radiol. 2004;1(4):265-9.
Exclusion: wrong intervention.

Park JM, Yang L, Laroia A, et al. Missed and/or misinterpreted lesions in breast ultrasound: reasons and solutions. Can Assoc Radiol J. 2011;62(1):41-9.
Exclusion: wrong study design for key question.

Parr N, Boyages J, Taylor R, et al. Projecting mammographic screens. J Med Screen. 2000;7(3):146-51.
Exclusion: wrong study design for key question.

Parris T, Wakefield D, Frimmer H. Real world performance of screening breast ultrasound following enactment of Connecticut Bill 458. Breast J. 2013;19(1):64-70.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Parsian S, Rahbar H, Allison KH, et al. Nonmalignant breast lesions: ADCs of benign and high-risk subtypes assessed as false-positive at dynamic enhanced MR imaging. Radiology. 2012;265(3):696-706.
Exclusion: wrong outcomes.

Partin MR, Casey-Paal AL, Slater JS, et al. Measuring mammography compliance: lessons learned from a survival analysis of screening behavior. Cancer Epidemiol Biomarkers Prev. 1998;7(8):681-7.
Exclusion: wrong outcomes.

Partin MR, Slater JS, Caplan L. Randomized controlled trial of a repeat mammography intervention: effect of adherence definitions on results. Prev Med. 2005;41(3-4):734-40.
Exclusion: wrong outcomes.

Partridge SC, DeMartini WB, Kurland BF, et al. Quantitative diffusion-weighted imaging as an adjunct to conventional breast MRI for improved positive predictive value. AJR Am J Roentgenol. 2009;193(6):1716-22.
Exclusion: wrong intervention.

Partridge SC, Rahbar H, Murthy R, et al. Improved diagnostic accuracy of breast MRI through combined apparent diffusion coefficients and dynamic contrast-enhanced kinetics. Magn Reson Med. 2011;65(6):1759-67.
Exclusion: wrong intervention.

Parvinen I, Helenius H, Pylkkanen L, et al. Service screening mammography reduces breast cancer mortality among elderly women in Turku. J Med Screen. 2006;13(1):34-40.
Exclusion: included in an included systematic review, not directly used.

Paskett E, Tatum C, Rushing J, et al. Randomized trial of an intervention to improve mammography utilization among a triracial rural population of women. J Natl Cancer Inst. 2006;98(17):1226-37.
Exclusion: wrong intervention.

Patani N, Mokbel K. The utility of MRI for the screening and staging of breast cancer. Int J Clin Pract. 2008;62(3):450-3.
Exclusion: review not meeting inclusion criteria.

Patel MR, Whitman GJ. Negative mammograms in symptomatic patients with breast cancer. Acad Radiol. 1998;5(1):26-33.
Exclusion: wrong population.

Payne JI, Caines JS, Gallant J, et al. A review of interval breast cancers diagnosed among participants of the Nova Scotia Breast Screening Program. Radiology. 2013;266(1):96-103.
Exclusion: wrong outcomes.

Pediconi F, Catalano C, Roselli A, et al. The challenge of imaging dense breast parenchyma: is magnetic resonance mammography the technique of choice? A comparative study with x-ray mammography and whole-breast ultrasound. Invest Radiol. 2009;44(7):412-21.
Exclusion: wrong intervention.

Pentecost MJ. Mammography and the risks of engagement. J Am Coll Radiol. 2004;1(11):797-9.
Exclusion: wrong publication type.

Pereira RR, Jr., Azevedo Marques PM, Honda MO, et al. Usefulness of texture analysis for computerized classification of breast lesions on mammograms. J Digit Imaging. 2007;20(3):248-55.
Exclusion: wrong outcomes.

Perez-Fidalgo JA, Miranda J, Chirivella I, et al. Impact of a mammography screening programme on the breast cancer population of the Region of Valencia (Spain). Clin Transl Oncol. 2008;10(11):745-52.
Exclusion: wrong comparison.

Perez-Gomez B, Ruiz F, Martinez I, et al. Women's features and inter-/intra-rater agreement on mammographic density assessment in full-field digital mammograms (DDM-SPAIN).[Erratum appears in Breast Cancer Res Treat. 2012 Dec;136(3):935]. Breast Cancer Res Treat. 2012;132(1):287-95.
Exclusion: wrong outcomes.

Perrier A, Roy PM, Sanchez O, et al. Multidetector-row computed tomography in suspected pulmonary embolism. N Engl J Med. 2005;352(17):1760-8.
Exclusion: wrong intervention.

Perry DK, Marable S, Darcy D. Breast cancer control report card: Rhode Island, 1999. Med Health R I. 1999;82(12):451-2.
Exclusion: wrong publication type.

Perry NM, Patani N, Milner SE, et al. The impact of digital mammography on screening a young cohort of women for breast cancer in an urban specialist breast unit. Eur Radiol. 2011;21(4):676-82.
Exclusion: wrong outcomes.

Peters NHGM, Borel Rinkes IHM, Zuithoff NPA, et al. Meta-analysis of MR imaging in the diagnosis of breast lesions. Radiology. 2008;246(1):116-24.
Exclusion: wrong intervention.

Petrakis IE, Paraskakis S. Breast cancer in the elderly. Arch Gerontol Geriatr. 2010;50(2):179-84.
Exclusion: wrong publication type.

Petralia G, Bonello L, Summers P, et al. Intraobserver and interobserver variability in the calculation of apparent diffusion coefficient (ADC) from diffusion-weighted magnetic resonance imaging (DW-MRI) of breast tumours. Radiol Med (Torino). 2011;116(3):466-76.
Exclusion: wrong outcomes.

Petticrew MP, Sowden AJ, Lister-Sharp D, et al. False-negative results in screening programmes: systematic review of impact and implications. Health Technol Assess. 2000;4(5):1-120.
Exclusion: review not meeting inclusion criteria.

Pharoah PDP, Sewell B, Fitzsimmons D, et al. Cost effectiveness of the NHS breast screening programme: life table model.[Erratum appears in BMJ. 2013;346:f3822]. BMJ. 2013;346:f2618.
Exclusion: wrong study design for key question.

Phillips CE, Rothstein JD, Beaver K, et al. Patient navigation to increase mammography screening among inner city women. J Gen Intern Med. 2011;26(2):123-9.
Exclusion: wrong intervention.

Phillips J, Smith ED. Breast cancer control and African American women: a review. Cancer Invest. 2001;19(3):273-80.
Exclusion: review not meeting inclusion criteria.

Phillips N, Coldman A. Comparison of nonbreast cancer incidence, survival and mortality between breast screening program participants and nonparticipants. Int J Cancer. 2008;122(1):197-201.
Exclusion: wrong outcomes.

Philpotts LE, Smith RA. Screening for breast cancer. Semin Roentgenol. 2003;38(1):19-33.
Exclusion: wrong publication type.

Piccoli CW, Greer JG, Mitchell DG. Breast MR imaging for cancer detection and implant evaluation: potential pitfalls. Radiographics. 1996;16(1):63-75.
Exclusion: review not meeting inclusion criteria.

Pickles MD, Turnbull LW. Breast MRI at 3.0 T in a high-risk familial breast cancer screening cohort: comparison with 1.5 T screening studies. Br J Radiol. 2012;85(1015):990-5.
Exclusion: wrong population.

Appendix A4. List of Excluded Studies

Pinker K, Grabner G, Bogner W, et al. A combined high temporal and high spatial resolution 3 Tesla MR imaging protocol for the assessment of breast lesions: initial results. Invest Radiol. 2009;44(9):553-8.
Exclusion: wrong intervention.

Pisani P, Forman D. Declining mortality from breast cancer in Yorkshire, 1983-1998: extent and causes. Br J Cancer. 2004;90(3):652-6.
Exclusion: wrong intervention.

Pisano E. Issues in breast cancer screening. Technol Cancer Res Treat. 2005;4(1):5-9.
Exclusion: wrong publication type.

Pisano ED, Earp JA, Gallant TL. Screening mammography behavior after a false positive mammogram. Cancer Detect Prev. 1998;22(2):161-7.
Exclusion: studies outside of search dates.

Pisano ED, Gatsonis C, Hendrick E, et al. Diagnostic performance of digital versus film mammography for breast-cancer screening.[Erratum appears in N Engl J Med. 2006 Oct 26;355(17):1840]. N Engl J Med. 2005;353(17):1773-83.
Exclusion: wrong comparison.

Pisano ED, Hendrick RE, Yaffe MJ, et al. Diagnostic accuracy of digital versus film mammography: exploratory analysis of selected population subgroups in DMIST. Radiology. 2008;246(2):376-83.
Exclusion: wrong intervention.

Pistolese CA, Ciarrapico AM, della Gatta F, et al. Inappropriateness of breast imaging: cost analysis. Radiol Med (Torino). 2013;118(6):984-94.
Exclusion: wrong outcomes.

Pistolese CA, Perretta T, Cossu E, et al. Value of the correct diagnostic pathway through conventional imaging (mammography and ultrasound) in evaluating breast disease. Radiol Med (Torino). 2011;116(4):584-94.
Exclusion: wrong outcomes.

Plecha D, Salem N, Kremer M, et al. Neglecting to screen women between 40 and 49 years old with mammography: what is the impact on treatment morbidity and potential risk reduction? AJR American Journal of Roentgenology. 2014;202(2):282-8.
Exclusion: wrong outcomes.

Pollan M, Pastor-Barriuso R, Ardanaz E, et al. Recent changes in breast cancer incidence in Spain, 1980-2004. J Natl Cancer Inst. 2009;101(22):1584-91.
Exclusion: wrong comparison.

Pons-Vigués M, Puigpinós R, Cano-Serral G, et al. Breast cancer mortality in Barcelona following implementation of a city breast cancer-screening program. Cancer Detect Prev. 2008;32(2):162-7.
Exclusion: included in an included systematic review, not directly used.

Ponti A, Lynge E, James T, et al. International variation in management of screen-detected ductal carcinoma in situ of the breast. Eur J Cancer. 2014;50(15):2695-704.
Exclusion: wrong outcomes.

Ponti A, Mano MP, Distante V, et al. Audit system on quality of breast cancer diagnosis and treatment (QT): results from the survey on screen-detected lesions in Italy, 2004. Epidemiol Prev. 2007;31(2-3 Suppl 2):69-75.
Exclusion: wrong study design for key question.

Ponti A, Mano MP, Distante V, et al. Audit system on Quality of breast cancer diagnosis and Treatment (QT): results from the survey on screen-detected lesions in Italy, 2003-2004. Epidemiol Prev. 2006;30(1 Suppl 3):59-63.
Exclusion: wrong intervention.

Ponti A, Rosso S, Zanetti R, et al. Re: Breast cancer incidence, 1980-2006: combined roles of menopausal hormone therapy, screening mammography, and estrogen receptor status. J Natl Cancer Inst. 2007;99(23):1817-8; author reply 9.
Exclusion: wrong publication type.

Ponzone R, Sismondi P, Baum M. Beyond randomized controlled trials: organized mammographic screening substantially reduces breast carcinoma mortality. Cancer. 2002;94(2):579-80; author reply 81-3.
Exclusion: wrong publication type.

Poplack SP, Tosteson AN, Grove MR, et al. Mammography in 53,803 women from the New Hampshire mammography network. Radiology. 2000;217(3):832-40.
Exclusion: wrong outcomes.

Poplack SP, Tosteson TD, Kogel CA, et al. Digital breast tomosynthesis: initial experience in 98 women with abnormal digital screening mammography. AJR Am J Roentgenol. 2007;189(3):616-23.
Exclusion: studies outside of search dates.

Porter GJR, Evans AJ, Burrell HC, et al. Interval breast cancers: prognostic features and survival by subtype and time since screening. J Med Screen. 2006;13(3):115-22.
Exclusion: wrong outcomes.

Porter PL, El-Bastawissi AY, Mandelson MT, et al. Breast tumor characteristics as predictors of mammographic detection: comparison of interval- and screen-detected cancers. J Natl Cancer Inst. 1999;91(23):2020-8.
Exclusion: wrong comparison.

Poulos A, Rickard M. Compression in mammography and the perception of discomfort. Australas Radiol. 1997;41(3):247-52.
Exclusion: included in an included systematic review, not directly used.

Powell KA, Obuchowski NA, Chilcote WA, et al. Film-screen versus digitized mammography: assessment of clinical equivalence. AJR Am J Roentgenol. 1999;173(4):889-94.
Exclusion: wrong comparison.

Powles TJ, Diem SJ, Fabian CJ, et al. Breast cancer incidence in postmenopausal women with osteoporosis or low bone mass using arzoxifene. Breast Cancer Res Treat. 2012;134(1):299-306.
Exclusion: wrong intervention.

Poynter JN, Inoue-Choi M, Ross JA, et al. Reproductive, lifestyle, and anthropometric risk factors for cancer in elderly women. Cancer Epidemiol Biomarkers Prev. 2013;22(4):681-7.
Exclusion: wrong comparison.

Prasad SN, Houserkova D. A comparison of mammography and ultrasonography in the evaluation of breast masses. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2007;151(2):315-22.
Exclusion: wrong population.

Prasad SN, Houserkova D, Campbell J. Breast imaging using 3D electrical impedence tomography. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2008;152(1):151-4.
Exclusion: wrong outcomes.

Price ER, Hargreaves J, Lipson JA, et al. The California breast density information group: a collaborative response to the issues of breast density, breast cancer risk, and breast density notification legislation. Radiology. 2013;269(3):887-92.
Exclusion: wrong publication type.

Price J, Chen SW. Screening for breast cancer with MRI: recent experience from the Australian Capital Territory. J Med Imaging Radiat Oncol. 2009;53(1):69-80.
Exclusion: wrong population.

Printz C. Advanced cancer risk similar with biennial vs. annual mammography in women aged 50 to 74. Cancer. 2013;119(16):2949.
Exclusion: wrong publication type.

Prionas ND, Lindfors KK, Ray S, et al. Contrast-enhanced dedicated breast CT: initial clinical experience. Radiology. 2010;256(3):714-23.
Exclusion: wrong outcomes.

Prior P, Woodman CB, Wilson S, et al. Reliability of underlying incidence rates for estimating the effect and efficiency of screening for breast cancer. J Med Screen. 1996;3(3):119-22.
Exclusion: wrong study design for key question.

Prizemin Y. Using "voting" in CAD for mammography to lower false-positive rates. Radiol Manage. 2010;32(1):13-5.
Exclusion: wrong publication type.

Provenzano E, Pinder SE. Pre-operative diagnosis of breast cancer in screening: problems and pitfalls. Pathology. 2009;41(1):3-17.
Exclusion: review not meeting inclusion criteria.

Puig-Vives M, Pollan M, Rue M, et al. Rapid increase in incidence of breast ductal carcinoma in situ in Girona, Spain 1983-2007. Breast. 2012;21(5):646-51.
Exclusion: wrong outcomes.

Puliti D, Miccinesi G, Collina N, et al. Effectiveness of service screening: a case-control study to assess breast cancer mortality reduction.[Erratum appears in Br J Cancer. 2008 Nov 18;99(10):1756]. Br J Cancer. 2008;99(3):423-7.
Exclusion: included in an included systematic review, not directly used.

Puliti D, Miccinesi G, Manneschi G, et al. Does an organised screening programme reduce the inequalities in breast cancer survival? Ann Oncol. 2012;23(2):319-23.
Exclusion: wrong outcomes.

Puliti D, Paci E. The other side of technology: risk of overdiagnosis of breast cancer with mammography screening. Fut Oncol. 2009;5(4):481-91.
Exclusion: wrong publication type.

Qian W, Song D, Lei M, et al. Computer-aided mass detection based on ipsilateral multiview mammograms. Acad Radiol. 2007;14(5):530-8.
Exclusion: wrong intervention.

Quek ST, Thng CH, Khoo JBK, et al. Radiologists' detection of mammographic abnormalities with and without a computer-aided detection system. Australas Radiol. 2003;47(3):257-60.
Exclusion: wrong outcomes.

Raabe NK, Fossaa SD. Primary invasive breast carcinoma in Oslo 1980-1989. Incidence and delay. Acta Oncol. 1996;35(1):9-15.
Exclusion: wrong outcomes.

Rack SK. Mammography screening: a current controversy. W V Med J. 2003;99(3):108-10.
Exclusion: wrong publication type.

Rafferty EA, Park JM, Philpotts LE, et al. Assessing radiologist performance using combined digital mammography and breast tomosynthesis compared with digital mammography alone: results of a multicenter, multireader trial. Radiology. 2013;266(1):104-13.
Exclusion: wrong outcomes.

Raftery J, Chorozoglou M. Possible net harms of breast cancer screening: updated modelling of Forrest report. BMJ. 2011;343:d7627.
Exclusion: wrong study design for key question.

Rakha EA, El-Sayed ME, Reed J, et al. Screen-detected breast lesions with malignant needle core biopsy diagnoses and no malignancy identified in subsequent surgical excision specimens (potential false-positive diagnosis). Eur J Cancer. 2009;45(7):1162-7.
Exclusion: wrong intervention.

Rakha EA, Lee AHS, Reed J, et al. Screen-detected malignant breast lesions diagnosed following benign (B2) or normal (B1) needle core biopsy diagnoses. Eur J Cancer. 2010;46(10):1835-40.
Exclusion: wrong intervention.

Ramirez AJ, Westcombe AM, Burgess CC, et al. Factors predicting delayed presentation of symptomatic breast cancer: A systematic review. Lancet. 1999;353(9159):1127-31.
Exclusion: wrong outcomes.

Randolph WM, Goodwin JS, Mahnken JD, et al. Regular mammography use is associated with elimination of age-related disparities in size and stage of breast cancer at diagnosis. Ann Intern Med. 2002;137(10):783-90.
Exclusion: wrong population.

Raneta O, Bella V, Bellova L, et al. The use of electrical impedance tomography to the differential diagnosis of pathological mammographic/sonographic findings. Neoplasma. 2013;60(6):647-54.
Exclusion: wrong intervention.

Rangayyan RM, Shen L, Shen Y, et al. Improvement of sensitivity of breast cancer diagnosis with adaptive neighborhood contrast enhancement of mammograms. IEEE Trans Inf Technol Biomed. 1997;1(3):161-70.
Exclusion: wrong intervention.

Ranger B, Littrup PJ, Duric N, et al. Breast ultrasound tomography versus MRI for clinical display of anatomy and tumor rendering: preliminary results. AJR Am J Roentgenol. 2012;198(1):233-9.
Exclusion: wrong intervention.

Rankin SC. MRI of the breast. Br J Radiol. 2000;73(872):806-18.
Exclusion: wrong publication type.

Rao S, Latha PS, Ravi A, et al. Ductal carcinoma in a multiple fibroadenoma: diagnostic inaccuracies. J Cancer Res Ther. 2010;6(3):385-7.
Exclusion: wrong study design for key question.

Rauscher GH, Hawley ST, Earp JAL. Baseline predictors of initiation vs. maintenance of regular mammography use among rural women. Prev Med. 2005;40(6):822-30.
Exclusion: wrong comparison.

Ravert PK, Huffaker C. Breast cancer screening in women: An integrative literature review. J Am Acad Nurse Pract. 2010;22(12):668-73.
Exclusion: review not meeting inclusion criteria.

Rayford CE, 2nd, Zhou W, Chen Y. Breast tomosynthesis imaging configuration analysis. International Journal of Computational Biology & Drug Design. 2013;6(3):255-62.
Exclusion: wrong outcomes.

Rayson D, Payne JI, Abdolell M, et al. Comparison of clinical-pathologic characteristics and outcomes of true interval and screen-detected invasive breast cancer among participants of a Canadian breast screening program: a nested case-control study. Clin Breast Cancer. 2011;11(1):27-32.
Exclusion: wrong comparison.

Raza S, Chikarmane SA, Neilsen SS, et al. BI-RADS 3, 4, and 5 lesions: value of US in management--follow-up and outcome. Radiology. 2008;248(3):773-81.
Exclusion: wrong population.

Redondo M, Funez R, Medina-Cano F, et al. Detection methods predict differences in biology and survival in breast cancer patients. BMC Cancer. 2012;12:604.
Exclusion: wrong comparison.

Reeves MJ, Newcomb PA, Remington PL, et al. Body mass and breast cancer. Relationship between method of detection and stage of disease. Cancer. 1996;77(2):301-7.
Exclusion: wrong outcomes.

Regentova E, Zhang L, Zheng J, et al. Detecting microcalcifications in digital mammograms using wavelet domain hidden Markov tree model. Conf Proc IEEE Eng Med Biol Soc. 2006;1:1972-5.
Exclusion: wrong outcomes.

Reinikainen H, Rissanen T, Paivansalo M, et al. B-mode, power Doppler and contrast-enhanced power Doppler ultrasonography in the diagnosis of breast tumors. Acta Radiol. 2001;42(1):106-13.
Exclusion: wrong population.

Reiser I, Nishikawa RM, Giger ML, et al. Computerized detection of mass lesions in digital breast tomosynthesis images using two- and three dimensional radial gradient index segmentation. Technol Cancer Res Treat. 2004;3(5):437-41.
Exclusion: wrong intervention.

Retsky M, Demicheli R, Hrushesky W. Breast cancer screening for women aged 40-49 years: screening may not be the benign process usually thought. J Natl Cancer Inst. 2001;93(20):1572.
Exclusion: wrong publication type.

Rettig B, Horton M. Breast cancer in Nebraska: recent trends in incidence, mortality, and screening. Nebr Med J. 1996;81(3):63-9.
Exclusion: wrong outcomes.

Rhodes DJ, Hruska CB, Phillips SW, et al. Dedicated dual-head gamma imaging for breast cancer screening in women with mammographically dense breasts. Radiology. 2011;258(1):106-18.
Exclusion: wrong intervention.

Ricci P, Cantisani V, Ballesio L, et al. Benign and malignant breast lesions: efficacy of real time contrast-enhanced ultrasound vs. magnetic resonance imaging. Ultraschall Med. 2007;28(1):57-62.
Exclusion: wrong outcomes.

Richardson A, Wells JE. Breast cancer screening: the effect of self selection for screening on comparisons of randomised controlled trials. J Med Screen. 1997;4(1):16-8.
Exclusion: wrong outcomes.

Richardson LC, Schulman J, Sever LE, et al. Early-stage breast cancer treatment among medically underserved women diagnosed in a national screening program, 1992-1995. Breast Cancer Res Treat. 2001;69(2):133-42.
Exclusion: wrong comparison.

Rickard M, Donnellan M. Diagnosis of small sized invasive breast cancer by an Australian mammography screening service: surrogate end-points for mortality reduction. Aust N Z J Surg. 1998;68(6):415-8.
Exclusion: wrong comparison.

Rickard M, Taylor R, Page A, et al. Cancer detection and mammogram volume of radiologists in a population-based screening programme. Breast. 2006;15(1):39-43.
Exclusion: wrong outcomes.

Rickard MT, Taylor RJ, Fazli MA, et al. Interval breast cancers in an Australian mammographic screening program. Med J Aust. 1998;169(4):184-7.
Exclusion: wrong comparison.

Riedl CC, Ponhold L, Flory D, et al. Magnetic resonance imaging of the breast improves detection of invasive cancer, preinvasive cancer, and premalignant lesions during surveillance of women at high risk for breast cancer. Clin Cancer Res. 2007;13(20):6144-52.
Exclusion: wrong population.

Rijnsburger AJ, van Oortmarssen GJ, Boer R, et al. Mammography benefit in the Canadian National Breast Screening Study-2: a model evaluation. Int J Cancer. 2004;110(5):756-62.
Exclusion: wrong study design for key question.

Rimer BK, Bluman LG. The psychosocial consequences of mammography. J Natl Cancer Inst. 1997(22):131-8.
Exclusion: wrong publication type.

Rimer BK, Lipscomb J. Enhancing the use of mammography: effectiveness and cost. Eff Clin Pract. 2000;3(5):250-5.
Exclusion: wrong publication type.

Ringash J, Canadian Task Force on Preventive Health C. Preventive health care, 2001 update: screening mammography among women aged 40-49 years at average risk of breast cancer. CMAJ. 2001;164(4):469-76.
Exclusion: review not meeting inclusion criteria.

Ripping TM, Verbeek ALM, van der Waal D, et al. Immediate and delayed effects of mammographic screening on breast cancer mortality and incidence in birth cohorts. Br J Cancer. 2013;109(9):2467-71.
Exclusion: wrong comparison.

Robbins AS, Clarke CA. Re: Declines in invasive breast cancer and use of postmenopausal hormone therapy in a screening mammography population. J Natl Cancer Inst. 2007;99(23):1815; author reply 6-7.
Exclusion: wrong publication type.

Roberts-Klein S, Iuanow E, Slanetz PJ. Avoiding pitfalls in mammographic interpretation. Can Assoc Radiol J. 2011;62(1):50-9.
Exclusion: wrong publication type.

Robinson JI, Crane CE, King JM, et al. The South Australian Breast X-Ray Service: results from a statewide mammographic screening programme. Br J Cancer. 1996;73(6):837-42.
Exclusion: wrong comparison.

Robsahm TE, Tretli S. Weak associations between sociodemographic factors and breast cancer: possible effects of early detection. Eur J Cancer Prev. 2005;14(1):7-12.
Exclusion: wrong outcomes.

Rockhill B, Spiegelman D, Byrne C, et al. Validation of the Gail et al. model of breast cancer risk prediction and implications for chemoprevention. J Natl Cancer Inst. 2001;93(5):358-66.
Exclusion: wrong outcomes.

Roder D, Houssami N, Farshid G, et al. Population screening and intensity of screening are associated with reduced breast cancer mortality: evidence of efficacy of mammography screening in Australia. Breast Cancer Res Treat. 2008;108(3):409-16.
Exclusion: wrong study design for key question.

Roder D, Webster F, Zorbas H, et al. Breast screening and breast cancer survival in Aboriginal and Torres Strait Islander women of Australia. Asian Pac J Cancer Prev. 2012;13(1):147-55.
Exclusion: wrong outcomes.

Rodger A, Kavanagh AM. Outcome measures of an Australian breast-screening program. Med J Aust. 1998;169(4):179-80.
Exclusion: wrong publication type.

Rodrigues PS, Giraldi GA, Provenzano M, et al. A new methodology based on q-entropy for breast lesion classification in 3-D ultrasound images. Conf Proc IEEE Eng Med Biol Soc. 2006;1:1048-51.
Exclusion: wrong study design for key question.

Roelofs AAJ, Karssemeijer N, Wedekind N, et al. Importance of comparison of current and prior mammograms in breast cancer screening. Radiology. 2007;242(1):70-7.
Exclusion: wrong outcomes.

Roelofs AAJ, van Woudenberg S, Otten JDM, et al. Effect of soft-copy display supported by CAD on mammography screening performance. Eur Radiol. 2006;16(1):45-52.
Exclusion: wrong intervention.

Roen EL, Roubidoux MA, Joe AI, et al. Adherence to screening mammography among American Indian women of the Northern Plains. Breast Cancer Res Treat. 2013;139(3):897-905.
Exclusion: wrong outcomes.

Rohan TE, Jain M, Howe GR, et al. A cohort study of dietary carotenoids and lung cancer risk in women (Canada). Cancer Causes Control. 2002;13(3):231-7.
Exclusion: wrong outcomes.

Rojas-Dominguez A, Nandi AK. Development of tolerant features for characterization of masses in mammograms. Comput Biol Med. 2009;39(8):678-88.
Exclusion: wrong study design for key question.

Rolnick SJ, O'Connor PJ, Jackson JM, et al. Early- and late-stage breast cancer in a managed care setting in relation to mammography screening. Cancer Detect Prev. 1998;22(6):495-8.
Exclusion: wrong study design for key question.

Roman M, Hubbard RA, Sebuodegard S, et al. The cumulative risk of false-positive results in the Norwegian Breast Cancer Screening Program: updated results. Cancer. 2013;119(22):3952-8.
Exclusion: wrong study design for key question.

Roman R, Sala M, De La Vega M, et al. Effect of false-positives and women's characteristics on long-term adherence to breast cancer screening. Breast Cancer Res Treat. 2011;130(2):543-52.
Exclusion: wrong outcomes.

Roman R, Sala M, Salas D, et al. Effect of protocol-related variables and women's characteristics on the cumulative false-positive risk in breast cancer screening. Ann Oncol. 2012;23(1):104-11.
Exclusion: wrong outcomes.

Romero C, Varela C, Munoz E, et al. Impact on breast cancer diagnosis in a multidisciplinary unit after the incorporation of mammography digitalization and computer-aided detection systems.[Erratum appears in AJR Am J Roentgenol. 2012 Jan;198(1):2]. AJR Am J Roentgenol. 2011;197(6):1492-7.
Exclusion: wrong outcomes.

Romero Castellano C, Varela Nunez C, Cuena Boy R, et al. [Impact of mammographic breast density on computer-assisted detection (CAD) in a breast imaging department]. Radiologia. 2011;53(5):456-61.
Exclusion: wrong intervention.

Rominger MB, Sax EV, Figiel JH, et al. Occurrence and positive predictive value of additional nonmass findings for risk stratification of breast microcalcifications in mammography. Can Assoc Radiol J. 2013;64(4):333-8.
Exclusion: wrong outcomes.

Rong XJ, Shaw CC, Johnston DA, et al. Microcalcification detectability for four mammographic detectors: flat-panel, CCD, CR, and screen/film). Med Phys. 2002;29(9):2052-61.
Exclusion: wrong intervention.

Roque AC, Andre TCSS. Mammography and computerized decision systems: a review. Ann N Y Acad Sci. 2002;980:83-94.
Exclusion: review not meeting inclusion criteria.

Rosen EL, Sickles E, Keating D. Ability of mammography to reveal nonpalpable breast cancer in women with palpable breast masses. AJR Am J Roentgenol. 1999;172(2):309-12.
Exclusion: wrong population.

Rosen S, Weintraub N. The efficacy of performing screening mammograms in the frail elderly population. J Am Med Dir Assoc. 2006;7(4):230-3.
Exclusion: wrong publication type.

Rosenberg RD, Hunt WC, Williamson MR, et al. Effects of age, breast density, ethnicity, and estrogen replacement therapy on screening mammographic sensitivity and cancer stage at diagnosis: review of 183,134 screening mammograms in Albuquerque, New Mexico. Radiology. 1998;209(2):511-8.
Exclusion: wrong comparison.

Rosenberg RD, Yankaskas BC, Abraham LA, et al. Performance benchmarks for screening mammography. Radiology. 2006;241(1):55-66.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Rostgaard K, Vaeth M, Holst H, et al. Age-period-cohort modelling of breast cancer incidence in the Nordic countries. Stat Med. 2001;20(1):47-61.
Exclusion: wrong study design for key question.

Roth EB, Jeffe DB, Margenthaler JA, et al. Method of breast cancer presentation and depressed mood 1 year after diagnosis in women with locally advanced disease. Ann Surg Oncol. 2009;16(6):1637-41.
Exclusion: wrong population.

Rothschild J, Lourenco AP, Mainiero MB. Screening mammography recall rate: does practice site matter? Radiology. 2013;269(2):348-53.
Exclusion: wrong outcomes.

Roubidoux MA, Wilson TE, Orange RJ, et al. Breast cancer in women who undergo screening mammography: relationship of hormone replacement therapy to stage and detection method. Radiology. 1998;208(3):725-8.
Exclusion: wrong comparison.

Rouse HC, Ussher S, Kavanagh AM, et al. Examining the sensitivity of ultrasound-guided large core biopsy for invasive breast carcinoma in a population screening programme. J Med Imaging Radiat Oncol. 2013;57(4):435-43.
Exclusion: wrong outcomes.

Royak-Schaler R, Chen S, Zang E, et al. Does access to screening through health maintenance organization membership translate into improved breast cancer outcomes for African American patients? J Am Med Womens Assoc. 2003;58(3):154-6.
Exclusion: wrong comparison.

Ruamsup S, Wiratkapun C, Wibulpolprasert B, et al. A comparison between short-interval and regular-interval follow-up for BI-RADS category 3 lesions. Singapore Med J. 2010;51(2):120-5.
Exclusion: wrong outcomes.

Rue M, Vilaprinyo E, Lee S, et al. Effectiveness of early detection on breast cancer mortality reduction in Catalonia (Spain). BMC Cancer. 2009;9:326.
Exclusion: wrong study design for key question.

Rutter CM, Taplin S. Assessing mammographers' accuracy. A comparison of clinical and test performance. J Clin Epidemiol. 2000;53(5):443-50.
Exclusion: wrong outcomes.

Rutter DR, Calnan M, Field S, et al. Predicting reattendance in the second round of the UK National Breast Screening Programme: A prospective 3-year longitudinal analysis. Breast. 1997;6(3):120-5.
Exclusion: included in an included systematic review, not directly used.

Saadatmand S, Tilanus-Linthorst MMA, Rutgers EJT, et al. Cost-effectiveness of screening women with familial risk for breast cancer with magnetic resonance imaging. J Natl Cancer Inst. 2013;105(17):1314-21.
Exclusion: wrong population.

Saarenmaa I, Salminen T, Geiger U, et al. The effect of age and density of the breast on the sensitivity of breast cancer diagnostic by mammography and ultasonography. Breast Cancer Res Treat. 2001;67(2):117-23.
Exclusion: wrong intervention.

Sadigh G, Carlos RC, Neal CH, et al. Ultrasonographic differentiation of malignant from benign breast lesions: a meta-analytic comparison of elasticity and BIRADS scoring. Breast Cancer Res Treat. 2012;133(1):23-35.
Exclusion: review not meeting inclusion criteria.

Sadjadi A, Hislop TG, Bajdik C, et al. Comparison of breast cancer survival in two populations: Ardabil, Iran and British Columbia, Canada. BMC Cancer. 2009;9:381.
Exclusion: wrong outcomes.

Sadler GR, Beerman PR, Lee K, et al. Promoting breast cancer screening among Asian American women: the Asian grocery store-based cancer education program. J Cancer Educ. 2012;27(4):612-7.
Exclusion: wrong outcomes.

Sadler GR, Ko CM, Wu P, et al. A cluster randomized controlled trial to increase breast cancer screening among African American women: the black cosmetologists promoting health program. J Natl Med Assoc. 2011;103(8):735-45.
Exclusion: wrong outcomes.

Sagen A, Kaaresen R, Sandvik L, et al. Upper limb physical function and adverse effects after breast cancer surgery: a prospective 2.5-year follow-up study and preoperative measures. Arch Phys Med Rehabil. 2014;95(5):875-81.
Exclusion: wrong comparison.

Sahiner B, Chan HP, Petrick N, et al. Improvement of mammographic mass characterization using spiculation meausures and morphological features. Med Phys. 2001;28(7):1455-65.
Exclusion: wrong outcomes.

Sahiner B, Chan H-P, Hadjiiski LM, et al. Multi-modality CADx: ROC study of the effect on radiologists' accuracy in characterizing breast masses on mammograms and 3D ultrasound images. Acad Radiol. 2009;16(7):810-8.
Exclusion: wrong outcomes.

Sahiner B, Chan H-P, Roubidoux MA, et al. Malignant and benign breast masses on 3D US volumetric images: effect of computer-aided diagnosis on radiologist accuracy. Radiology. 2007;242(3):716-24.
Exclusion: wrong intervention.

Sahiner B, Chan H-P, Roubidoux MA, et al. Computerized characterization of breast masses on three-dimensional ultrasound volumes. Med Phys. 2004;31(4):744-54.
Exclusion: wrong intervention.

Sala M, Comas M, Macia F, et al. Implementation of digital mammography in a population-based breast cancer screening program: effect of screening round on recall rate and cancer detection. Radiology. 2009;252(1):31-9.
Exclusion: wrong comparison.

Appendix A4. List of Excluded Studies

Sala M, Salas D, Belvis F, et al. Reduction in false-positive results after introduction of digital mammography: analysis from four population-based breast cancer screening programs in Spain.[Erratum appears in Radiology. 2011 Jul;260(1):308]. Radiology. 2011;258(2):388-95.
Exclusion: wrong comparison.

Salas D, Ibanez J, Roman R, et al. Effect of start age of breast cancer screening mammography on the risk of false-positive results. Prev Med. 2011;53(1-2):76-81.
Exclusion: wrong outcomes.

Salz T, Richman AR, Brewer NT. Meta-analyses of the effect of false-positive mammograms on generic and specific psychosocial outcomes. Psychooncology. 2010;19(10):1026-34.
Exclusion: review not meeting inclusion criteria.

Salzmann P, Kerlikowske K, Phillips K. Cost-effectiveness of extending screening mammography guidelines to include women 40 to 49 years of age.[Erratum appears in Ann Intern Med 1998 May 15;128(10):878]. Ann Intern Med. 1997;127(11):955-65.
Exclusion: wrong outcomes.

Samei E, Poolla A, Ulissey MJ, et al. Digital mammography: comparative performance of color LCD and monochrome CRT displays. Acad Radiol. 2007;14(5):539-46.
Exclusion: wrong outcomes.

Samei E, Saunders RS, Jr., Baker JA, et al. Digital mammography: effects of reduced radiation dose on diagnostic performance. Radiology. 2007;243(2):396-404.
Exclusion: wrong intervention.

Samnakay N, Tinning J, Ives A, et al. Rates for mastectomy are lower in women attending a breast-screening programme. ANZ J Surg. 2005;75(11):936-9.
Exclusion: wrong outcomes.

Sampalis FS, Denis R, Picard D, et al. International prospective evaluation of scintimammography with (99m)technetium sestamibi. Am J Surg. 2003;185(6):544-9.
Exclusion: wrong intervention.

Samulski M, Hupse R, Boetes C, et al. Using computer-aided detection in mammography as a decision support. Eur Radiol. 2010;20(10):2323-30.
Exclusion: wrong intervention.

Samulski M, Karssemeijer N. Optimizing Case-based detection performance in a multiview CAD system for mammography. IEEE Trans Med Imaging. 2011;30(4):1001-9.
Exclusion: wrong intervention.

Sanchez Gomez S, Torres Tabanera M, Vega Bolivar A, et al. Impact of a CAD system in a screen-film mammography screening program: a prospective study. Eur J Radiol. 2011;80(3):e317-21.
Exclusion: wrong intervention.

Sanders MA, Roland L, Sahoo S. Clinical implications of subcategorizing BI-RADS 4 breast lesions associated with microcalcification: a radiology-pathology correlation study. Breast J. 2010;16(1):28-31.
Exclusion: wrong outcomes.

Sanderson M, Daling JR, Doody DR, et al. Perinatal factors and mortality from breast cancer. Cancer Epidemiol Biomarkers Prev. 2006;15(10):1984-7.
Exclusion: wrong outcomes.

Sandin B, Chorot P, Valiente RM, et al. Adverse psychological effects in women attending a second-stage breast cancer screening. Journal of psychosomatic research. 2002;52(5):303-9.
Exclusion: studies outside of search dates.

Sandin B, Chorot P, Valiente RM, et al. Adverse psychological effects in women attending a second-stage breast cancer screening. Journal of psychosomatic research. 2002;52(5):303-9.
Exclusion: included in an included systematic review, not directly used.

Sandstrom-Wakeling SK, Nied L, Gambino K, et al. The importance of mammography screening in elderly women. Nurse Pract. 2003;28(5):50-3.
Exclusion: wrong study design for key question.

Sankaranarayanan R, Ramadas K, Thara S, et al. Clinical breast examination: preliminary results from a cluster randomized controlled trial in India. J Natl Cancer Inst. 2011;103(19):1476-80.
Exclusion: wrong intervention.

Sardanelli F. MultiHance for dynamic MR imaging of the breast. Eur Radiol. 2004;14 Suppl 7:O65-70; discussion O84-5.
Exclusion: wrong outcomes.

Sardanelli F, Fausto A, Iozzelli A, et al. Dynamic breast magnetic resonance imaging. Effect of changing the region of interest on early enhancement using 2D and 3D techniques. J Comput Assist Tomogr. 2004;28(5):642-6.
Exclusion: wrong outcomes.

Sarkeala T. Performance and effectiveness of organised breast cancer screening in Finland. Acta Oncol. 2008;47(8):1618.
Exclusion: wrong publication type.

Sarkeala T, Anttila A, Saarenmaa I, et al. Validity of process indicators of screening for breast cancer to predict mortality reduction. J Med Screen. 2005;12(1):33-7.
Exclusion: wrong outcomes.

Sarkeala T, Heinavaara S, Anttila A. Breast cancer mortality with varying invitational policies in organised mammography. Br J Cancer. 2008;98(3):641-5.
Exclusion: included in an included systematic review, not directly used.

Sarkeala T, Heinavaara S, Anttila A. Organised mammography screening reduces breast cancer mortality: a cohort study from Finland. Int J Cancer. 2008;122(3):614-9.
Exclusion: wrong comparison.

Sarkissyan M, Wu Y, Vadgama JV. Obesity is associated with breast cancer in African-American women but not Hispanic women in South Los Angeles. Cancer. 2011;117(16):3814-23.
Exclusion: wrong outcomes.

Sassi F, Luft HS, Guadagnoli E. Reducing racial/ethnic disparities in female breast cancer: screening rates and stage at diagnosis. Am J Public Health. 2006;96(12):2165-72.
Exclusion: wrong comparison.

Satake H, Nishio A, Ikeda M, et al. Predictive value for malignancy of suspicious breast masses of BI-RADS categories 4 and 5 using ultrasound elastography and MR diffusion-weighted imaging. AJR Am J Roentgenol. 2011;196(1):202-9.
Exclusion: wrong outcomes.

Sauer T, Young K, Thoresen SO. Fine needle aspiration cytology in the work-up of mammographic and ultrasonographic findings in breast cancer screening: an attempt at differentiating in situ and invasive carcinoma. Cytopathology. 2002;13(2):101-10.
Exclusion: wrong comparison.

Saunders RS, Jr., Samei E, Lo JY, et al. Can compression be reduced for breast tomosynthesis? Monte carlo study on mass and microcalcification conspicuity in tomosynthesis. Radiology. 2009;251(3):673-82.
Exclusion: wrong outcomes.

Sauven P, Bishop H, Patnick J, et al. The National Health Service Breast Screening Programme and British Association of Surgical Oncology audit of quality assurance in breast screening 1996-2001. Br J Surg. 2003;90(1):82-7.
Exclusion: wrong outcomes.

Savoca CJ. Re: "Technology evaluation center assessment synopsis: use of magnetic resonance imaging to avoid a biopsy in women with suspicious primary breast lesions". J Am Coll Radiol. 2005;2(10):869; author reply -70.
Exclusion: wrong publication type.

Sayegh RA, Slanetz PJ. Breast density, hormones, and screening mammography: should women be less concerned? Menopause. 2009;16(6):1085-6.
Exclusion: wrong study design for key question.

Scaf-Klomp W, Sanderman R, van de Wiel HB, et al. Distressed or relieved? Psychological side effects of breast cancer screening in The Netherlands. J Epidemiol Community Health. 1997;51(6):705-10.
Exclusion: studies outside of search dates.

Schell MJ, Yankaskas BC, Ballard-Barbash R, et al. Evidence-based target recall rates for screening mammography. Radiology. 2007;243(3):681-9.
Exclusion: wrong outcomes.

Schilling K. Positron emission mammography: better than magnetic resonance mammography? Eur J Radiol. 2012;81 Suppl 1:S139-41.
Exclusion: wrong outcomes.

Schleicher UM, Ammon J. Mode of breast cancer detection: a study from the German part of the Maas-Rhine-EUREGIO. Eur J Cancer Prev. 1998;7 Suppl 1:S41-6.
Exclusion: wrong intervention.

Schmitz AC, Peters NHGM, Veldhuis WB, et al. Contrast-enhanced 3.0-T breast MRI for characterization of breast lesions: increased specificity by using vascular maps. Eur Radiol. 2008;18(2):355-64.
Exclusion: wrong outcomes.

Schnall M, Orel S. Breast MR imaging in the diagnostic setting. Magn Reson Imaging Clin N Am. 2006;14(3):329-37.
Exclusion: wrong intervention.

Schnall MD. Application of magnetic resonance imaging to early detection of breast cancer. Breast Cancer Res. 2001;3(1):17-21.
Exclusion: review not meeting inclusion criteria.

Schnall MD. Breast MR imaging. Radiol Clin North Am. 2003;41(1):43-50.
Exclusion: wrong publication type.

Schnall MD, Blume J, Bluemke DA, et al. Diagnostic architectural and dynamic features at breast MR imaging: multicenter study. Radiology. 2006;238(1):42-53.
Exclusion: wrong outcomes.

Schnur JB, Montgomery GH, Hallquist MN, et al. Anticipatory psychological distress in women scheduled for diagnostic and curative breast cancer surgery. Int J Behav Med. 2008;15(1):21-8.
Exclusion: wrong outcomes.

Schonberg MA, Breslau ES, McCarthy EP. Targeting of mammography screening according to life expectancy in women aged 75 and older. J Am Geriatr Soc. 2013;61(3):388-95.
Exclusion: wrong outcomes.

Schonberg MA, McCarthy EP, Davis RB, et al. Breast cancer screening in women aged 80 and older: results from a national survey. J Am Geriatr Soc. 2004;52(10):1688-95.
Exclusion: wrong outcomes.

Schootman M, Fuortes LJ. Breast and cervical carcinoma: the correlation of activity limitations and rurality with screening, disease incidence, and mortality. Cancer. 1999;86(6):1087-94.
Exclusion: wrong outcomes.

Schootman M, Fuortes LJ. Early indicators of the effect of a breast cancer screening program for low-income women. Cancer Detect Prev. 2001;25(2):138-46.
Exclusion: wrong study design for key question.

Schootman M, Jeffe D, Reschke A, et al. The full potential of breast cancer screening use to reduce mortality has not yet been realized in the United States. Breast Cancer Res Treat. 2004;85(3):219-22.
Exclusion: wrong study design for key question.

Schootman M, Jeffe DB, Lian M, et al. Surveillance mammography and the risk of death among elderly breast cancer patients. Breast Cancer Res Treat. 2008;111(3):489-96.
Exclusion: wrong population.

Schootman M, Lian M, Deshpande AD, et al. Temporal trends in area socioeconomic disparities in breast-cancer incidence and mortality, 1988-2005. Breast Cancer Res Treat. 2010;122(2):533-43.
Exclusion: wrong comparison.

Schootman M, Walker MS, Jeffe DB, et al. Breast cancer screening and incidence in communities with a high proportion of uninsured. Am J Prev Med. 2007;33(5):379-86.
Exclusion: wrong outcomes.

Schott G, Reichel M, Junkermann H, et al. Retrospective quantification of background incidence and stage distribution of breast cancer for the mammography screening pilot project in Wiesbaden, Germany. J Cancer Res Clin Oncol. 2008;134(1):29-35.
Exclusion: wrong outcomes.

Schousboe JT, Kerlikowske K, Loh A, et al. Personalizing mammography by breast density and other risk factors for breast cancer: analysis of health benefits and cost-effectiveness. Ann Intern Med. 2011;155(1):10-20.
Exclusion: wrong outcomes.

Schouten LJ, de Rijke JM, Huveneers JAM, et al. Rising incidence of breast cancer after completion of the first prevalent round of the breast cancer screening programme. J Med Screen. 2002;9(3):120-4.
Exclusion: wrong outcomes.

Schouten LJ, de Rijke JM, Schlangen JT, et al. Evaluation of the effect of breast cancer screening by record linkage with the cancer registry, The Netherlands. J Med Screen. 1998;5(1):37-41.
Exclusion: wrong comparison.

Schroen AM, Wobbes T, van der Sluis RF. Infiltrating lobular carcinoma of the breast detected by screening. Br J Surg. 1998;85(3):390-2.
Exclusion: wrong intervention.

Schwartz LM, Woloshin S, Sox HC, et al. US women's attitudes to false positive mammography results and detection of ductal carcinoma in situ: cross sectional survey. BMJ. 2000;320(7250):1635-40.

Exclusion: wrong study design for key question.

Scinto JD, Gill TM, Grady JN, et al. Screening mammography: Is it suitably targeted to older women who are most likely to benefit? J Am Geriatr Soc. 2001;49(8):1101-4.
Exclusion: wrong outcomes.

Scotland NHSQI. Comparison of digital mammography and film screen mammography. 2004
Exclusion: wrong outcomes.

Sechopoulos I, Suryanarayanan S, Vedantham S, et al. Radiation dose to organs and tissues from mammography: Monte Carlo and phantom study. Radiology. 2008;246(2):434-43.
Exclusion: wrong population.

Seemayer CA, Breuer E, Kroll G, et al. Incidence and tumour stages of breast cancer in the region of Aachen, Germany. Eur J Cancer Care (Engl). 2002;11(1):16-24.
Exclusion: wrong outcomes.

Seidenwurm D, Rosenberg R. Quality of life and diagnostic imaging outcomes. J Am Coll Radiol. 2010;7(4):265-8.
Exclusion: wrong study design for key question.

Seigneurin A, Exbrayat C, Labarere J, et al. Comparison of interval breast cancer rates for two- versus single-view screening mammography: a population-based study. Breast. 2009;18(5):284-8.
Exclusion: wrong outcomes.

Seigneurin A, Exbrayat C, Labarere J, et al. Association of diagnostic work-up with subsequent attendance in a breast cancer screening program for false-positive cases. Breast Cancer Res Treat. 2011;127(1):221-8.
Exclusion: wrong outcomes.

Seiler S, Lenkinski RE. Dedicated PET device for breast PET and MRI/PET correlations. Eur J Radiol. 2012;81 Suppl 1:S149-50.
Exclusion: wrong publication type.

Sekine K, Tsunoda-Shimizu H, Kikuchi M, et al. DCIS showing architectural distortion on the screening mammogram - comparison of mammographic and pathological findings. Breast Cancer. 2007;14(3):281-4.
Exclusion: wrong outcomes.

Selinko VL, Middleton LP, Dempsey PJ. Role of sonography in diagnosing and staging invasive lobular carcinoma. J Clin Ultrasound. 2004;32(7):323-32.
Exclusion: wrong population.

Sellers TA, King RA, Cerhan JR, et al. Fifty-year follow-up of cancer incidence in a historical cohort of Minnesota breast cancer families. Cancer Epidemiol Biomarkers Prev. 1999;8(12):1051-7.
Exclusion: wrong population.

Semiglazov VF, Manikhas AG, Moiseenko VM, et al. [Results of a prospective randomized investigation [Russia (St.Petersburg)/WHO] to evaluate the significance of self-examination for the early detection of breast cancer]. Vopr Onkol. 2003;49(4):434-41.
Exclusion: wrong outcomes.

Semiglazov VF, Moiseyenko VM, Bavli JL, et al. The role of breast self-examination in early breast cancer detection (results of the 5-years USSR/WHO randomized study in Leningrad). Eur J Epidemiol. 1992;8(4):498-502.
Exclusion: studies outside of search dates.

Sener SF, Winchester DJ, Winchester DP, et al. Survival rates for breast cancers detected in a community service screening mammogram program. Am J Surg. 2006;191(3):406-9.
Exclusion: wrong comparison.

Sener SF, Winchester DJ, Winchester DP, et al. Spectrum of mammographically detected breast cancers. Am Surg. 1999;65(8):731-5; discussion 5-6.
Exclusion: wrong outcomes.

Sennerstam RB, Wiksell H, Schassburger K-U, et al. Breast cancer and clinical outcome among women over 60 years of age: a plead for more screening and alternative treatments. Anal Quant Cytol Histol. 2012;34(4):189-94.
Exclusion: wrong comparison.

Sentis M. Imaging diagnosis of young women with breast cancer. Breast Cancer Res Treat. 2010;123 Suppl 1:11-3.
Exclusion: review not meeting inclusion criteria.

Seo BK, Pisano ED, Kuzmiak CM, et al. The positive predictive value for diagnosis of breast cancer full-field digital mammography versus film-screen mammography in the diagnostic mammographic population. Acad Radiol. 2006;13(10):1229-35.
Exclusion: wrong outcomes.

Appendix A4. List of Excluded Studies

Seppanen J, Heinavaara S, Anttila A, et al. Effects of different phases of an invitational screening program on breast cancer incidence. Int J Cancer. 2006;119(4):920-4.
Exclusion: wrong study design for key question.

Seppanen J, Heinavaara S, Hakulinen T. Influence of alternative mammographic screening scenarios on breast cancer incidence predictions (Finland). Cancer Causes Control. 2006;17(9):1135-44.
Exclusion: wrong outcomes.

Seppanen J, Heinavaara S, Hakulinen T. Predicting impacts of mass-screening policy changes on breast cancer mortality. Stat Med. 2008;27(25):5235-51.
Exclusion: wrong outcomes.

Seradour B, Allemand H, Weill A, et al. Changes by age in breast cancer incidence, mammography screening and hormone therapy use in France from 2000 to 2006. Bull Cancer. 2009;96(4):E1-6.
Exclusion: wrong outcomes.

Seradour B, Esteve J, Heid P, et al. Hormone replacement therapy and screening mammography: analysis of the results in the Bouches du Rhone programme. J Med Screen. 1999;6(2):99-102.
Exclusion: wrong comparison.

Setti E, Trecate G, Ferrari M, et al. Breast magnetic resonance imaging: a computer-based analysis of enhancement curves. J Digit Imaging. 2001;14(2 Suppl 1):226-8.
Exclusion: wrong study design for key question.

Setz-Pels W, Duijm LEM, Coebergh JW, et al. Re-attendance after false-positive screening mammography: a population-based study in the Netherlands. Br J Cancer. 2013;109(8):2044-50.
Exclusion: wrong outcomes.

Setz-Pels W, Duijm LEM, Louwman MWJ, et al. Characteristics and screening outcome of women referred twice at screening mammography. Eur Radiol. 2012;22(12):2624-32.
Exclusion: wrong population.

Shapiro S. Determining the efficacy of breast cancer screening. Cancer. 1989;63(10):1873-80.
Exclusion: studies outside of search dates.

Shapiro S, Strax P, Venet L, et al. Proceedings: Changes in 5-year breast cancer mortality in a breast cancer screening program. Proceedings National Cancer Conference. 1972;7:663-78.
Exclusion: studies outside of search dates.

Shaw CM, Flanagan FL, Fenlon HM, et al. Consensus review of discordant findings maximizes cancer detection rate in double-reader screening mammography: Irish National Breast Screening Program experience. Radiology. 2009;250(2):354-62.
Exclusion: wrong comparison.

Shen W-C, Chang R-F, Moon WK, et al. Breast ultrasound computer-aided diagnosis using BI-RADS features. Acad Radiol. 2007;14(8):928-39.
Exclusion: wrong intervention.

Shen Y, Parmigiani G. A model-based comparison of breast cancer screening strategies: mammograms and clinical breast examinations. Cancer Epidemiol Biomarkers Prev. 2005;14(2):529-32.
Exclusion: wrong study design for key question.

Shen Y, Yang Y, Inoue LYT, et al. Role of detection method in predicting breast cancer survival: analysis of randomized screening trials. J Natl Cancer Inst. 2005;97(16):1195-203.
Exclusion: review not meeting inclusion criteria.

Shen Y, Zelen M. Screening sensitivity and sojourn time from breast cancer early detection clinical trials: mammograms and physical examinations. J Clin Oncol. 2001;19(15):3490-9.
Exclusion: review not meeting inclusion criteria.

Shile PE, Pilgram TK. Variability in the interpretation of screening mammograms by US radiologists. Acad Radiol. 1996;3(10):879-81; discussion 81-2.
Exclusion: wrong publication type.

Shimada M, Senoo A, Hayashi S, et al. Assessment of breast cancer with dynamic gadolinium-enhanced MR imaging combined with magnetization transfer contrast using a newly developed breast surface coil for the supine position. Radiat Med. 1997;15(2):85-90.
Exclusion: wrong intervention.

Shin HJ, Kim HH, Cha JH, et al. Automated ultrasound of the breast for diagnosis: interobserver agreement on lesion detection and characterization. AJR Am J Roentgenol. 2011;197(3):747-54.
Exclusion: wrong intervention.

Shrestha S, Poulos A. The effect of verbal information on the experience of discomfort in mammography. Radiography. 2001;7(4):271-7.
Exclusion: included in an included systematic review, not directly used.

Sickles E, D'Orsi C. ACR BI-RADS Follow-up and outcome monitoring. ACR BI-RADS Atlas: Breast Imaging Data Reporting System. 2013:17.
Exclusion: wrong publication type.

Sickles EA. Breast cancer screening outcomes in women ages 40-49: clinical experience with service screening using modern mammography. J Natl Cancer Inst. 1997;Monographs.(22):99-104.
Exclusion: wrong publication type.

Sickles EA. Quality assurance. How to audit your own mammography practice. Radiol Clin North Am. 1992;30(1):265-75.
Exclusion: wrong publication type.

Sickles EA. The use of breast imaging to screen women at high risk for cancer. Radiol Clin North Am. 2010;48(5):859-78.
Exclusion: wrong study design for key question.

Sickles EA, Miglioretti DL, Ballard-Barbash R, et al. Performance benchmarks for diagnostic mammography. Radiology. 2005;235(3):775-90.
Exclusion: wrong intervention.

Siegal EC, Angelakis EJ, Hartman A. Can peer review contribute to earlier detection of breast cancer? A quality initiative to learn from false-negative mammograms. Breast J. 2008;14(4):330-4.
Exclusion: wrong intervention.

Sihto H, Lundin J, Lehtimaki T, et al. Molecular subtypes of breast cancers detected in mammography screening and outside of screening. Clin Cancer Res. 2008;14(13):4103-10.
Exclusion: wrong comparison.

Sim LSJ, Hendriks JHCL, Bult P, et al. US correlation for MRI-detected breast lesions in women with familial risk of breast cancer. Clin Radiol. 2005;60(7):801-6.
Exclusion: wrong population.

Simpson WL, Jr., Hermann G, Rausch DR, et al. Ultrasound detection of nonpalpable mammographically occult malignancy. Can Assoc Radiol J. 2008;59(2):70-6.
Exclusion: wrong comparison.

Sinclair N, Littenberg B, Geller B, et al. Accuracy of screening mammography in older women. AJR Am J Roentgenol. 2011;197(5):1268-73.
Exclusion: wrong comparison.

Singh S, Kumar V, Verma HK, et al. SVM based system for classification of microcalcifications in digital mammograms. Conf Proc IEEE Eng Med Biol Soc. 2006;1:4747-50.
Exclusion: wrong intervention.

Singh V, Saunders C, Wylie L, et al. New diagnostic techniques for breast cancer detection. Fut Oncol. 2008;4(4):501-13.
Exclusion: wrong publication type.

Singhal H, O'Malley FP, Tweedie E, et al. Axillary node dissection in patients with breast cancer diagnosed through the Ontario Breast Screening Program: a need for minimally invasive techniques. Can J Surg. 1997;40(5):377-82.
Exclusion: wrong study design for key question.

Singletary SE. New approaches to surgery for breast cancer. Endocr Relat Cancer. 2001;8(4):265-86.
Exclusion: review not meeting inclusion criteria.

Sjolin M, Maerker M. [Effects of information on and reflection of women's pain experience during mammography]. Vard i Norden. 1994;14(1):11-5.
Exclusion: included in an included systematic review, not directly used.

Skaane P. The additional value of US to mammography in the diagnosis of breast cancer. A prospective study. Acta Radiol. 1999;40(5):486-90.
Exclusion: wrong comparison.

Skaane P. Nationwide mammography screening registers: the best way to go for mortality evaluation - but there is no free lunch. Acta Radiol. 2011;52(3):235.
Exclusion: wrong publication type.

Skaane P. Studies comparing screen-film mammography and full-field digital mammography in breast cancer screening: updated review. Acta Radiol. 2009;50(1):3-14.
Exclusion: review not meeting inclusion criteria.

Skaane P. Ultrasonography as adjunct to mammography in the evaluation of breast tumors. Acta Radiol Suppl. 1999;420:1-47.
Exclusion: wrong intervention.

Skaane P, Balleyguier C, Diekmann F, et al. Breast lesion detection and classification: comparison of screen-film mammography and full-field digital mammography with soft-copy reading--observer performance study. Radiology. 2005;237(1):37-44.
Exclusion: wrong comparison.

Skaane P, Bandos AI, Gullien R, et al. Prospective trial comparing full-field digital mammography (FFDM) versus combined FFDM and tomosynthesis in a population-based screening programme using independent double reading with arbitration. Eur Radiol. 2013;23(8):2061-71.
Exclusion: wrong outcomes.

Skaane P, Engedal K, Skjennald A. Interobserver variation in the interpretation of breast imaging. Comparison of mammography, ultrasonography, and both combined in the interpretation of palpable noncalcified breast masses. Acta Radiol. 1997;38(4 Pt 1):497-502.
Exclusion: wrong outcomes.

Skaane P, Hofvind S, Skjennald A. Randomized trial of screen-film versus full-field digital mammography with soft-copy reading in population-based screening program: follow-up and final results of Oslo II study. Radiology. 2007;244(3):708-17.
Exclusion: wrong comparison.

Skaane P, Kshirsagar A, Hofvind S, et al. Mammography screening using independent double reading with consensus: is there a potential benefit for computer-aided detection? Acta Radiol. 2012;53(3):241-8.
Exclusion: wrong intervention.

Skaane P, Kshirsagar A, Stapleton S, et al. Effect of computer-aided detection on independent double reading of paired screen-film and full-field digital screening mammograms. AJR Am J Roentgenol. 2007;188(2):377-84.
Exclusion: wrong comparison.

Skaane P, Skjennald A. Screen-film mammography versus full-field digital mammography with soft-copy reading: randomized trial in a population-based screening program--the Oslo II Study. Radiology. 2004;232(1):197-204.
Exclusion: wrong comparison.

Skandarajah AR, Mann GB. The role of magnetic resonance imaging in early breast cancer. Asia Pac J Clin Oncol. 2012;8(1):24-30.
Exclusion: wrong intervention.

Smart CR, Byrne C, Smith RA, et al. Twenty-year follow-up of the breast cancers diagnosed during the Breast Cancer Detection Demonstration Project. CA Cancer J Clin. 1997;47(3):134-49.
Exclusion: wrong comparison.

Smith CL, Kricker A, Armstrong BK. Breast cancer mortality trends in Australia: 1921 to 1994.[Erratum appears in Med J Aust 1998 Mar 2;168(5):225]. Med J Aust. 1998;168(1):11-4.
Exclusion: wrong study design for key question.

Smith-Bindman R, Chu P, Miglioretti DL, et al. Physician predictors of mammographic accuracy. J Natl Cancer Inst. 2005;97(5):358-67.
Exclusion: wrong outcomes.

Smith-Bindman R, Kerlikowske K. Is there a downside to elderly women undergoing screening mammography? J Natl Cancer Inst. 1998;90(18):1322-3.
Exclusion: wrong publication type.

Smith-Bindman R, Kerlikowske K, Gebretsadik T, et al. Is screening mammography effective in elderly women? Am J Med. 2000;108(2):112-9.
Exclusion: wrong comparison.

Sohlich RE, Sickles EA, Burnside ES, et al. Interpreting data from audits when screening and diagnostic mammography outcomes are combined. AJR Am J Roentgenol. 2002;178(3):681-6.
Exclusion: wrong outcomes.

Sohn Y-M, Kim MJ, Kim E-K, et al. Sonographic elastography combined with conventional sonography: how much is it helpful for diagnostic performance? J Ultrasound Med. 2009;28(4):413-20.
Exclusion: wrong intervention.

Sohn Y-M, Kim MJ, Kwak JY, et al. Breast ultrasonography in young Asian women: analyses of BI-RADS final assessment category according to symptoms. Acta Radiol. 2011;52(1):35-40.
Exclusion: wrong population.

Solin LJ, Fourquet A, Vicini FA, et al. Mammographically detected ductal carcinoma in situ of the breast treated with breast-conserving surgery and definitive breast irradiation: long-term outcome and prognostic significance of patient age and margin status. Int J Radiat Oncol Biol Phys. 2001;50(4):991-1002.
Exclusion: wrong intervention.

Solin LJ, Gray R, Baehner FL, et al. A multigene expression assay to predict local recurrence risk for ductal carcinoma in situ of the breast. J Natl Cancer Inst. 2013;105(10):701-10.
Exclusion: wrong intervention.

Solin LJ, McCormick B, Recht A, et al. Mammographically detected, clinically occult ductal carcinoma in situ treated with breast-conserving surgery and definitive breast irradiation. Cancer J Sci Am. 1996;2(3):158-65.
Exclusion: wrong population.

Solin LJ, Schultz DJ, Hanchak NA, et al. Patterns of treatment for older women with newly diagnosed breast carcinoma. Am J Clin Oncol. 1999;22(2):107-13.
Exclusion: wrong outcomes.

Solin LJ, Schultz DJ, Kessler HB, et al. Downstaging of Breast Carcinomas in Older Women Associated with Mammographic Screening. Breast J. 1999;5(2):94-100.
Exclusion: wrong intervention.

Song E, Jiang L, Jin R, et al. Breast mass segmentation in mammography using plane fitting and dynamic programming. Acad Radiol. 2009;16(7):826-35.
Exclusion: wrong intervention.

Song L, Fletcher R. Breast cancer rescreening in low-income women. Am J Prev Med. 1998;15(2):128-33.
Exclusion: wrong outcomes.

Sontag L, Axelrod DE. Evaluation of pathways for progression of heterogeneous breast tumors. J Theor Biol. 2005;232(2):179-89.
Exclusion: wrong study design for key question.

Sorelli PG, Cosgrove DO, Svensson WE, et al. Can contrast-enhanced sonography distinguish benign from malignant breast masses? J Clin Ultrasound. 2010;38(4):177-81.
Exclusion: wrong outcomes.

Souza FH, Wendland EM, Rosa MI, et al. Is full-field digital mammography more accurate than screen-film mammography in overall population screening? A systematic review and meta-analysis. Breast. 2013;22(3):217-24.
Exclusion: review not meeting inclusion criteria.

Sox H. Screening mammography for younger women: back to basics. Ann Intern Med. 2002;137(5 Part 1):361-2.
Exclusion: wrong publication type.

Spanu A, Sanna D, Chessa F, et al. The clinical impact of breast scintigraphy acquired with a breast specific -camera (BSGC) in the diagnosis of breast cancer: incremental value versus mammography. Int J Oncol. 2012;41(2):483-9.
Exclusion: wrong intervention.

Spencer DB, Potter JE, Chung MA, et al. Mammographic screening and disease presentation of breast cancer patients who die of disease. Breast J. 2004;10(4):298-303.
Exclusion: wrong outcomes.

Spillane AJ, Kennedy CW, Gillett DJ, et al. Screen-detected breast cancer compared to symptomatic presentation: an analysis of surgical treatment and end-points of effective mammographic screening. ANZ J Surg. 2001;71(7):398-402.
Exclusion: wrong comparison.

Sprague BL, Trentham-Dietz A, Burnside ES. Socioeconomic disparities in the decline in invasive breast cancer incidence. Breast Cancer Res Treat. 2010;122(3):873-8.
Exclusion: wrong outcomes.

Spratt JS, Gaines BM, Aaron WS, et al. What are the benefits and costs of screening mammograms on Kentucky women aged 40-49? J Surg Oncol. 1996;63(2):71-6.
Exclusion: wrong publication type.

Stang A, Kaab-Sanyal V, Hense H-W, et al. Effect of mammography screening on surgical treatment for breast cancer: a nationwide analysis of hospitalization rates in Germany 2005-2009. Eur J Epidemiol. 2013;28(8):689-96.
Exclusion: wrong outcomes.

Stefanick ML, Anderson GL, Margolis KL, et al. Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy. JAMA. 2006;295(14):1647-57.
Exclusion: wrong intervention.

Steinemann SK, Chun MBJ, Huynh DH, et al. Breast cancer worry among women awaiting mammography: is it unfounded? Does prior counseling help? Hawaii Med J. 2011;70(7):149-50.
Exclusion: wrong intervention.

Sterns EE. Relation between clinical and mammographic diagnosis of breast problems and the cancer/biopsy rate. Can J Surg. 1996;39(2):128-32.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Stoblen F, Landt S, Stelkens-Gebhardt R, et al. First evaluation of the diagnostic accuracy of an automated 3D ultrasound system in a breast screening setting. Anticancer Res. 2011;31(8):2569-74.
Exclusion: wrong outcomes.

Stout NK, Rosenberg MA, Trentham-Dietz A, et al. Retrospective cost-effectiveness analysis of screening mammography. J Natl Cancer Inst. 2006;98(11):774-82.
Exclusion: wrong outcomes.

Stoutjesdijk MJ, Futterer JJ, Boetes C, et al. Variability in the description of morphologic and contrast enhancement characteristics of breast lesions on magnetic resonance imaging. Invest Radiol. 2005;40(6):355-62.
Exclusion: wrong outcomes.

Strigel RM, Eby PR, Demartini WB, et al. Frequency, upgrade rates, and characteristics of high-risk lesions initially identified with breast MRI. AJR Am J Roentgenol. 2010;195(3):792-8.
Exclusion: wrong outcomes.

Suhrke P, Maehlen J, Schlichting E, et al. Effect of mammography screening on surgical treatment for breast cancer in Norway: comparative analysis of cancer registry data. BMJ. 2011;343:d4692.
Exclusion: wrong study design for key question.

Sun J, Chapman J, Gordon R, et al. Survival from primary breast cancer after routine clinical use of mammography. Breast J. 2002;8(4):199-208.
Exclusion: wrong study design for key question.

Suzuki A, Kuriyama S, Kawai M, et al. Age-specific interval breast cancers in Japan: estimation of the proper sensitivity of screening using a population-based cancer registry. Cancer Sci. 2008;99(11):2264-7.
Exclusion: wrong outcomes.

Suzuki R, Iwasaki M, Yamamoto S, et al. Leisure-time physical activity and breast cancer risk defined by estrogen and progesterone receptor status--the Japan Public Health Center-based Prospective Study. Prev Med. 2011;52(3-4):227-33.
Exclusion: wrong outcomes.

Suzuki R, Ye W, Rylander-Rudqvist T, et al. Alcohol and postmenopausal breast cancer risk defined by estrogen and progesterone receptor status: a prospective cohort study. J Natl Cancer Inst. 2005;97(21):1601-8.
Exclusion: wrong outcomes.

Svahn T, Andersson I, Chakraborty D, et al. The diagnostic accuracy of dual-view digital mammography, single-view breast tomosynthesis and a dual-view combination of breast tomosynthesis and digital mammography in a free-response observer performance study. Radiat Prot Dosimetry. 2010;139(1-3):113-7.
Exclusion: wrong outcomes.

Svane G, Azavedo E, Lindman K, et al. Clinical experience of photon counting breast tomosynthesis: comparison with traditional mammography. Acta Radiol. 2011;52(2):134-42.
Exclusion: wrong population.

Svartbo B, Bygren LO, Bucht G, et al. False-negative cases of breast cancer deaths in mammography screening evaluations. Breast J. 2003;9(2):142-3.
Exclusion: wrong publication type.

Svensson WE, Pandian AJ, Hashimoto H. The use of breast ultrasound color Doppler vascular pattern morphology improves diagnostic sensitivity with minimal change in specificity. Ultraschall Med. 2010;31(5):466-74.
Exclusion: wrong outcomes.

Swedish Organised Service Screening Evaluation G. Effect of mammographic service screening on stage at presentation of breast cancers in Sweden. Cancer. 2007;109(11):2205-12.
Exclusion: wrong study design for key question.

Swedish Organised Service Screening Evaluation Group. Reduction in breast cancer mortality from organized service screening with mammography: 1. Further confirmation with extended data. Cancer Epidemiol Biomarkers Prev. 2006;15(1):45-51.
Exclusion: included in an included systematic review, not directly used.

Sylvester PA, Vipond MN, Kutt E, et al. A comparative audit of prevalent, incident and interval cancers in the Avon breast screening programme. Ann R Coll Surg Engl. 1997;79(4):272-5.
Exclusion: wrong comparison.

Tabár L, Chen HH, Duffy SW, et al. Primary and adjuvant therapy, prognostic factors and survival in 1053 breast cancers diagnosed in a trial of mammography screening. Jpn J Clin Oncol. 1999;29(12):608-16.
Exclusion: wrong population.

Tabár L, Dean PB. Mammography and breast cancer: the new era. Int J Gynaecol Obstet. 2003;82(3):319-26.
Exclusion: wrong publication type.

Tabár L, Duffy SW, Burhenne LW. New Swedish breast cancer detection results for women aged 40-49. Cancer. 1993;72(4 Suppl):1437-48.
Exclusion: studies outside of search dates.

Tabár L, Duffy SW, Chen HH. Re: Quantitative interpretation of age-specific mortality reductions from the Swedish Breast Cancer-Screening Trials. J Natl Cancer Inst. 1996;88(1):52-5.
Exclusion: wrong publication type.

Tabár L, Duffy SW, Krusemo UB. Detection method, tumour size and node metastases in breast cancers diagnosed during a trial of breast cancer screening. Eur J Cancer Clin Oncol. 1987;23(7):959-62.
Exclusion: studies outside of search dates.

Tabár L, Duffy SW, Yen MF, et al. All-cause mortality among breast cancer patients in a screening trial: support for breast cancer mortality as an end point. J Med Screen. 2002;9(4):159-62.
Exclusion: studies outside of search dates.

Tabár L, Fagerberg G, Day NE, et al. The Swedish two-county trial of mammographic screening for breast cancer: recent results on mortality and tumor characteristics. Pathologie-biologie. 1992;39(9):846.
Exclusion: studies outside of search dates.

Tabár L, Gad A, Holmberg L, et al. Significant reduction in advanced breast cancer. Results of the first seven years of mammography screening in Kopparberg, Sweden. Diagn Imaging Clin Med. 1985;54(3-4):158-64.
Exclusion: studies outside of search dates.

Tabár L, Larsson LG. Breast-cancer screening with mammography in women aged 40-49 years. Int J Cancer. 1996;68(6):693-9.
Exclusion: no original data to include; publication or dataset with longer followup, more complete data, or same data already included in review.

Tabár L, Vitak B, Chen HH, et al. Beyond randomized controlled trials: organized mammographic screening substantially reduces breast carcinoma mortality. Cancer. 2001;91(9):1724-31.
Exclusion: wrong comparison.

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Exclusion: wrong outcomes.

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Randomized, Controlled Trials (RCTs) and Cohort Studies[1,2]

Criteria:

- Initial assembly of comparable groups**:**
  - for RCTs: adequate randomization, including first concealment and whether potential confounders were distributed equally among groups
  - for cohort studies: consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts
- Maintenance of comparable groups (includes attrition, crossovers, adherence, contamination)
- Important differential loss to followup or overall high loss to followup
- Measurements: equal, reliable, and valid (includes masking of outcome assessment)
- Clear definition of interventions
- Important outcomes considered
- Analysis: adjustment for potential confounders for cohort studies, or intention-to-treat analysis for RCTs.

Definition of ratings based on above criteria:

Good: Meets all criteria: Comparable groups are assembled initially and maintained throughout the study (followup at least 80 percent); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; important outcomes are considered; and appropriate attention to confounders in analysis. In addition, for RCTs, intention to treat analysis is used.

Fair: Studies will be graded "fair" if any or all of the following problems occur, without the fatal flaws noted in the "poor" category below: Generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred in followup; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for. Intention to treat analysis is done for RCTs.

Poor: Studies will be graded "poor" if any of the following fatal flaws exists: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied at all equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. For RCTs, intention to treat is lacking.

Case Control Studies[1,2]

Criteria:

- Accurate ascertainment of cases
- Nonbiased selection of cases/controls with exclusion criteria applied equally to both
- Response rate
- Diagnostic testing procedures applied equally to each group
- Measurement of exposure accurate and applied equally to each group
- Appropriate attention to potential confounding variable

Definition of ratings based on criteria above:

Good: Appropriate ascertainment of cases and nonbiased selection of case and control participants; exclusion criteria applied equally to cases and controls; response rate equal to or greater than 80 percent; diagnostic procedures and measurements accurate and applied equally to cases and controls; and appropriate attention to confounding variables.

Fair: Recent, relevant, without major apparent selection or diagnostic work-up bias but with response rate less than 80 percent or attention to some but not all important confounding variables.

Poor: Major selection or diagnostic work-up biases, response rates less than 50 percent, or inattention to confounding variables.

Systematic Reviews[2-5]

Criteria:

- Search dates reported?
- Search methods reported?
- Comprehensive search?
- Inclusion criteria reported?
- Selection bias avoided?
- Validity criteria reported?
- Validity assessed appropriately?
- Methods used to combine studies reported?
- Findings combined appropriately?
- Conclusions supported by data?

Definitions of ratings based on above criteria:

Good: Meets all criteria: reports comprehensive and reproducible search methods and results; reports pre-defined criteria to select studies and reports reasons for excluding potentially relevant studies; adequately evaluates quality of included studies and incorporates assessments of quality when synthesizing data; reports methods for synthesizing data and uses appropriate methods to combine data qualitatively or quantitatively; conclusions supported by the evidence reviewed.

Fair: Studies will be graded fair if they fail to meet one or more of the above criteria, but the limitations are not judged as being major.

Poor: Studies will be graded poor if they have a major limitation in one or more of the above criteria.

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Breast Cancer Surveillance Consortium

In 1994 the National Cancer Institute (NCI) established the Breast Cancer Surveillance Consortium (BCSC) to study breast cancer screening practices in the United States, with the recognition that results from controlled clinical trials of mammography may differ from the results of community screening practices. Each of the Consortium's breast imaging registries collects population-based screening and diagnostic mammography data and links it to state or regional cancer registries. The following BCSC registries contributed data to this report: the Carolina Mammography Registry (North Carolina), Group Health Cooperative (Seattle Puget Sound region), New Hampshire Mammography Network, San Francisco Mammography Registry, and Vermont Breast Cancer Surveillance System. Mammography data are also linked to pathology databases, which include benign as well as malignant outcomes. A comparison of women represented in the BCSC against 2000 Census data shows that Consortium sites are located in counties that contain slightly more than 5 percent of the U.S. population, and represent the population in important sociodemographic respects.[1]

Currently, the Consortium's database contains information on 10.7 million mammography examinations (including 2.6 million digital), 2.5 million women, and 130,000 breast cancer cases. Information on the distribution of key variables, mammographic data, characteristics of cases, and screening performance, among others, are detailed on the BCSC website: http://breastscreening.cancer.gov/data/. Data are pooled at a central Statistical Coordinating Center.

Registries and the Coordinating Center received institutional review board approval for active or passive consenting processes or a waiver of consent to enroll participants, link data, and perform analysis. All procedures were Health Insurance Portability and Accountability Act compliant, and registries and the coordinating center received a federal Certificate of Confidentiality and other protections for the identities of women, physicians, and facilities.

BCSC data include screening as well as diagnostic mammography. Screening mammography examinations are those designated as such by the ordering provider or radiologist performed more than 9 months after a previous imaging examination in women without a history of breast cancer or breast augmentation. Unilateral exams are excluded. Mammography information includes breast density, Breast Imaging Reporting And Data System (BI-RADS) assessment score, and recommendations for further work-up. In addition, prior to each mammography examination, a woman fills out a questionnaire that includes demographic and medical history information, including previous mammography information. Each screening mammography examination is given initial BI-RADS score based on the screening views only, which categorizes it as "positive" or "negative." In our analysis, an initial score of 0, 4, 5, or 3 with a recommendation for immediate work-up is considered positive, whereas a score of 1, 2 or 3 without a recommendation for immediate work-up is negative.

In this report, BCSC data from 2003 to 2011 are included to examine the 1) frequency of recommendations for additional imaging and biopsy procedures resulting from positive screening mammography, 2) potential adverse effects of mammography screening, 3) incidence of ductal carcinoma in situ and invasive cancers detected by mammography screening; and 4) differences

in outcomes between groups based on age, risk factors, and time since last mammography screening. Information for women under age 40 years or who have histories of breast augmentation or previous breast cancer diagnosis has been excluded.

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Key Question 1. What is the effectiveness of routine mammography screening in reducing breast cancer–specific and all-cause mortality, and how does it differ by age, risk factor, and screening interval?

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Key Question 5. What are the harms of routine mammography screening, and how do they differ by age, risk factor, and screening interval?

Psychological Harms

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Appendix B1. Quality Ratings of Systematic Reviews

Author, year, title	Study design pre-determined?	Dual review of studies and data abstraction?	Comprehensive literature search?	Publication status used as inclusion criteria?	List of included and excluded studies provided?	Characteristics of included studies provided?
Armstrong et al, 2007[14]	Yes	Yes	Yes	Unclear	Included studies: Yes Excluded studies: No	Yes
Bond et al, 2013[185]	Yes	Dual review of abstracts Dual checking of data	Yes	No	Included studies: Yes Excluded studies: No	Yes
Brett et al, 2005[183]	Unclear	Yes	Yes	No	Included studies: Yes Excluded studies: No	Yes
Brewer et al, 2007[184]	Unclear	Yes	Yes	No	Included studies: Yes Excluded studies: No	Yes
Broeders et al, 2012[98]	Yes	Not reported	Yes	No	Included studies: Yes Excluded studies: No	Yes
Hafslund and Nortvedt, 2009[194]	Unclear	Not reported	Yes	No	Included studies: Yes Excluded studies: No	Yes
Harris et al, 2011[99]	Yes	Dual review of abstracts Dual checking of data	Yes	No	Included studies: Yes Excluded studies: No	Yes
Marmot et al, 2013[163]	Unclear	Not reported	Unclear	No	Included studies: Yes Excluded studies: No	Yes
Miller et al, 2008[210]	Yes	Yes	Yes	No	Included studies: Yes Excluded studies: Yes	Yes
Moss et al, 2012[97]	Yes	Not reported	Yes	No	Included studies: Yes Excluded studies: No	Yes
Njor et al, 2012[96]	Yes	Not reported	Yes	No	Included studies: Yes Excluded studies: No	Yes
Puliti et al, 2012[161]	Yes	Not reported	Yes	No	Included studies: Yes Excluded studies: No	Yes
Whelehan et al, 2013[211]	Yes	Dual review of abstracts Dual checking of data	Yes	Unclear	Included studies: Yes Excluded studies: No	Not all studies

Author, year, title	Included studies quality assessed?	Quality of included studies considered in formulating conclusions?	Appropriate methods used to combine studies?	Publication bias assessed?	Conflict of interest stated?	Quality rating
Armstrong et al, 2007[14]	Yes	Yes	Unclear	No	Yes	Good
Bond et al, 2013[185]	Yes	Unclear	Yes	No	Yes	Good
Brett et al, 2005[183]	No	Unclear	Yes	No	No	Fair
Brewer et al, 2007[184]	Coded variables, but not formally assessed with criteria	Unclear	Yes	No	Yes	Fair
Broeders et al, 2012[98]	No	Unclear	Yes	No	Yes	Good
Hafslund and Nortvedt, 2009[194]	Yes	Unclear	Yes	No	No	Fair

Appendix B1. Quality Ratings of Systematic Reviews

Author, year, title	Included studies quality assessed?	Quality of included studies considered in formulating conclusions?	Appropriate methods used to combine studies?	Publication bias assessed?	Conflict of interest stated?	Quality rating
Harris et al, 2011[99]	Yes	Yes	Yes	No	No	Good
Marmot et al, 2013[163]	No	Unclear	Yes	No	No	Fair
Miller et al, 2008[210]	Yes	Yes	Yes	No	Yes	Good
Moss et al, 2012[97]	No	Unclear	Yes	No	Yes	Good
Njor et al, 2012[96]	No	Unclear	Yes	No	Yes	Good
Puliti et al, 2012[161]	No	Unclear	Yes	No	Yes	Fair
Whelehan et al, 2013[211]	Yes	Yes	Yes	No	Yes	Fair

Appendix B2. Evidence Table of Results of New Studies of Psychological Harms

Author, year	Study design	Age, *years* (mean or %); setting; population	Comparisons	Measures	Outcomes	Quality rating; limitations
Bredal et al, 2013[207]	Before-after study	57.7; women recalled in a screening program in Oslo, Norway	FP (n=560) and TP (n=80) at recall vs. 4 weeks later	HADS (score ≥11)	**Recall vs. 4 weeks later:** anxiety (% cases): FP 15% vs. 5.5% (NS), TP 19% vs. 16.7% (NS); depression (% cases): FP 1.4% vs. 1.3% (NS), TP 1.3% vs. 6.9% (NS). Factors predicting anxiety or depression in multivariate models: low general life expectations, previous history of anxiety and/or depression, anxiety at baseline, satisfaction with information (predicts depression only).	NA*
Brodersen and Siersma, 2013[203]	Nested case-control	28% 50-54, 32% 55-59, 23% 60-64, 17% ≥65; women in screening programs in Copenhagen and Funen, Denmark; cases=recalled; controls=normal results in the same clinic and day as cases	FP (n=272) vs. Normal screen (n=864) vs. TP (n=174)	COS-BC	**After screening mammography:** Normal screen vs. FP and TP had significantly better scores on subscales for sense of dejection, anxiety, negative impact on behavior, sleep, or sexuality, breast examination, and on single items of feeling less attractive and keeping mind off things ($p<0.001$ for all outcomes); no differences between FP and TP on any subscales. **3 year followup:** TP vs. FP and Normal screen had significantly worse scores on subscales of sense of dejection, anxiety, negative impact on behavior, sleep, or sexuality, social network, and on single items of feeling less attractive and keeping mind off things ($p<0.001$ for all outcomes) and additional differences vs. Normal screen on subscales of inner calm, social networking, and existential values ($p<0.001$ for all outcomes); FP vs. Normal screen had significantly worse scores on subscales for sense of dejection, anxiety, negative impact on behavior, sleep, or sexuality, breast examination, inner calm, social network, existential values, and on single items of feeling less attractive and keeping mind off things ($p<0.05$).	Good
Espasa et al, 2012[206]	Case-control	55% 50-59, 45% 60-69; women in screening program in Spain; cases=FP; controls=TN matched on age, education, marital and working status, and previous mammograms	FP (n=100) vs. Normal screen (n=50)	HADS, structured interview	**After 22 days of followup:** FP vs. Normal screen worried about having breast cancer (49% vs. 10%, $p<0.0001$) and had worries that affected mood or daily activities (31% vs. 2%, $p<0.0001$); but no differences in anxiety (11% vs. 14%, $p=0.83$) or depression (2% vs. 2%).	Fair; enrolled selected group of women; 2:1 ratio of cases to controls; did not control for confounders

Appendix B2. Evidence Table of Results of New Studies of Psychological Harms

Author, year	Study design	Age, *years* (mean or %); setting; population	Comparisons	Measures	Outcomes	Quality rating; limitations
Fitzpatrick et al, 2011[200]	Retrospective cohort	Mean age: NR, range: 50-62; women screened through the National Breast Screening Programme in Ireland	FP (n=9,746) vs. Normal screen (n=148,589)	Re-attendance	**Rate of re-attendance:** 90.7% vs. 89.0%, p<0.001; age group 50-54 years: 91.0% vs. 89.6%, p<0.001; age group 55-59 years: 90.4% vs. 88.7%, p<0.001; age group 60-62 years: 90.4% vs. 87.4%, p<0.001 **Adjusted OR of predictors of re-attendance (95% CI):** 0.8 (0.7 to 0.9) for age group 55-59 years and 0.8 (0.6 to 0.9) for age group 60-62 years vs. age group 50-54; 1.8 (1.5 to 2.2) for subsequent screen vs. initial screen; 0.9 (0.8 to 1.1) for core biopsy and 0.4 (0.3 to 0.6) for open benign biopsy vs. no tissue sampling; 0.997 (0.994 to 0.999) for every additional day from recall to assessment to non-malignant diagnosis	Fair, unclear if random or consecutive sample; baseline data not provided; did not control for confounders
Gibson et al, 2009[198]	Prospective cohort	6% <50, 32% 50-59, 34% 60-69, 22% 70-79, 6% ≥80; women registered in the New Hampshire Mammography Network and the New Hampshire Women for Health study	FP (n=2,107) vs. Normal screen (n=11,384) reference group	WHQ	**OR for depression (95% CI)**: overall FP 0.96 (0.72 to 1.28); white FP 0.84 (0.62 to 1.15); non-white FP 3.23 (1.32 to 7.91).	Fair; unclear how women were selected; baseline data not provided for groups of interest; outcomes self-reported
Hafslund et al, 2012[205]	Nested case-control	57 (SD 5.8) for FP vs. 58 (SD 5.5) for TN; women from Hordaland, Sogn, and Fjordane Counties, Norway; cases=FP; controls=TN	FP (n=128) vs. Normal screen (n=195)	SF-36, HADS	**6 months followup:** FP vs. Normal screen clinical anxiety (mean HADS-A) 4.1 vs. 4.0, p=0.81; clinical depression (mean HADS-D) 3.2 vs. 2.4, p=0.045; mental function (mean SF-36) 80.6 vs. 85.0; p=0.03; vitality (mean SF-36) 70.3 vs. 77.0; p=0.02.	Fair; enrolled selected group of women; higher response rate in control group
Keyzer-Dekker, 2012[199]	Prospective cohort	50 (SD 0.8) for 1st screen recalls vs. 61 (SD 5.9) for repeat screen recalls, p<0.001; women with abnormal results referred to hospitals in The Netherlands	1st screen recalls (n=186) vs. repeat screen recalls (n=296)	STAI, NEO-FFI, CES-D, WHOQOL	**After recall before diagnosis:** anxiety (mean STAI) 13.3 vs. 12.8, p=0.209; depression (mean CES-D) 8.9 vs. 9.0, p=0.836). **6 month followup:** anxiety (mean STAI estimated from graph) 10.6 vs. 10.3, p<0.001 for change over time for both groups; depression p<0.001 for change over time for both groups (data not shown), with no differences between groups.	Fair; older women in repeat screen group; outcomes were self-reported; did not report attrition

Appendix B2. Evidence Table of Results of New Studies of Psychological Harms

Author, year	Study design	Age, *years* (mean or %); setting; population	Comparisons	Measures	Outcomes	Quality rating; limitations
Klompen-houwer et al, 2014[202]	Retrospective cohort	Mean age: NR, range: 50-75; women being screened in one of the specialized screening units in The Netherlands	Normal screen (n=373,474) vs. 1st screen recalls (n=6,672) vs. repeat screen recalls for different lesion (n=161) vs. repeat screen recalls for same lesion (n=89)	Re-attendance rates	**Rate of re-attendance:** 93.2% (95% CI, 93.1% to 93.3%) vs. 65.4% (95% CI, 64.0% to 66.8%) vs. 56.7% (95% CI, 47.1% to 66.4%) vs. 44.3% (95% CI, 31.4% to 57.1%); and 52.1% (95% CI, 44.4% to 59.8%) for all recalled groups combined	Fair, baseline data not provided for groups; did not control for confounders
Maxwell et al, 2013[201]	Retrospective cohort	Mean age: NR, range: 49-66; women screened at 1 of 5 breast screening programs in the United Kingdom	FP (n-9,367) vs. Normal screen (n=243,650) and Prevalent screen (n=54,716) vs. incident screen (n=198,301)	Re-attendance rates	**Rate of re-attendance:** 87.7% of prevalent FP screen vs. 86.0% of prevalent normal screen, difference of 1.61% (95% CI, 0.54% to 2.62%); 92.0% of incident FP vs. 92.4% of incident normal screen, difference of -0.04% (95% CI, -1.18% to 0.31%); 86.2% of all prevalent screens vs. 92.4% of all incident screens **OR (95% CI) of re-attendance after additional procedures (reference is normal screen):** needle sampling only after prevalent screen 1.06 (0.90 to 1.24); needle sampling only after incident screen 0.88 (0.84 to 0.92); open biopsy after prevalent screen 0.64 (0.31 to 1.33); open biopsy after incident screen 0.40 (0.25 to 0.66); no tissue sampling after prevalent screen 1.20 (1.10 to 1.30); no tissue sampling after incident screen 1.00 (0.91 to 1.09) **OR (95% CI) of re-attendance by age:** 0.89 (0.86 to 0.93) for older age at prevalent screen with a reduction in the odds of re-attendance of 11% for each year's increase in a women's age; 0.99 (0.98 to 0.99) for older age at incident screen with a reduction in the odds of re-attendance of 1% for each year's increase in a women's age	Fair, baseline data not provided for groups; did not control for confounders
Tosteson et al, 2014[202]	Nested case-control	41% <50, 45% 50-64, 14% ≥65 years; women participating in DMIST in the United States; cases=FP; controls=TN matched by institution and age	FP (n=494) vs. Normal screen (n=534)	STAI, EuroQOL EQ-5D	**After mammography:** FP vs. Normal screen anxiety (mean STAI) 35 vs. 33, p=NR; QOL (mean EQ-5D) 0.90 vs. 0.90, p=NR. **1 year followup:** FP anxiety (STAI mean difference) -1.53 (SD 13.14), p=0.01; QOL (EQ-5D mean difference) 0.001 (SD 0.13), p=0.13); Normal screen anxiety and QOL did not change over time.	Good

*Quality rating criteria not available for this study design.

Appendix B2. Evidence Table of Results of New Studies of Psychological Harms

Abbreviations: CES-D=Center for Epidemiological Studies-Depression Scale; CI=confidence interval; COS-BC=Consequences of Screening in Breast Cancer; DMIST=Digital Mammographic Imaging Screening Trial; FP=false-positive; HADS=Hospital Depression and Anxiety Scale; HADS-A=HADS-Anxiety Subscale; HADS-D=HADS-Depression Subscale; n=number; NA=not available; NEO-FFI=Neuroticism-Extraversion-Openness-Five Factor Inventory; NR=not reported; NS=not significant; OR=odds ratio; QOL=quality of life; SD=standard deviation; SF-36=Short-form 36 Health Survey; STAI=Spielberger State-Trait Anxiety Inventory; TP=true positive; vs.=versus; WHOQOL=World Health Organization Quality of Life Assessment Instrument; WHQ=Women's Health Questionnaire.

Appendix B3. Quality Ratings of Cohort Studies

Author, Year	Did the study attempt to enroll a random sample or consecutive patients meeting inclusion criteria (inception cohort)?	Were the groups comparable at baseline?	Did the study use accurate methods for ascertaining exposures, potential confounders, and outcomes?	Were outcome assessors and/or data analysts blinded to treatment?	Did the article report attrition?
Bredal et al, 2013[207]	Yes	Unclear	Yes	No - self report	Yes
Elmore et al, 1998[149]	Yes	Yes	Unclear	No	Not applicable
Fitzpatrick et al, 2011[200]	Unclear	Unclear	Yes	No	Not applicable
Gibson et al, 2009[198]	Unclear	Unclear	Yes	No - self report	Yes
Hellquist et al, 2011[123]	Yes	Mostly, ages women were included changed over time	Yes	No	Not applicable
Hubbard et al, 2011[143]	Yes	Yes	Yes	No	Yes
Kerlikowske et al, 2013[144]	Yes	Yes	Yes	No	Yes
Keyzer-Dekker et al, 2012[199]	Yes	Mostly, older women in repeat screen group (p<0.001)	Yes	No - self report	No
Klompenhouwer et al, 2014[202]	Yes	Unclear	Yes	No	Not applicable
Maxwell et al, 2013[201]	Yes	Unclear	Yes	No	Not applicable

Author, Year	Did the study perform appropriate statistical analyses on potential confounders?	Is there important differential loss to followup or overall high loss to followup?	Were outcomes prespecified and defined, and ascertained using accurate methods?	Quality rating
Bredal et al, 2013[207]	Unclear	Unclear	Yes	Fair
Elmore et al, 1998[149]	Unclear	Unclear	Yes	Fair
Fitzpatrick et al, 2011[200]	Unclear	Unclear	Yes	Fair
Gibson et al, 2009[198]	Yes	Unclear	Yes	Fair
Hellquist et al, 2011[123]	Yes	Unclear	Yes	Fair
Hubbard et al, 2011[143]	Yes	Yes (5.5% of women had 1 year of followup and 2.9% observed for 10 or more years)	Yes	Fair

Appendix B3. Quality Ratings of Cohort Studies

Author, Year	Did the study perform appropriate statistical analyses on potential confounders?	Is there important differential loss to followup or overall high loss to followup?	Were outcomes prespecified and defined, and ascertained using accurate methods?	Quality rating
Kerlikowske et al, 2013[144]	Yes	Unclear	Yes	Fair
Keyzer-Dekker et al, 2012[199]	Yes	Unclear	Yes	Fair
Klompenhouwer et al, 2014[202]	Unclear	Unclear	Yes	Fair
Maxwell et al, 2013[201]	Unclear	Unclear	Yes	Fair

Appendix B4. Quality Ratings for Case-Control Studies

Author, year	Did the study attempt to enroll all or random sample of cases using pre-defined criteria?	Were the controls derived from the same population as the cases?	Were the groups comparable at baseline on key prognostic factors?	Were enrollment rates similar in cases and controls invited to participate?	Did the study use accurate methods for identifying outcomes?	Did the study use accurate methods for ascertaining exposures and potential confounders?	Did the study perform appropriate statistical analyses on potential confounders?	Quality rating
Brodersen and Siersma, 2013[203]	Yes	Yes	Yes, age is different, but would be expected	Yes	Yes	Yes	Yes	Good
Espasa et al, 2012[206]	Unclear	Yes	Yes, matched	Unclear	Yes	Yes	Unclear	Fair
Hafslund et al, 2012[205]	Unclear	Yes	Yes	No, more controls responded (85% vs. 52%)	Yes	Yes	Yes	Fair
Tosteson et al, 2014[204]	Yes	Yes	Yes, age is different, but would be expected	Unclear	Yes	Yes	Yes	Good