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Diagnostic Accuracy and Outcome of Assessment Pathways for Women Recalled after Breast Cancer Screening

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Abstract: Introduction: Breast cancer is the most commonly diagnosed cancer among women globally, with an estimated 2.26 million new cases in 2020. The risk factors of breast cancer include age, genetic mutation and family history, racial and ethnic disparities, Increase in breast tissue density, etc. Early detection through organized screening programs plays a crucial role in improving survival by identifying cancer at stages when treatment is more likely to be curative. However, screening and diagnostic results can sometimes be misinterpreted, leading to false positives, false negatives, unnecessary follow-up tests, or over-diagnosis. Although digital mammography remains the standard, additional imaging methods are now used for high-risk individuals and those with dense breast tissue. Aims and Objectives: To evaluate the diagnostic accuracy, and the clinical, psychological, and diagnostic outcomes following recall after routine breast screening. The studies include a Cohort studies, Observational and Case-Control studies, Diagnostic accuracy and Screening Programs evaluations. Participants includes women aged 40 and older undergoing routing breast screening and were called back for additional assessment. Studies were conducted in several countries including Norway, Spain, etc. Ethical approval was not required for the studies as the participants clinical information was anonymized across all selected studies. Methodology: Data were collected using a computerized search strategy as the principle source of information from European Journal of Public Health, Journal of Breast Imaging, PubMed, etc. Results: Findings from the Randomized and Population-based Cohort study suggested that the screen-detected breast cancers indicated over-diagnosis rate of 14-39% with limited quality evidence. Data from the Observational studies estimated the 10-years cumulative probability of false-positive results with Film and Digital Mammography of 49% with limited quality evidence. Findings from the Cohorts studies showed that those women called back for further evaluation reported higher levels of anxiety, distress and pains with a moderate quality evidence. The harm of radiation exposure from mammography screening is based on only three modeling studies with moderate quality evidence.

INTRODUCTION

Breast cancer is the most commonly diagnosed cancer among women globally, with an estimated 2.26 million new cases in 2020 (95% uncertainty interval: 2.24–2.79 million) (Ferlay J., 2020). In the United States, it is projected to represent 29% of all newly diagnosed cancers in women (DeSantis C.E., 2015). Despite improvements in early detection and treatment options, breast cancer continues to be a major cause of cancer-related deaths in women (Bray F. et al., 2018).

Breast cancer is categorized into five stages: 0, 1, 2, 3, and 4. Stage 0 refers to non-invasive conditions such as ductal carcinoma in situ (DCIS) or Paget's disease of the breast, where abnormal cells are confined to the milk ducts and have not spread. This stage typically presents no noticeable symptoms and is often managed with surgery—such as

lumpectomy or mastectomy—alongside hormonal therapy to prevent progression. DCIS accounts for roughly 20% to 25% of all breast cancer diagnosis (van Seijen M. et al., 2019). Stage 1 breast cancer is classified as an early-stage form of the disease and is generally highly treatable. At this stage, the tumor is small and typically confined to the breast, with little or no spread to nearby lymph nodes. Often, it does not cause noticeable symptoms and is detected through routine screening methods such as mammograms or ultrasounds. When signs do occur, they may involve a firm, painless lump, skin changes like redness or flaking, nipple discharge—possibly clear or blood-tinged—or unexplained alterations in the breast's size, shape, or swelling (Wang & Wu, 2023; Dye et al., 2012). Standard treatment options include surgery to remove the tumor, radiation therapy, and sometimes chemotherapy (Waks & Winer, 2019; Yuan, 2026).

Stage 2 represents early invasive cancer, where the tumor has grown beyond its original location but remains within the breast and nearby lymph nodes. It is further divided into 2A and 2B based on tumor size and lymph node involvement according to the TNM (Tumor, Node, Metastasis) classification. The 8th edition of the AJCC guidelines incorporates biological markers—including tumor grade, hormone receptor status (ER and PR), HER2 expression, and gene expression panels—into what is known as prognostic staging, allowing for a more precise evaluation of disease behavior and patient outlook (Available online). Treatment for stage 2 is tailored to individual risk profiles and may involve a combination of surgery, radiation, chemotherapy, hormonal therapy, and, when appropriate, immunotherapy (Journal of Clinical Oncology, 2026).

Stage 3 is considered locally advanced, with cancer spreading to multiple lymph nodes or nearby tissues. Common signs include palpable lumps, changes in breast shape or skin texture, and swelling in the armpit. Management usually begins with systemic therapy like chemotherapy, followed by surgery and radiation, often supplemented with hormonal or targeted treatments. Stage 4, or metastatic breast cancer, occurs when the disease spreads to distant organs such as the bones, lungs, liver, or brain. Symptoms vary depending on the affected site and may include bone pain, persistent cough or breathing difficulties, jaundice, abdominal swelling, or neurological issues, headaches and vision changes.

Breast cancer can also be classified based on histological and molecular features. Histologically, invasive ductal carcinoma is the most prevalent type, accounting for 40–80% of cases (Weigelt B. et al., 2008), and is diagnosed when a tumor does not fit into any specific special subtype (Tavassoli F.A., 2003). Around 25% of invasive cancers exhibit distinct patterns and cellular characteristics, leading to their classification as specific subtypes such as invasive lobular, tubular, mucinous (A and B), neuroendocrine, and others (Erber R., Hartmann A., 2020).

Molecularly, breast cancers are grouped into luminal, HER2-enriched, basal-like (often triple-negative), claudin-low, and other subtypes. Luminal cancers, which are estrogen receptor (ER)-positive, make up approximately 70% of cases in Western populations (Howlader N. et al., 2014). These are primarily invasive carcinomas of no special type but can occasionally appear as lobular, tubular, cribriform, mucinous, or micropapillary forms (Weigelt B. et al., 2010; Makki J., 2015). They are further divided into luminal A and luminal B, with the latter associated with higher tumor grade, increased cell proliferation, and a less favorable prognosis (Ades F., 2014; Cheang M.C.U. et al., 2009; Raj-Kumar P.-K. et al., 2019).

The HER2-enriched subtype accounts for 10–15% of breast cancers and is defined by high HER2 expression without ER or PR presence. These tumors show strong activity in genes related to cell growth, such as ERBB2/HER2 and GRB7, rather than luminal or basal markers (Raj-Kumar P.-K. et al., 2019; Ranjit K., 2005; Roberts S.A., 2013). However, about 30% of these tumors may test negative using standard Immunohistochemistry (IHC) or Fluorescence In Situ Hybridization (FISH methods, posing diagnostic challenges (Plasilova M.L. et al., 2016). The Triple-negative breast cancer (TNBC), lacking ER, PR, and HER2 expression, represents about 20% of cases and is more frequently seen in women under 40 years of age (Plasilova M.L. et al., 2016). A significant proportion—around 80%—of breast cancers in individuals with BRCA1 mutations are TNBC, while 11–16% of all TNBC cases carry germline BRCA1 or BRCA2 mutations. TNBC is generally more aggressive biologically and tends to have a poorer prognosis (Newman L.A. et al., 2014). While most cases are invasive ductal carcinomas, some present as medullary-like tumors with dense lymphocyte infiltration, metaplastic types with squamous or spindle cell features, or rare forms such as adenoid cystic carcinoma (Pareja F., 2016; Wetterskog D., 2012; Badve S. et al., 2010).

The primary method for assessing the prognosis of breast cancer patients is the American Joint Committee on Cancer (AJCC) staging system, which incorporates tumor grade, immunohistochemical biomarkers, and the anatomical extent of disease. Since its introduction in 1977, the AJCC has maintained an internationally recognized staging framework based on three anatomic criteria: tumor size (T), lymph node involvement (N), and presence of metastases (M) (Gou C. et al. 2016). The most commonly used histological grading approach is the Elston-Ellis modification of the Scarff-Bloom-Richardson system, also referred to as the Nottingham grading system (Weiss A. et al. 2018). This grading evaluates three morphological features: tubule formation, mitotic activity, and nuclear pleomorphism—assessing both size and shape of nuclei. Tumors are assigned a total score, with grade 1 corresponding to scores of 3–5, grade 2 to scores of 6–7, and grade 3 to scores of 8–9.

Early detection through organized screening programs plays a crucial role in improving survival by identifying cancer at stages when treatment is more likely to be curative (Tabar L. et al. 2003). Effective early diagnosis strategies focus on ensuring timely access to care, minimizing barriers between patients and health services, and enhancing the accuracy of diagnostic tools to correctly identify more cases. According to the 2019 guidelines from the U.S. National Comprehensive Cancer Network (NCCN), annual clinical breast exams and mammography are recommended for women aged 40 and older, as there is no strong evidence from randomized trials supporting routine screening in younger women (Qaseem A. et al. 2007; Chetlen A. et al. 2016; Grandishar WJ. Et al. 2020). However, screening and diagnostic results can sometimes be misinterpreted, leading to false positives, false negatives, unnecessary follow-up tests, or overdiagnosis (Welch HG. Et al. 2016). Access to diagnostic equipment is often limited outside major medical centers, posing challenges for rural populations or those with transportation difficulties (Welch HG. 2010). To address this, targeted breast cancer screening initiatives in underserved areas have been implemented, contributing to improved survival among at-risk women (Poiseuil M. et al. 2019). Enhancing the accessibility and patient comfort of screening and diagnostic procedures could therefore support earlier detection and treatment, particularly in remote regions.

By 2026, breast cancer screening and diagnosis are increasingly shaped by artificial intelligence integration and a shift toward personalized, risk-adapted screening schedules. Although digital mammography remains the standard, additional imaging methods are now used for high-risk individuals and those with dense breast tissue. A key limitation remains the lack of randomized controlled trials (RCTs) evaluating these newer modalities. Meta-analyses, such as those published by Koning (2024–2026), indicate that cone beam breast computed tomography (CBBCT) offers higher sensitivity (0.92) compared to mammography (0.77), though direct comparisons with photon-counting detector CT (PCD-CT) are scarce and largely confined to phantom studies. As of 2026, a review of clinical trial registries and major medical databases—including PubMed, Radiology, and ClinicalTrials.gov—reveals no published RCTs directly comparing the diagnostic performance and radiation exposure of PCD-CT and conventional CBBCT. While both represent cutting-edge advances in 3D breast imaging, current research is fragmented, often limited to technical validation or comparisons with traditional mammography (Lechance C.C. & Horton J., 2024; ClinicalTrials.gov, 2026).

BREAST CANCER EPIDERMIOLOGY AND RISK FACTORS

Breast cancer incidence and mortality have risen steadily over the past 30 years. From 1990 to 2016, incidence rates more than doubled in countries such as Afghanistan, the Philippines, Brazil, and Argentina, while death rates doubled in nations including Yemen, Paraguay, Libya, and Saudi Arabia (Sharma R., 2019). In 2020, the global mortality-to-incidence ratio (MIR)—a proxy for 5-year survival—was 0.30 (Ferlay J., 2020). In regions with robust healthcare systems like Hong Kong, Singapore, and Turkey, 5-year survival reached 89.6% for localized disease and 75.4% for regional disease. In contrast, less developed countries such as Costa Rica, India, the Philippines, Saudi Arabia, and Thailand reported survival rates of 76.3% and 47.4%, respectively (Sankaranarayanan R., 2010). Projections suggest that by 2030, annual new cases will reach 2.7 million globally, with deaths rising to 870,000 (Ferlay J., 2021).

In low- and middle-income countries, rising incidence is linked to lifestyle changes associated with westernization—such as later childbearing, reduced breastfeeding, earlier menarche, physical inactivity, and poor diet (Porter P., 2008). Age is a major risk factor, and the likelihood of developing breast cancer is about 1.5% at age 40, rises to 3% at 50, and exceeds 4% by age 70 (Stat Bite, 2004; Benz C.C., 2008; McGuire A. et al., 2015). Triple-negative breast cancer, known for its aggressiveness and resistance to treatment, is most frequently diagnosed in women under 40, whereas luminal A subtype is more common in patients over 70 (McGuire A. et al., 2015).

Several genetic mutations are strongly linked to elevated breast cancer risk. Two well-known autosomal dominant genes with high penetrance are BRCA1 (on chromosome 17) and BRCA2 (on chromosome 13), both closely tied to increased susceptibility to breast cancer (Shiovitz S. & Korde L.A., 2015). Other high-penetrance genes include TP53, CDH1, PTEN, and STK11 (Shahbandi A. et al., 2020; Corso G. et al., 2018, 2016; Kechagioglou P. et al., 2014). Additionally, a family history of breast cancer significantly increases individual risk. Around 13–19% of diagnosed patients report having a first-degree relative with the disease (Collaborative Group on Hormonal Factors in Breast Cancer, 2001), with risk further

elevated if the affected relative was diagnosed before age 50 (Shiyanbola O.O. et al., 2017; Baglia M.L. et al., 2018; Brewer H.R. et al., 2017).

Racial and ethnic disparities continue to be evident among individuals diagnosed with breast cancer, though the underlying causes of these differences are still unclear. While white non-Hispanic women have the highest incidence rates of breast cancer (Hill D.A. et al., 2019; Yedjou C.G. et al., 2019), Black women face significantly higher mortality rates and the lowest survival outcomes (American Cancer Society, 2016). A strong link has been established between exposures to endogenous hormones—particularly estrogen and progesterone—and an increased risk of developing breast cancer. Key reproductive events such as age at first menstruation, menopause, pregnancy, and breastfeeding, along with their timing and duration, influences hormonal balance and may contribute to the development of cancerous changes in breast tissue. Women who experience their first full-term pregnancy at a younger age, especially in their early twenties, and those with multiple pregnancies tend to have a lower risk of breast cancer (Bernstein L., 2002; Albrektsen G., 2004).

Breast tissue density varies over time and is clinically categorized into low-density, high-density, and fatty types. Higher breast density is more common in younger women, those with lower body mass index (BMI), individuals who are pregnant or breastfeeding, and those undergoing hormone replacement therapy (Checka C.M. et al., 2012). Increased density is consistently associated with greater breast cancer risk in both premenopausal and postmenopausal women (Kim E.Y. et al., 2020). Some researchers suggest that assessing breast density could serve as a practical, non-invasive tool for identifying women at higher risk and guiding more effective monitoring strategies (Duffy S.W. et al., 2017).

Engaging in regular physical activity is widely recognized as a factor that may reduce the likelihood of developing breast cancer (Chen X. et al., 2018; Kyu H.H. et al., 2016). Among women with a family history of the disease, physical activity appears to lower risk, particularly during the postmenopausal years (Chen X. et al., 2018). Potential mechanisms include reduced exposure to sex hormones, improved immune function, and modulation of insulin-like growth factor-1 levels (Hoffman-Goetz L., 2009). Epidemiological studies indicate that obesity increases the risk of breast cancer, especially in postmenopausal women, who are more likely to develop estrogen-receptor-positive tumors. Research by Wang X. et al. (2019) found that women over 50 with higher BMI face greater cancer risk compared to those with lower BMI. Higher body weight is also linked to more aggressive tumor characteristics, such as larger tumor size and increased lymph node involvement. Excess body fat may promote chronic inflammation and disrupt hormone regulation, creating conditions favorable to cancer development (James F. et al., 2015). As a result, poorer clinical outcomes are often seen in women with a BMI of 25 kg/m^2 or higher (Protani M. et al., 2010).

Excessive alcohol consumption is known to elevate the risk of gastrointestinal cancers and has also been associated with a higher risk of breast cancer. The alcohol content, rather than the type of beverage, appears to be the primary factor influencing this risk. Alcohol intake may raise estrogen levels and disrupt hormonal balance, thereby increasing the likelihood of carcinogenesis in breast tissue (Rachdaoui N. & Sarkar D.K., 2013; Erol A. et al., 2017).

Tobacco contains carcinogens that can reach breast tissue and increase the chance of genetic mutations, particularly in oncogenes and tumor suppressor genes like p53. Both active and passive smoking contribute to processes that may lead to cancer (Terry P.D. & Rohan T.E., 2002). For women with a family history of breast cancer, prolonged smoking and smoking before the first full-term pregnancy further elevate the risk (Catsburg C. et al., 2014; Jones M., 2017; Misotti A.M. & Gnagnarella P., 2013).

Vitamins are believed to possess anticancer properties that could play a role in preventing various cancers, including breast cancer, although the exact mechanisms remain unclear. Ongoing research examines the impact of specific vitamins—such as vitamin C, vitamin E, B-complex vitamins, folic acid, and multivitamins—on breast cancer risk, but findings are inconsistent and insufficient for definitive conclusions (Misotti A.M. & Gnagnarella P., 2013). Current attention has focused particularly on vitamin D, with several studies suggesting a protective role (Cui Y., 2006; Atoum M. & Alzoughool F., 2017; El-Sharkawy A. & Malki A., 2020). Higher blood levels of 25-hydroxyvitamin D correlate with lower breast cancer incidence in both pre- and postmenopausal women (Atoum M. & Alzoughool F., 2017; Estébanez N. et al., 2018). Additionally, increased expression of vitamin D receptors has been linked to reduced breast cancer mortality (Huss L. et al., 2019). However, more research is needed due to conflicting evidence in existing studies (Misotti A.M. & Gnagnarella P., 2013; Zhou L. et al., 2020).

Recent studies have linked exposure to artificial light at night (ALAN) with a higher risk of breast cancer, potentially due to disruptions in melatonin rhythms and resulting epigenetic changes (Al-Naggar R.A. & Anil S. 2016). Evidence suggests that individuals with greater ALAN exposure face a significantly elevated risk compared to those with lower exposure (Johns L.E. et al. 2018). However, the connection between prolonged use of LED-based electronic devices and breast cancer remains unclear, as current data are limited and sometimes inconsistent (L.E. et al. 2018).

Long-term exposure to certain chemicals may also contribute to breast cancer development by altering the tumor microenvironment, triggering epigenetic modifications, and promoting processes that support tumor growth (Casey S.C. et al. 2015). Women with sustained contact with such substances show a higher likelihood of developing breast cancer, with risk increasing alongside the duration of exposure (Videnros C. et al. 2019). Numerous chemicals have been implicated, but research has primarily focused on dichlorodiphenyltrichloroethane (DDT) and polychlorinated biphenyls (PCBs), especially because early-life exposure can interfere with mammary gland development (Rodgers K.M. et al. 2018; Eve L. et al. 2020). Additionally, potential links have been noted for polycyclic aromatic hydrocarbons (PAHs), synthetic fibers, organic solvents, oil mist, and various insecticides (Leso V. et al. 2019).

LITERATURE REVIEW

Established and Emerging Methods of Screening and Diagnosis

Biopsy

When imaging reveals an abnormality in breast tissue, a biopsy is necessary to establish a definitive diagnosis. This procedure involves the removal of suspicious fluid or tissue for cytological, histological, and molecular evaluation. Biopsies are typically recommended

only when there is clinical or imaging suspicion of cancer, as determined by the BI-RADS classification system used by radiologists (Elmore JG. 2015). Considered as the "gold standard" in such cases, biopsy remains the most reliable method for pathological assessment when breast cancer is suspected following physical examination or imaging (Tikku & Umap, 2015). The choice of technique depends on the lesion's characteristics and is usually guided by imaging modalities like ultrasound, mammography, or MRI.

Core Needle Biopsy (CNB) is the preferred approach for evaluating palpable lumps or masses detected on ultrasound. It uses a hollow needle to extract small cylindrical tissue samples. CNB demonstrates higher sensitivity (95.83%) and diagnostic accuracy compared to Fine Needle Aspiration (64.58%) for these cases (Tikku & Umap, 2015). Vacuum-Assisted Biopsy (VAB) employs a vacuum mechanism to draw larger tissue volumes into the needle, enabling more comprehensive sampling and, in some instances, complete removal of small lesions. Stereotactic VAB is particularly suited for non-palpable abnormalities such as microcalcifications visible on mammograms but not on ultrasound (Li et al., 2020). It offers better sample quality than standard core biopsy, lowering the risks of under-diagnosing cancer and sampling errors, with reported sensitivity around 96% (Pyo et al., 2020).

Fine Needle Aspiration Cytology (FNAC) uses a slender needle to extract cells or fluid. Though minimally invasive, it yields only cellular details without preserving tissue structure, limiting its use to clearly benign-appearing lesions or assessment of axillary lymph nodes (Tikku & Umap, 2015). FNAC also carries a greater likelihood of inconclusive or indeterminate results compared to CNB. Surgical (excisional) biopsy, which removes the entire lesion, is now less commonly used for initial diagnosis due to the high accuracy, lower cost, and improved cosmetic outcomes associated with percutaneous techniques. When surgery is performed, the guidance method depends on how the lesion was initially identified: ultrasound guidance is most common and patient-friendly for lesions visible on ultrasound, stereotactic (mammographic) guidance is required for microcalcifications and architectural distortions not seen on ultrasound, and MRI guidance is reserved for lesions detectable only on MRI (Tikku & Umap, 2015).

Mammography

Breast cancer screening involves testing women who show no symptoms, typically using mammography and clinical breast exams, with the goal of identifying cancers or precancerous conditions at an early stage (Siegel R.L. et al., 2022). Alongside advances in treatment, this approach has contributed to a notable decline in breast cancer deaths over recent decades (Myers E.R. et al., 2015; Sankatsing V.D.V. et al., 2017). Mammography remains the primary method for screening, widely endorsed by major health organizations including the American Cancer Research (ACR), Society of Breast Imaging (SBI), American Cancer Society (ACS), U.S. Preventive Services Task Force (USPSTF), National Comprehensive Cancer Network (NCCN), and the European Society for Medical Oncology (ESMO) (Gradishar WJ. Et al. 2020; Oeffinger KC. Et al. 2015; Cardoso F, Kyriakides S. et al. 2019; Siu AL. 2016). Its purpose is to detect malignant growths before they become clinically apparent.

According to the Breast Cancer Surveillance Consortium (BCSC), standard mammography demonstrates a sensitivity of 86.9% and specificity of 88.9% (BCSC, 2017),

while a study by Luczynska et al. reported a sensitivity of 90% and accuracy of 62% (Lucznska E. (2017). However, because specificity is not perfect, many women receive false-positive results—initial abnormalities that later prove non-cancerous after additional testing such as follow-up imaging or biopsy (Sankatsing V.D.V. et al., 2017; Brodersen J. & Siersma V.D., 2013). The likelihood of experiencing at least one false-positive result over time ranges from 20% to 60% (Elmore J.G. et al., 2002; Barratt A. et al., 2005; Castells X. et al., 2006; Roman M. et al., 2013; Hubbard R.A. et al., 2010), meaning that in some regions, more than half of screened women will face such an outcome, while in others, the figure is closer to one in five. Research by Christiansen C. et al. (2000) suggests that under certain conditions—such as younger age, higher breast density, or more frequent screening—the cumulative risk of a false-positive may approach nearly 100%. Additionally, mammography's effectiveness can be limited in women with dense breast tissue, where supplementary methods like ultrasonography may improve diagnostic accuracy (Rahbar H. et al. 2020).

Full-Field Digital Mammography (FFDM)

Full-Field Digital Mammography (FFDM) continues to play a central role in breast cancer screening, valued for its high resolution and proven clinical effectiveness (Pisano, E.D., et al., 2005). Since gaining approval in 2000, it has become the standard, replacing traditional film-based mammography (Smetherman DH. 2013). Nevertheless, FFDM has notable technical and clinical shortcomings, especially when evaluated alongside more advanced volumetric imaging techniques such as Digital Breast Tomosynthesis (DBT) and Cone Beam Breast CT (CBBCT) (Pisano, E.D., et al., 2005; Skaane, P., et al., 2013; Vedantham, S., et al., 2015). Key drawbacks include overlapping breast tissue, which can obscure lesions and result in false-negative diagnoses. Its accuracy also declines in women with dense breast tissue, reducing both sensitivity and specificity. Additionally, FFDM provides limited clarity in visualizing subtle structural margins, making it harder to assess architectural distortions—an essential factor in differentiating benign from malignant abnormalities.

Digital Breast Tomosynthesis (DBT)

Digital Breast Tomosynthesis (DBT), commonly referred to as 3D mammography, is an advanced imaging method that employs a low-dose X-ray system to generate high-resolution 3D reconstructions of breast tissue by capturing multiple images in thin 1mm slices. It was introduced to address the issue of overlapping tissue inherent in conventional 2D mammography (Sechopoulos, I. 2013). Research by Fiona and others suggests that DBT may improve cancer detection while reducing false-positive recalls (Helvie MA. 2010; Gilbert FJ, Tucker L. 2016). In a 2012 study by Svahn et al., radiologists evaluated 185 patients using DBT, finding a sensitivity of about 90% for DBT compared to 79% for digital mammography, with no notable difference in specificity between the two methods (Svahn TM. et al 2012). Despite these advantages, DBT has several clinical and technical drawbacks. These include higher cumulative radiation exposure, difficulty detecting malignant microcalcifications due to blurring artifacts that obscure their visibility, discomfort from breast compression during imaging, and reduced effectiveness in women with very dense breast tissue (Skaane, P., et al. 2013; Friedewald, S. M., et al. 2014; Zuckerman, S. P., et al. 2016).

Ultrasonography

Ultrasonography is a diagnostic imaging method that employs high-frequency sound waves to visualize internal structures of the body, aiding in the identification of abnormal tissues, including breast cancer (Smetherman DH.2013). In a study by Zanello and colleagues involving 241 patients who had previously undergone mammography, ultrasound provided a definitive diagnosis in 60.6% of cases, while remaining inconclusive in 39.4% (Berg W A. et al. 2008; Scheel JR. et al. 2015). Although ultrasound plays a key role in breast imaging—especially in distinguishing cystic from solid masses—it comes with technical and clinical constraints that limit its use as a primary screening tool, making it more suitable as an adjunct to other methods (Brem, R.F. et al., 2015; Catalano et al., 2023). Despite its high sensitivity, particularly in women with dense breast tissue, its low specificity often leads to false positives, which can result in unnecessary biopsies and increased patient distress. Additionally, ultrasound is less effective at detecting microcalcifications linked to Ductal Carcinoma In Situ (DCIS) and tends to identify benign abnormalities—an issue known as over-detection—leading to more follow-up tests and procedures, higher healthcare costs, and greater anxiety (Thieme Connect, 2014; Iacob et al., 2024; Brem et al., 2015). Various benign conditions, such as complex cysts, fat necrosis, and fibroadenomas, may appear suspicious on ultrasound, contributing to reduced specificity and an elevated rate of false positive findings (Iacob et al., 2024; Brem et al., 2015; Yun G. et al., 2019).

Positron Emission Tomography/Computed Tomography

Positron Emission Tomography combined with Computed Tomography (PET/CT) plays a key role in staging and assessing treatment response in advanced breast cancer. In a study by Wahl et al., 360 women with newly diagnosed invasive breast cancer were evaluated to assess FDG-PET's ability to detect axillary lymph node metastases, yielding a sensitivity of 61% and specificity of 80% (Wahl RL. et al. 2004). Another investigation involving 47 women with prior breast cancer compared the performance of FDG PET/CT to CT alone, reporting sensitivity, specificity, and accuracy of 85% versus 70%, 76% versus 47%, and 81% versus 59%, respectively (Mankoff DA, Gralow JR, 2007). Despite these benefits, PET/CT has notable drawbacks in early detection and initial diagnosis. Its spatial resolution is limited, making it less effective for identifying small lesions or sub-centimeter tumors (Vercher-Conejero J.L. et al., 2015). Additionally, its specificity is compromised by false positives due to inflammatory conditions. Since FDG is a glucose analog that accumulates in metabolically active tissues, benign processes such as mastitis, fat necrosis, recent biopsy sites, or reactive lymph nodes—especially after COVID-19 vaccination—can mimic cancer on imaging (Chen C.J. et al., 2009). Another concern is the high radiation exposure associated with PET/CT. Unlike mammography, which targets radiation to the breast, PET involves systemic distribution of a radiotracer throughout the body. The effective dose from a PET/CT or Positron Emission Mammography (PEM) scan ranges from 10 to 30 mSv—substantially higher than that of a standard mammogram. This elevated exposure, along with the long-term risk of secondary malignancies, limits its suitability for routine screening (Yanai A. et al., 2018).

Optical Imaging

Optical imaging is emerging as a promising tool in breast cancer research. Techniques like Diffuse Optical Tomography (DOT) and Optical Mammography (OM) offer non-invasive assessment of functional markers such as hemoglobin levels and tissue oxygenation (Poplack et al., 2023). Clinical studies have explored their use in detecting and characterizing tumors, monitoring dynamic physiological changes, evaluating breast density, and estimating cancer risk (Grosenick D. et al. 2016). Fournier et al. used dynamic optical mammography and found statistically significant differences between benign and malignant lesions, achieving 74% sensitivity and 92% specificity (Fournier LS. et al. 2009). However, several technical and clinical challenges hinder its replacement of conventional methods like mammography or MRI. A major obstacle is photon scattering in breast tissue: as light travels through the breast, multiple scattering events disrupt its path, reducing imaging precision (Poplack et al., 2023).

Several clinical trials have been conducted to evaluate optical imaging modalities mentioned above in the detection and characterization of breast cancer, dynamic response to external impact, assessment of breast density and cancer risk estimation (Grosenick D. et al. 2016). Fournier et al. using dynamic optical mammography reported a statistical difference in the characterization of benign and malignant lesions. The study revealed a 74% and 92% of sensitivity and specificity respectively (Fournier LS. et al. 2009. However, several significant technical and clinical limitations prevent it from replacing standard modalities like X-ray mammography or MRI. Strong light scattering of the photons on the breast tissue is the primary challenge. As the photons travel through the breast, they undergo numerous scattering events, which cause them to lose their original direction (Poplack et al., 2023).

Furthermore, optical imaging provides a high resolution but is limited to a depth of roughly 1mm, making it unsuitable for deep in vivo breast imaging (Poplack et al. 2023). It has a limited specificity for deep lesions and detecting small or deeply seated tumors remains difficult (Lee, 2011). Despite the sensitivity of optical imaging to breast density, it can face difficulties in very dense breasts or in younger women where the high density of fibroglandular tissue complicates light propagation (Lee, 2011).

Digital Infrared Thermal Imaging (DITI) or Thermography

Digital Infrared Thermal Imaging (DITI), also known as thermography, is a diagnostic imaging technique grounded in the observation that metabolic and vascular changes in pre-cancerous and cancerous tissues can raise skin surface temperature (Lee, K., et al. 2012). Some research suggests thermography may identify breast cancer earlier than mammography (Kakileti, S.T., et al. 2017), yet it remains a subject of debate within the medical community (Lee, K., et al. 2012). A major drawback of DITI is its limited ability to detect tumors located deep within breast tissue, as the method relies on measuring infrared radiation emitted from the skin surface—making deeper lesions harder to capture (FDA, 2019; UCHealth, 2022).

Additionally, there is currently no standardized protocol for image acquisition or software analysis, contributing to inconsistent results across different clinics and practitioners (JOCPR, 2018). Another significant concern is the high rate of false positives. Increased breast temperature, which thermography detects, is not exclusive to cancer and can stem from benign causes such as inflammation, infection, hormonal shifts, or recent

physical activity, potentially leading to unnecessary stress and further testing (Healthline, 2024). While certain small studies have reported strong detection rates, broader systematic reviews generally show DITI performs less effectively than mammography. For example, Kontos et al. evaluated DITI's accuracy in 63 patients with confirmed breast lesions—both benign and malignant—who had undergone biopsy or surgery. Their findings revealed a sensitivity of just 25% (Molina Healthcare, 2013; NZ Medical Journal, 2012) and a specificity of 85% (Kontos M. et al. 2011).

Contrast Enhanced Mammography (CEM)

Contrast-enhanced mammography (CEM) is an imaging method that employs X-rays, a dual-energy technique, and a standard iodine-based intravenous contrast agent to detect breast abnormalities by assessing both new blood vessel formation and the structural characteristics of lesions. As an advanced functional imaging approach, it integrates dual-energy digital mammography with contrast enhancement. Studies indicate that CEM offers higher sensitivity and specificity than conventional 2D mammography, and when compared to contrast-enhanced MRI (CE-MRI), it demonstrates comparable diagnostic performance, reduced costs, and a shorter examination time (Philps J. et al. 2019). In a study by Mokhtar and Mahmoud involving 60 women with suspected breast abnormalities identified via mammography or ultrasound, CEM showed a sensitivity of 97.7% and a specificity of 50%, leading the authors to conclude it is more effective than standard mammography, particularly in women with dense breast tissue (Mokhta O, & Mahmoud S. 2014).

Although CEM achieves sensitivity levels similar to MRI, its clinical use faces several limitations related to biology, diagnostics, technology, and safety. Like MRI, CEM images can be affected by Background Parenchymal Enhancement (BPE)—the normal enhancement of glandular breast tissue (Covington et al., 2024). Elevated BPE may obscure small tumors or result in false-positive interpretations, with potential influence from the patient's menstrual cycle (Tari, 2025). From a safety standpoint, CEM delivers a higher radiation dose—between 15% and 80% more—than standard 2D digital mammography (Moffa et al., 2023; Covington et al., 2024). Another concern is the risk of adverse reactions to the contrast agent. Since CEM requires an iodinated contrast medium, there is a small chance of allergic responses. While severe reactions such as anaphylaxis are very rare—occurring in approximately 0.002% of cases—the need for intravenous access and monitoring during contrast administration adds complexity to the procedure compared to routine mammography (Moffa et al., 2023; Covington et al., 2024). Furthermore, despite its high sensitivity—typically ranging from 89% to 97.7%—CEM is generally viewed as slightly less accurate than breast MRI in overall diagnostic performance, especially in identifying certain subtle or hidden lesions (Tari, 2025).

Scintimammography

Scintimammography is a functional imaging method that employs radioactive tracers, such as Technetium-99m sestamibi (99mTc-MIBI), to evaluate breast abnormalities initially identified through mammography. It is considered a forerunner to more advanced techniques like Breast-Specific Gamma Imaging (BSGI) and Molecular Breast Imaging (MBI). The tracer accumulates in breast tissue and emits gamma rays, which are captured by a

dedicated camera. The resulting images offer insights into both the structure and metabolic activity of the breast, aiding in cancer detection and providing clues about tumor aggressiveness. This approach may help monitor treatment response or serve as an alternative when conventional imaging—such as mammography—is inconclusive or when MRI cannot be used (Greene LR & Wilkinson D.2015; Berg WA.2016; American College of Radiology, 2016). It may also benefit women with dense breast tissue or those with breast implants (Berg WA, 2016, Mettler FA. Et al. 2008).

Despite these potential uses, the clinical role of scintimammography has diminished over time due to several technical and practical drawbacks. A major issue is its limited spatial resolution—typically around 7 to 10 mm—far lower than that of mammography (sub-millimeter) or MRI, making it less effective for identifying small lesions or microcalcifications (Barone et al., 2024). Another concern is the high rate of false positives, as the tracer can accumulate in benign conditions like fibroadenomas, fat necrosis, or inflammatory breast disease (mastitis). This non-specific uptake reduces its reliability in confirming or excluding cancer (Nawaz et al., 2023; Jadvar, 2024). Additionally, safety and logistical challenges arise from radiation exposure. Unlike MRI or ultrasound, scintimammography involves injecting a radiopharmaceutical, leading to systemic radiation. The overall radiation dose is generally higher than that of a standard mammogram, limiting its suitability for regular screening purposes (Barone et al., 2024; Nawaz et al., 2023).

Magnetic Resonance Elastography (MRE)

Magnetic Resonance Elastography (MRE) is an evolving imaging method that functions as a form of "virtual palpation," assessing tissue stiffness—specifically viscoelastic properties—by tracking the movement of shear waves through tissue. Although it holds strong potential for distinguishing benign from malignant breast lesions, integrating MRE into standard clinical breast imaging remains challenging. One major issue is the overlap in elasticity measurements between some soft malignant tumors, like mucinous or high-grade necrotic carcinomas, and harder benign conditions, such as dense fibroadenomas or localized fibrosis. This similarity in mechanical properties can lower the test's ability to accurately identify cancer, reducing its positive predictive value (BCBSM Medical Policy, 2026).

Additional challenges stem from practical workflow considerations. Routine breast MRI examinations typically last between 30 and 50 minutes, and incorporating MRE requires extra time and specialized equipment, such as pneumatic drivers or active transducers. This prolongs the scan, increasing the likelihood of patient discomfort and motion-related image distortions (PMC, 2026). Furthermore, there is currently no standardized framework for interpreting breast elastography results. In contrast to the widely adopted BI-RADS classification in mammography, breast MRE lacks a consistent stiffness threshold or uniform color-coding system for elastograms, contributing to variability in how different radiologists interpret the findings (BCBSM Medical Policy, 2026).

Acoustic Radiation Force Impulse (ARFI)

Acoustic Radiation Force Impulse (ARFI) imaging is a non-invasive elastography method that uses ultrasound to emit a focused, high-intensity "push pulse," generating shear waves within

tissue. As an emerging ultrasound-based technique, ARFI offers both quantitative and semi-quantitative assessments of tissue stiffness or strain in lesions (Jayaraman. et al. 2017). Research indicates that malignant tumors typically exhibit greater stiffness than benign ones, with corresponding differences in shear wave propagation (Baltzer PAT. et al. 2017; Jayaraman J. et al. 2017). For instance, Jayaraman et al. found that the average shear wave velocity in 34 benign lesions was 2.08 m/s, noticeably lower than the 6.28 m/s observed in 16 malignant samples. Although ARFI reduces operator dependency compared to manual strain elastography, it is not without technical and clinical challenges. One major limitation is the low Signal-to-Noise Ratio (SNR) in fatty breast tissue, where the push pulse is significantly weakened in breasts with high fat content (Taylor & Francis, 2025). This attenuation can result in failed measurements or unreliable SWV data. Additionally, certain benign conditions—such as focal fibrosis, prior scarring, or hyalinized fibroadenomas—can display stiffness levels similar to those of malignant.

Diffusion-Weighted Magnetic Resonance Imaging (DW-MRI) or Diffusion Weighted Imaging (DWI.)

In oncology, diffusion-weighted magnetic resonance imaging (DW-MRI), also known as diffusion-weighted imaging (DWI), serves as a valuable tool for improving the detection and biological assessment of breast tumors. DW-MRI helps distinguish benign from malignant lesions by measuring the apparent diffusion coefficient (ADC), which tends to be lower in malignant tissues (Chilla GS, et al. 2015; Partridge SC, et al. 2017). When used alongside contrast-enhanced MRI (CE-MRI), DW-MRI may help reduce false positive findings, potentially decreasing the need for unnecessary biopsies when evaluating suspicious lesions identified through conventional imaging (Partridge SC, et al. 2017). Bickel et al. conducted a retrospective analysis of ADC values from 170 primary malignant breast tumors to assess DW-MRI's ability to differentiate invasive breast cancer from ductal carcinoma in situ (DCIS), reporting a sensitivity of 78.06% and a specificity of 90.5% (Bickel H. et al. 2015).

Despite its utility as a non-contrast method for evaluating tissue cellularity in the breast, broader clinical adoption of DWI remains limited due to several technical and interpretive challenges. A major obstacle is the absence of standardized imaging protocols. Variations in key parameters such as b-values, echo times (TE), and repetition times (TR) across different MRI systems contribute to inconsistent ADC measurements (Lee et al., 2021). This variability prevents the establishment of a universal ADC threshold for distinguishing benign from malignant lesions, limiting the integration of DWI results into the BI-RADS classification system (Lee et al., 2021; Partridge & Amornisiripanitch, 2017). DWI is also prone to artifacts and often suffers from suboptimal image quality, which can mask small lesions or lead to diagnostic errors (Lee et al., 2021).

Certain benign conditions, including fibroadenomas and papillomas, may show low ADC values resembling those of cancers, increasing the risk of false positives (Mendez et al., 2022; Lo Gullo et al., 2024). While DWI performs well in characterizing enhancing masses, its effectiveness is reduced for non-mass enhancement (NME) lesions, where it frequently offers little added value over standard MRI (Lo Gullo et al., 2024). Additionally, standard DWI typically provides lower spatial resolution than dynamic contrast-enhanced (DCE) MRI, complicating the evaluation of very small abnormalities (Lo et al., 2024).

Ductoscopy and Ductal Ravage (DDL)

Ductoscopy combined with ductal lavage (DDL), also known as fiberoptic ductoscopy (FDS), enables direct examination of the mammary duct lining by inserting a thin scope through the nipple opening. In parallel, ductal lavage involves flushing the milk ducts to collect epithelial cells for cytological evaluation, primarily aiming to identify precancerous or cancerous changes in women at high risk for breast cancer. In a study by Liu et al. involving 1,048 women, the sensitivity of FDS alone was found to be 94.2%, while combining FDS with cytology increased sensitivity to 98.1% (Liu G.Y. et al 2008). Although DDL methods offer minimally invasive access to the breast duct system, they have not supplanted conventional imaging or biopsy techniques due to several drawbacks. While ductoscopy provides visual insight into the duct lumen, it is technically challenging and often yields inconsistent diagnostic results.

A major obstacle is the difficulty in successfully cannulating the duct, along with the absence of uniform standards for interpreting suspicious findings. Distinguishing benign papillomas from early intraductal cancers typically still requires surgical removal for definitive diagnosis (Bahl et al., 2015). Ductal lavage functions as a form of "liquid biopsy" by harvesting cells for cytological assessment, but its effectiveness in detecting breast cancer is limited by low sensitivity. It is more reliable in detecting high-risk cellular abnormalities than invasive cancer. False-negative results are common, as many tumors do not release sufficient cells into the lavage fluid. Technical issues such as low cell yield or inadequate sample volume are frequent—up to 25–40% of procedures fail to obtain enough epithelial cells for a conclusive analysis (Hery et al., 2011). Additionally, the method cannot pinpoint the location of abnormal cells within the breast, creating diagnostic uncertainty and complicating decisions about targeted biopsy or surgical intervention (Bahl et al., 2015; Khan et al., 2004). Despite being less invasive, the need for duct dilation and fluid infusion can cause discomfort and prolong the procedure compared to standard fine-needle aspiration, affecting patient tolerance.

Radomics

Over the past twenty years, medical image analysis has advanced rapidly, driven by major improvements in diagnostic imaging technologies, giving rise to the field of radiomics (Gillies RJ. et al. 2016). This approach focuses on extracting large amounts of quantitative data from one or more digital medical images, with applications in cancer detection, diagnosis, and outcome prediction (Valdora F. et al. 2018; Tran WT. et al. 2019; Conti A. et al. 2020). In breast cancer, radiomics features capture both morphological characteristics—such as tumor size, shape, intensity, and texture—and functional aspects like blood flow and cellular metabolism (Tran WT. et al. 2019; Crivelli P. et al. 2018). Radiomics shows promise not only for identifying breast tumors but also for characterizing them, predicting their behavior, assessing treatment response, and estimating recurrence risk, thereby supporting personalized patient care and monitoring. In 2017, Zhang et al. introduced a radiomics method using ultrasound imaging to distinguish between benign and malignant breast lesions. Their technique involved extracting high-throughput features from sonoelastograms to measure tumor shape, stiffness, and heterogeneity, followed by classification analysis. The method achieved a sensitivity of 85.7% and a specificity of 89.3% (Zhang Q. et al. 2017).

Despite its potential to act as a non-invasive "digital biopsy," radiomics still faces significant challenges that hinder its widespread adoption in clinical breast imaging. A major obstacle is the lack of standardization and the variability in data collection. Radiomic results are highly influenced by imaging acquisition parameters, and without consistent protocols for image normalization or voxel resampling, the same scan can yield different outcomes when processed by different software platforms (Li et al., 2024; MDPI, 2026). Although manual delineation of the Region of Interest (ROI) is considered the current gold standard, it is subject to variability between and within observers. This introduces segmentation bias, limits reproducibility, complicates interpretation, and poses difficulties in distinguishing between Luminal A and Luminal B subtypes of breast cancer (PMC, 2026).

Magnetic Resonance Imaging (MRI)

Breast MRI is a non-invasive method for detecting tumors and has demonstrated high sensitivity, significantly enhancing breast cancer screening for women at elevated risk (Gillies R.et al.2017; Mann. et al. 2015). In a prospective study by Schelfout et al., contrast-enhanced (CE)-MRI showed superior performance in identifying both ipsilateral and contra-lateral breast tumors compared to other imaging methods. The results indicated that CE-MRI detected 96% of multifocal and 95% of multicentric tumors, whereas mammography identified only 37% and 18%, and ultrasound 41% and 9%, respectively (K. et al. 2004).

MRI is widely regarded as the most sensitive imaging technique for breast cancer detection, with sensitivity rates ranging from 98% to 100%. However, its clinical application faces several challenges related to diagnosis, technology, and patient factors. A common issue is the detection of enhancing foci—areas that appear suspicious on imaging but turn out to be benign after biopsy. MRI often cannot reliably differentiate malignant lesions from benign conditions like fibroadenomas, leading to false positives, Schelfout overdiagnosis, increased recall rates, unnecessary biopsies, and added psychological burden (Chhetri et al., 2020; Eremici et al., 2024). Another drawback is its limited ability to detect microcalcifications. Unlike mammography, MRI does not effectively visualize these small calcium deposits, which hampers accurate diagnosis of Ductal Carcinoma in Situ (DCIS). From a public health standpoint, the infrastructure needed for MRI presents a significant barrier. The high cost of equipment and ongoing maintenance makes MRI approximately ten times more expensive than mammography, limiting its feasibility as a widespread screening tool. This cost factor further restricts its role in routine breast imaging. For example, a study by the UK Magnetic Resonance Imaging in Breast Screening group involving 279 women with a strong family history of breast cancer found that the additional cost per cancer detected in those with BRCA1 or BRCA2 mutations was £11,800 (Kriege M. et al., 2004).

Photon-counting Detector (PCD) Technology

Photon-counting detector (PCD) technology is making significant strides in breast cancer diagnosis by overcoming the traditional compromise between image clarity and radiation exposure. Unlike conventional energy-integrating detectors (EIDs), PCDs convert X-ray photons directly into electrical signals and categorize them based on their energy levels. This capability delivers enhanced spatial resolution—typically around 0.16–0.2 mm^2—and

improved contrast resolution, enabling more sensitive detection of small lesions, microcalcifications, and subtle structural abnormalities that may go unnoticed with standard mammography or tomosynthesis.

Early research indicates that photon-counting breast CT (PC-BCT) identifies suspicious masses in about 85% of cases detected by MRI, with strong agreement in tumor size measurements (Aunt Minnie Europe, 2026). In comparative studies, images obtained with photon-counting systems were rated as equally or more clearly visible than those from conventional systems in 94% of cases (PubMed, 2025).

Additionally, because PCDs reduce electronic noise and utilize X-ray photons more efficiently, they can produce high-quality diagnostic images at significantly lower Average Glandular Dose (AGD) levels. Clinical studies have demonstrated dose reductions of 45–60% compared to EID systems without sacrificing image quality (AJR, 2024), a crucial advantage for routine screening safety. Another key benefit of PCDs is their ability to sort photons into distinct energy bins, supporting spectral or multi-energy imaging. This feature improves the ability to distinguish iodine uptake in tumors from dense breast tissue without requiring multiple scans. Quantitative analysis of iodine distribution offers accurate cancer staging and restaging, with performance approaching that of MRI (AuntMinnieEurope, 2026).

Limitations of Different Imaging Modalities

The constraints and limitations on different imaging modalities (for breast cancer screening and diagnosis) serve as a focus for (doctorate) research into 3D Photon-Counting Detector (PCD-CT) Technology. The limitations offer a strong rationale for exploring PCD-CT as a promising alternative. In PhD research, the focus will center on a comparative evaluation of Photon-Counting Detectors and conventional Integrating Energy Detectors (used in Cone Beam Breast CT), particularly assessing differences in diagnostic accuracy and radiation dose.

Characteristics of Cancers Detected by Breast Imaging

Cancers detected through screening tend to have a better prognosis than those found outside of screening programs, regardless of tumor size, stage, or lymph node involvement. This difference may reflect inherent biological characteristics—screen-detected cancers are often slower-growing and less likely to spread aggressively. Screening is more likely to identify indolent tumors, while faster-growing cancers typically emerge between scheduled screenings. A 10-year Finnish study of 1,983 women with invasive breast cancer showed that detection method is an independent predictor of outcome. Even after adjusting for age, tumor size, and nodal status, screen-detected cases had lower relapse rates and improved survival. Women whose cancers were diagnosed outside screening faced a nearly twofold higher risk of death (HR 1.90; 95% CI, 1.15–3.11), despite being more likely to receive adjuvant treatment (Joensuu et al., 2004).

Similar results emerged from an analysis of three major randomized trials—the Health Insurance Plan, NBSS-1, and NBSS-2—which found that screened patients had better outcomes even when accounting for stage, node status, and tumor size. Compared to screen-detected cancers, the risk of death was 1.53 times higher (95% CI, 1.17–2.00) for

interval or incident cancers and 1.36 times higher (95% CI, 1.10–1.68) for those in control groups (Wishart et al., 2008). Another study of 5,604 English women diagnosed between 1998 and 2003 confirmed these findings: after adjusting for tumor grade, size, nodal status, and age, screen-detected cases still showed superior survival, with a hazard ratio of 0.79 (95% CI, 0.63–0.99) for symptomatic cases (Joensuu et al., 2004; Wishart et al., 2008). These patterns support the idea that some screen-detected cancers are low-risk and may represent overdiagnosis.

Assessment of Screening Performance and Diagnostics Accuracy

Evaluating the performance of breast screening programs involves standardized metrics that assess both initial screening effectiveness and the precision of follow-up diagnostics. According to the American College of Radiology's BI-RADS system, monitoring these measures is essential for quality control and improving patient care (Newell et al., 2025). Comprehensive evaluation typically includes input, process, and outcome indicators (Frontiers, 2025).

Sensitivity

Mammography remains the primary tool for breast cancer screening (DeAngelis & Fontanarosa, 2010). Its sensitivity—the proportion of actual cancers correctly identified—averages around 79%, but varies based on tumor characteristics, breast density, patient age, hormonal factors, imaging quality, and radiologist expertise. It tends to be lower in younger women and those with dense breasts (36–38%).

Diagnostic Accuracy of Imaging Modalities

Accuracy is defined by the modality's ability to correctly identify both malignant (sensitivity) and benign (specificity) findings. Diagnostic accuracy in breast cancer imaging varies significantly across different imaging and biopsy modalities. While digital mammography remains the screening standard, newer technologies like Digital Breast Tomosynthesis, Magnetic Resonance Imaging, Photon-Counting Detector and Artificial Intelligent are redefining accuracy benchmarks (Sprague et al., 2023; PMC, 2026).

Specificity and False-positive Rate

Specificity measures how well a test identifies healthy tissue, directly influencing the false-positive rate (FPR = 1 – specificity). High specificity is key to reducing harms like anxiety, unnecessary radiation exposure, and benign biopsies. Breast density is the most influential factor. In dense tissue (BI-RADS C and D), overlapping structures can mimic tumors, increasing false positives result. Specificity reaches about 98% in fatty breasts (BI-RADS A) but drops notably in extremely dense tissue (UCLA Health, 2026). Over time, repeated screening increases the chance of a false alarm—women undergoing annual exams from age 40 have a 50% to 61% cumulative risk of at least one false-positive recall over a decade (Annals of Internal Medicine, 2026).

Recent clinical data emphasizes that while newer technologies improve detection, they often come with a trade-off in specificity. Breast density remains the most significant biological factor affecting specificity. In dense breast tissue (BI-RADS C and D), the overlapping of fibroglandular tissue can mimic a lesion, leading to a ‘‘summation’’false positive. A 2026 cohort study indicated that specificity remains highest in ‘‘fatty’’ breast (BI-RADS A) at approximately 98%, while dropping significantly in ‘‘extremely dense’’ breasts (UCLA Health, 2026).

For patients undergoing regular screening, the statistical likehood of a false positive increases over time. Women who start annual screening at age 40 and continue for 10 years have a 50% to 61% cumulative risk of at least one false-positive recall (Annals of Internal Medicine, 2026).

Recall Rate

This refers to the proportion of screening exams requiring additional imaging or diagnostic follow-up. It serves as a key indicator of program efficiency, balancing early detection against unnecessary procedures and patient stress (Grabler et al., 2017). While ideal recall rates are generally considered to be between 5% and 12%, recent studies report rates as high as 30.6% (ResearchGate, 2026). Women with extremely dense breasts face significantly higher recall rates—up to 14%–16%—even with advanced imaging (ResearchGate, 2026).

Cancer Detection Rate (CDR)

CDR measures the number of cancers found per 1,000 screenings and is a core indicator of screening effectiveness. As of 2026, the adoption of Photon Counting Detector 3D imaging and AI tools has boosted detection rates compared to traditional 2D mammography. Recent data show CDRs near 12.3 per 1,000 in certain populations (Lowry et al., 2020; Yoon et al., 2023; Sprague et al., 2023; ResearchGate, 2026). For women with dense breasts, MRI remains the most effective method, with an odds ratio of 4.16 for cancer detection compared to other modalities (PMC, 2026).

Interval Cancers

Interval cancers refer to tumors diagnosed between 12 and 24 months following a screening that showed no abnormalities. The reported incidence is 5.4 cases per 1,000 screenings (ResearchGate, 2026). Research indicates these cancers are more commonly found in women under 50 and tend to exhibit mucinous or lobular subtypes, high histological grade, and strong cell proliferation, despite appearing relatively benign on mammograms and lacking calcifications. In contrast, cancers detected through screening are typically tubular in histology, smaller, at an earlier stage, hormone receptor-positive, and often include a significant component of ductal carcinoma in situ (Porter PL. et al., 2020). Overall, interval cancers often display features associated with aggressive growth (Porter PL. et al., 2020), are usually identified at a more advanced stage, and are linked to worse outcomes (Niraula S. et al., 2020).

Diagnostic Resolution Rate (DRR)

DRR has recently emerged as a key quality measure in breast cancer screening, shifting focus from traditional indicators such as "screening uptake" to evaluate the overall efficiency of the diagnostic process. Unlike conventional metrics that assess test accuracy at a single moment, DRR tracks how quickly and consistently patients with inconclusive (BI-RADS 0) or suspicious (BI-RADS 4/5) findings receive a definitive diagnosis—either benign or malignant—within a set period, usually 60 to 90 days (AJMC, 2026). It reflects a program's ability to guide patients through to conclusive clinical outcomes. A high DRR suggests effective follow-up systems, while a low rate signals gaps in care where patients fall through the cracks (AJMC, 2026). In this way, DRR serves as a critical safety net for diagnostic reliability. Even with advanced imaging technologies like Photon-Counting CT, diagnostic value is undermined if patients do not complete the pathway to a final assessment.

Effectiveness of Population-Based Screening Programs

The success of population-wide breast cancer screening is evaluated based on its capacity to lower mortality by detecting cancer early, while also considering potential downsides such as overdiagnosis and false-positive results (Soren R. et al. 2022). As of 2026, major health organizations including the World Health Organization (WHO) and the American College of Radiology (ACR) maintain that structured screening programs are among the most impactful public health strategies for reducing deaths from cancer. The main objective of these programs is to detect cancers earlier, when treatment is more effective, rather than at advanced stages. Nations with well-established screening systems have seen a 40% decline in late-stage diagnoses between the 1980s and 2020s (WHO 2026). Research models indicate that biennial screening for women aged 50 to 74 is effective, but switching to annual screenings beginning at age 40 could prevent an estimated 10,000 additional deaths annually in the United States (ACR/SBI, 2026).

Radiologist Experience in Interpretation of Breast Imaging Results

The accuracy of breast imaging interpretation varies considerably and is strongly shaped by a radiologist's experience, the number of cases they review annually, and their level of sub-specialization. In this field, clinical judgment and advanced technology intersect, making the radiologist's role pivotal. Skilled radiologists draw on patient history, prior imaging, and nuanced visual patterns to support critical diagnostic decisions. Although innovations such as artificial intelligence, photon-counting detector (PCD) technology, and MRI are transforming the field, human expertise—particularly in terms of reading volume and specialized training—remains central to diagnostic effectiveness.

A high annual interpretive volume is one of the most reliable indicators of diagnostic precision. Radiologists who interpret more than 2,000 mammograms per year tend to show greater sensitivity in cancer detection (Barlow et al., 2004; Miglioretti et al., 2007). This higher volume is also associated with improved positive predictive value (PPV), meaning a larger proportion of their biopsy recommendations lead to confirmed cancer diagnoses (Coldman et al., 2006).

Additionally, a radiologist's training path significantly influences their performance trajectory. Those who complete a dedicated breast imaging fellowship typically begin practice at a high level of proficiency, avoiding the steep learning curve often seen among general radiologists (Miglioretti et al., 2009). In contrast, non-specialized radiologists usually show the most notable improvements in interpretation—especially in reducing false positives—during their first three years of practice. Overall, breast imaging specialists tend to achieve higher cancer detection rates and better diagnostic sensitivity than their generalist counterparts (Miglioretti et al., 2007; Wong et al., 2023).

The emergence of photon-counting detector technology represents a major advancement in breast imaging, enhancing the tools available to radiologists. A key benefit for interpreters is the improved contrast resolution and spatial detail provided by PCD systems. As with any new modality, radiologists' ability to interpret PCD imaging effectively is expected to grow through experience, particularly when findings are reviewed alongside clinical and pathological data (Miglioretti et al., 2015).

AIMS AND OBJECTIVES

With the availability of documented evidences, the aims of this study are to evaluate the clinical, psychological, and diagnostic outcomes following recall after routine breast screening. The following research questions were addressed:

1. Among women recalled after screening mammography, what outcome occurs during diagnostic assessment and follow up?
2. Does integrating Photon-Counting Detector Technology in Breast Imaging improves diagnostic accuracy, improves the detection of microcalcification and reduces unnecessary recall after breast screening?

MATERIALS AND METHODS

Eligibility Criteria and Study Selection

Studies were included in the systematic review if they meet the following criteria:

1. The population included women aged 40 years and above undergoing routine breast screening and recalled for further assessment.
2. Cohort studies, Observational studies of pre-specified harms, Diagnostic accuracy studies, Clinical audit studies and Screening programme evaluations for the benefits and harms.
3. Included studies that were most clinically relevant to practice which was determined by practice setting, population, date of publication, and use of technologies and therapies in current practice.
4. Included evidence for the benefits and harms of breast cancer screening

Studies were excluded if they contain:

1. Case reports

2. Animal studies
3. Editorials report
4. Non-screening population

Principle Source of Information and Search Strategy

A computerized search strategy was conducted using the following principle source of information and database:

1. European Journal of Public Health
2. European Journal of Surgical Oncology
3. Journal of Breast Imaging
4. Korean Journal of Radiology
5. Canadian Journal of Health Technology
6. Journal of Clinical Medicine
7. American Journal of Roentgenology
8. British Journal of Radiology
9. Data from PubMed, Google Scholar, etc.

Data Extraction and Quality Assessments

Information on study design, patient characteristics, screening methods, interventions, analytical approaches, follow-up procedures, and outcomes was extracted from an online database search. The quality of this review was assessed competently, reviewed and evaluated by (Ugochukwu O. Maluze).

For a structural evaluation, a validated appraisal QUADAS-2 tools was used to assess the risk of bias (internal validity) and Applicability (external validity). The quality was based on the studies observed from the articles evaluating the diagnostic accuracy and the outcomes of assessment pathways for women recalled after routine breast screening.

Diagnostic accuracy and screening outcomes were evaluated using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool. To assess the strength of evidence regarding benefits and harms, criteria from the U.S. Preventive Services Task Force were applied, categorizing studies as providing strong, moderate, or limited evidence. Overall, the quality of the review is rated as moderate, with a final quality score of 62%.

Type of Participants

The study included women aged 40 and older who were undergoing routine breast screening and were called back for additional assessment. Participants were drawn from cohort studies, diagnostic accuracy studies, observational studies, clinical audit studies, and research evaluating screening programs. To maintain consistency, only studies conducted in Norway, Spain, Denmark, the United Kingdom, the Netherlands, Canada, and the United

States, etc. were considered, ensuring alignment with findings from prior research by other investigators. When results from these studies align with those involving the same age group in population-based screening, they support broader generalizability.

Levels of Evidence for the Selected Studies

- Strong Evidence +++
- Moderate Evidence ++
- Limited Evidence +

Ethical Consideration

No ethical approval was needed for the systematic review, as it was not required. The review included only published studies that met the predefined inclusion and eligibility criteria. Participant clinical information was anonymized across all selected studies.

Searched Words

The following searched key words was used in this review; ‘‘Breast cancer screening, Imaging modalities, risk factors for breast cancer, Overdiagnosis, False Positive, etc.

RESULTS/FINDINGS

Study Selection

The initial electronic search identified 326 articles. After applying the inclusion and eligibility criteria, only 58 studies were selected for this systematic review. Among these, two observational studies reported false positive results in women who underwent screening. Over-diagnosis rates in the screened population were examined in three randomized controlled trials and thirteen case-control studies. Twenty-five Cohort studies focused on outcomes related to anxiety and distress. Five studies explored the link between pain and screening outcomes in women. Seven randomized controlled trials were designed as interventions to reduce pain associated with mammography. Additionally, three observational studies assessed radiation exposure linked to various imaging techniques.

Description of Studies

The studies included in this systematic review are summarized in Tables 1 through 3. Table 1 presents a comparison between false positive results and normal results from screening. Table 2 outlines the study designs and the instruments used to assess clinical and psychological outcomes linked to screening. These studies were carried out in several countries, including Norway, Spain, Denmark, the United Kingdom, Canada, the United States, and the Netherlands. Table 3 provides a summary of the evidence on screening outcomes across the various studies, along with their respective limitations. Table 4 details

the assessment tools based on the QUADAS-2 framework. All studies followed a population-based approach. Most were conducted in Norway, Spain, Denmark, the United Kingdom, the United States, and the Netherlands to ensure consistency between their findings on diagnostic accuracy and screening outcomes and those reported in earlier research by other authors.

False Positive Mammography Results

Table 1 presents a comparison of screening outcomes between women who received false-positive results and those with normal results. Table 2 outlines the study design and the instruments used to assess clinical and psychological outcomes linked to screening, while Table 3 compiles evidence on screening outcomes from various studies.

Data from two observational studies, based on a large U.S. population breast cancer surveillance database (Hubbard RA et al., 2011; Kerlikowske K et al., 2013), estimated the 10-year cumulative probability of false-positive results with film and digital mammography. When screening started at age 40, nearly half (49%) of women experienced at least one false-positive result over a decade. Among those beginning screening between ages 40 and 49, the 10-year cumulative rate of biopsy due to a false-positive result reached 56% with annual screening. In contrast, for women starting at age 50 or older, the 10-year biopsy recommendation rate was 6% (95% CI: 6%–7%) with annual screening and 9% (95% CI: 7%–12%) with biennial screening. Further analysis showed that among women aged 40–49, those with extremely dense breasts or using combination hormone therapy had the highest false-positive rates—65.5% and 65.8%, respectively (Kerlikowske K et al., 2013). For women aged 50–70 with fibroglandular density undergoing biennial or triennial screening, false-positive rates were lower, at 39.7% and 21.9%.

A separate prospective cohort study on community-based screening found that annual screening led to a higher proportion of women experiencing at least one false-positive result over 10 years compared to biennial screening, regardless of breast density. The cumulative likelihood of a false-positive result was 7.4% (95% CI: 6.4%–8.5%) after the first mammogram, rising to 26.0% (95% CI: 24.0%–28.2%) by the fifth, and 43.1% (95% CI: 36.6%–53.6%) by the ninth. Among women in their 40s with scattered fibroglandular density, the 10-year rates were 68.9% with annual screening versus 46.3% with biennial. For women aged 50–74 in the same density group, the rates were 49.8% and 30.7%, respectively (Christiansen CL et al., 2000; Kerlikowske K et al., 2013).

The overall cumulative risk of a false-positive result was influenced by four patient-related factors—younger age, more prior breast biopsies, family history of breast cancer, and current estrogen use—and three radiology-related factors: longer intervals between screenings, failure to compare current and prior mammograms, and individual radiologists' tendencies to interpret findings as abnormal. Of these, the radiologist's individual interpretation style was the most significant contributor to false-positive results

Over Diagnosis

Overdiagnosis happens when screening identifies cancers that would never have caused symptoms or posed a health risk without screening. This is a significant concern because,

while detecting such cancers offers no benefit to the individual, the processes involved in diagnosis and treatment can lead to substantial harm. One way to estimate overdiagnosis is by comparing breast cancer rates in populations that undergo screening with those that do not. However, such comparisons can be influenced by differences between groups, including time periods, geographic location, lifestyle factors, and hormone use. A common method for calculating overdiagnosis is the excess incidence approach, which measures the ongoing difference in cancer rates between screened and unscreened groups, divided by the number of cancers found through screening.

Findings from 29 randomized studies in Denmark indicated overdiagnosis rates of 14% to 39% in screened populations (Jørgensen KJ. et al., 2017). In the Netherlands, a population-based cohort study suggested that roughly half of all screen-detected breast cancers, including ductal carcinoma in situ (DCIS), may be cases of overdiagnosis—results that align with other research pointing to high levels of overdiagnosis linked to screening (Autier P., 2017). In the United States, a cross-country analysis found that higher use of mammography screening correlated with increased rates of overdiagnosis (Harding C. et al., 2015).

The Canadian National Breast Screening Study, a randomized trial, also provided insights into overdiagnosis. After five rounds of screening, 142 more invasive breast cancers were diagnosed in the mammography group than in the control group (Miller AB. et al., 2014; Marmot MG. et al., 2013). By the 15-year mark, this excess had decreased to 106 additional cases in the screened group, translating to an overdiagnosis rate of 22% among the 484 invasive cancers detected by screening. With 25 years of follow-up, the study revised its estimates by age: about 30% of screen-detected invasive cancers in women aged 40–49 and up to 20% in those aged 50–59 were deemed overdiagnosed. When DCIS cases were included, the figures rose to 40% for women 40–49 and 30% for those 50–59. These calculations again used the excess incidence method.

A systematic review that analyzed 13 observational studies reported unadjusted overdiagnosis rates ranging from 0% to 54%, while adjusted estimates from six of those studies fell between 1% and 10% (Puliti D. et al., 2015). More reliable distinctions between early detection and overdiagnosis come from three randomized comparison studies—the Malmö I trial and two Canadian NBSS trials—with long-term follow-up (Marmot MG. et al., 2013; Independent UK Panel on Breast Cancer Screening, 2012). The Malmö I trial considered all breast cancer cases, whereas the Canadian studies focused only on screen-detected ones. By comparing the overall incidence of breast cancer (including both invasive and DCIS) in screened versus unscreened groups, researchers estimated overdiagnosis at 10.7% (95% CI: 9.3%–12.2%) when limited to the screening period, and 19.0% (95% CI: 15.2%–22.7%) when including cases diagnosed during both screening and follow-up.

Anxiety, Distress, Psychological response and Pains during Screening Procedures

Ten observational studies (Gibson CJ. et al. 2009; Keyzer-Dekker CM. et al. 2012; Brodersen J. & Siersma VD. 2013; Tosteson AN. et al. 2014; Espasa R. et al. 2012; Schou Bredal I. et al. 2013; Hafslund B. et al. 2012; Fitzpatrick P. et al. 2011; Klompenhouwer EG. et al. 2014; Maxwell AJ. et al. 2013) (Table 2) were published alongside four systematic reviews studies (Brett J. et al. 2005; Brewer NT. et al. 2007; Hafslund B. & Nortvedt MW. 2009; Bond M. et

al. 2013) (Table 2). The systematic reviews showed that women who received clear notification of a negative mammogram result generally experienced low levels of anxiety. In contrast, those called back for further evaluation reported higher levels of anxiety, distress, and concerns specifically related to breast cancer (Brett J. et al. 2005; Hafslund B. & Nortvedt MW. 2009; Hislop TG. et al. 2002; Brett J. & Austoker J. 2001). Among studies examining repeat screening attendance, two found that women with false-positive results were less likely to return for subsequent screenings (Brett J. & Austoker J. 2001; McCann J. et al. 2002).

A telephone survey of 308 women conducted three months after screening found that roughly a quarter of the 68 women recalled for additional tests still felt ongoing worry affecting their mood or daily life, despite cancer having been ruled out (Lerman C. et al. 1991). A 2002 Spanish cohort study observed short-term psychological effects following a false-positive mammogram, though these typically faded within months (Sandin B. et al. 2002). However, a Danish cohort study from 2013 identified lasting psychological impacts several years after a false-positive result.

Two systematic reviews—incorporating Five observational studies and 7 randomized controlled trials—examined pain associated with screening mammography and strategies to reduce it (Armstrong K. et al. 2007; Whelehan P. et al. 2013; Miller D. et al. 2008) (Table 3, available at www.annals.org). Findings indicated that reports of pain during the procedure varied widely, ranging from 1% to 77% of women, although most did not view it as a barrier to future participation (Armstrong K. et al. 2007). Still, five studies noted that between 11% and 46% of women expressed reluctance to undergo screening again (Whelehan P. et al. 2013).

Interventions aimed at reducing discomfort during mammography (Miller D. et al. 2008) showed that offering verbal or written information helped lower pain, discomfort, stress, and anxiety (Alimoglu E. et al. 2004; Shrestha S. & Poulos A. 2001).

Radiation Exposure

The primary risk factors for radiation-related breast cancer are exposure at a young age and the radiation dose received. However, a small number of women have an inherited sensitivity to radiation damage and should avoid exposure regardless of age (Swift M. et al. 1991). For most women over 40, the advantages of regular mammography screening generally exceed the potential harms. A standard two-view screening mammogram delivers an average of 4 mSv to the breasts and 0.29 mSv to the whole body (Suleiman OH. et al. 1999). This level of exposure could lead to approximately one radiation-induced breast cancer per 1,000 women who undergo yearly mammograms from age 40 to 80. The risk doubles for women with larger breasts, who require higher radiation doses, and for those with breast implants, who often need extra imaging views. Shifting from annual screening starting at 40 to biennial screening beginning at 50 can reduce the incidence of radiation-induced cancers by a factor of five (Miglioretti DL. et al. 2016).

Two modeling studies have estimated radiation exposure, associated breast cancer cases, and mortality (Hendrick RE, 2010; Yaffe MJ. & Mainprize JG. 2011; Dai X. et al. 2016). One model projected that radiation-induced deaths from a single digital mammogram could range from 2 per 100,000 women aged 50–59 undergoing biennial

screening to 11 per 100,000 among those aged 40–59 receiving annual screening (Semenza GI. Et al. 2015).

However, a diagnostic study assessed as having high risk of bias and low applicability across all QUADAS-2 domains (Table 4) is considered of very low quality. The findings are likely highly unreliable, potentially generating misleading results, including an invalid estimate of the false positive rate, making them unsuitable for clinical use.

Table 1: Screening outcomes in Women with False Positive (FP) result vs. Normal results (NR)

Screening re-attendance	Anxiety	Depression	Breast Cancer-Specific Worry/Distress	Quality Rating
2 studies: Lower with FP results. One study: Higher with FP.	2 studies: No difference.	2 studies: No difference	3 studies: Higher with FP result.	Good
United States: 5 studies: lower with FP result (RR 1.07, 95% Cl, 1.02 – 1.12).	4 studies: Higher with FP results. 4 studies: No differences	1 study: Lower with FP result	4 studies: Higher with FP results. 3 studies: No differences.	Fair
Canada: 2 studies: lower with NR (RR 0.63, Cl 0.5-0.8)	Not reported	Not reported	Not reported	Not reported
Europe: 5 studies: No differences (RR 0.97, 95% Cl 0.93 – 1.01)	Not reported	Not reported	Not reported	Not reported

NN = Normal Result, FP = False Positive, RR = Relative Risk, CI = Confidence Interval

Table 2: Results of New Studies of Psychological effect on Brest Cancer Screening.

Author, Year (Reference)	Study Design	Population	Comparisons (No of Participants)	Measures
Schou Bredal et al. 2013	Case-control	Women recalled in a screening program in Norway	A:FP: At recall (640) B:NR: 4 wk later	HADS (scores ≥11).
Espasa et al. 2012.	Case-control	Screening population program in Spain.	A:FP: (100) B:NR: (50).	HADS, structured interview.
Brodersen & Siersma.	Nested case-control.	Screening programs in Denmark.	A: FP (272) B: NR (864) C: TP (174)	
Fitzpatrick et al. 2011	Retrospective cohort	Screening population program in the United Kingdom	A:FP: (9746) B:NR: (148589)	Reattendance
Gibson et al. 2009	Prospective cohort studies	New-Hampshire Mammography and the NHWH study	A:FP: (2017) B:NR: (11;384)	WHO
Hafslund et al. 2012.	Nested case-control studies	Screening program in Norway	A:FP: (128) B:NR: (195)	SF-36, HADS
Keyzer-Dekker et al. 2012	Prospective cohort studies	Women with abnormal results in the Netherlands.	A: First screen recalls (186). B: Repeated screen recalls (296).	STAI, CES-D, WHOQOL.
Klompenhouwer et al. 2014	Retrospective cohort	Screening program in the Netherlands.	A: Normal screen 9373,474). B. First screen recalls (6672). Repeated screen recalls for different lesion (161). D: Repeated screen recalls for same lesions	Reattendance

Maxwell et al. 2013.	Retrospective cohort	Screening program in the United Kingdom	First screening: A; Open biopsy (110). Needled biopsy sampling (1052). C: No tissue sampling (4009).	Re-attedance

HADs = Hospital anxiety and depression scale, FP = False Positive, NR = Normal Results, TP = True Positive, NHWH = New Hampshire Women for Health. STAI = State Trait Anxiety Inventory, CES-D = Centre for Epidemiologic Studies Depression Scale, WHOQL = World Health Organisation Quality of Life.

Table 3: Summary of Evidence of the screening outcomes of different studies

Primary Findings from Previous USPSTF Reviews	Number and Type of Studies	Overall Quality	Limitations	Summary of Findings	Ratings
False-positive and false-negative results. Younger women had higher rates of false-positive mammography results per screening cycle. Cumulative 10-years rates for false-positive mammography results were 49% overall and 56% for ages 40-49 y; cumulative 10-y rate of biopsies due to false-postive mammography results was 19%	Two observational studies of women screened in the United State.	Low	Not all risk factors were examined	10-y cumulative rates of false-positive mammography results and biopsies were higher with annual vs. biennial screening (61% vs. 42% and 7% vs. 5%, and for women with heterogeneously or extremely dense breasts, those aged 40-49 y, and those using combination of hormonal therapy.	Limited Evidence (+)
Overdiagnosis Estimates of overdiagnosis ranged from 0% to 50%.	1 meta-analysis of 3 RCT; 1 systematic review of 13 studies.	Low	No established definition or methods to determine over-diagnosis; Studies were highly heterogenous, and estimates varied depending on the analytical approach.	Estimates of over-diagnosis ranged from 0% to 54% overall and from 11% to 22% in randomized trials.	Limited Evidence (+)
Anxiety and distress Many women have anxiety with mammography, but it is generally transiet and is not a deterrent to future screening.	2 systematic reviews of 25 Cohort studies.	Moderate	Studies used different outcome measures and thresholds; effects based on age, risk factors, and screening intervals were not determined.	Women with false-positive results had more anxiety, distress, and breast cancer-specific worry than those with negative results, particularly those who had biopsies, fine- needle aspirations, and early recall. Distress was persistent for some women, but in some women, distress was inconsistent. Some women with false positive results did not return for screening.	Moderate Evidence (++)
Pains Many women have pain with mammography,	1 systematic review of 5	High	Studies used different outcome measures and	Although many women had pain during mammography (which ranges from 1% to	Strong Evidence (+++)

but it is generally inconsistent and it is not a deterrent to future screening. Pain could be reduced by providing helpful information and advice to patients.	observational studies. 1 systematic review of 7 RCT (interventional studies) to reduce pain).		thresholds; effects based on age, risk factors, and screening intervals were not determined	77%), but the proportion of those experiencing pain who did not attend future screening varied (11% to 46%).	
Radiation exposure	3 observational studies	Moderate	Not stated	Two view Screening mammography exposes the breast to a mean dose of 4 mSv and the whole body to 0.29 mSv. Breast cancer may be induced per 1,000 women undergoing annual mammograms from ages 40 to 80 years. Such risk is doubled in women with large breasts who require increased radiation doses and in women who required additional views. For women who begin biennial screening at age 50 years rather than annually at 40 years, radiation-induced breast cancers may be reduced five fold.	Moderate (++)

Table 4: QUADAS-2 Framework Assessment Tools

Screening Assessment Outcomes	Patient Selection (Bias issue)	Patient Selection (Applicability concern)	Index Test (Bias issue)	Index Test (Applicability concern)	Ref. Standard (Bias issue)	Ref. Standard (Applicability concern)	Flow & Timing (Bias issue)	Overall Quality of the study.
False Positive Results	High	Low	High	Low	High	Low	High	Low quality
Over-diagnosis	High	Low	High	Low	High	Moderate	High	Low quality
Anxiety & Distress	High	Low	Low	Low	Low	Low	High	Moderate quality
Pain	Low	Moderate	Low	Moderate	Low	Low	Moderate	High quality
Radiation Exposure	High	High	Low	Low	Moderate	Low	High	Moderate quality

DISCUSSION

A summary of the evidence is provided in Table 3. Two large observational studies of women screened in the Breast Cancer Surveillance Consortium provided limited quality evidence about cumulative rates of false-positive mammography results and biopsies over 10 years. In these studies, rates of false positive results were higher with annual than biennial screening (mammography, 61% vs. 42%; biopsy, 7% vs. 5%). The rates was also higher among women with heterogeneously or extremely dense breasts, those aged 40 to 49 years, and those using combination hormone therapy. Another observational study described false-positive results with the use of tomosynthesis. This evidence is limited by the lack of

randomized trials, uncertainty about the comparability of comparison groups, and differences in outcome measures.

However, a U.S. study comparing tomosynthesis and mammography versus mammography alone reported a significant reduction of 16 recalls but an increase of 1.3 biopsies per 1000 women. This evidence is limited by the lack of randomized trials, uncertainty about the comparability of comparison groups, and differences in outcome measures on the number, quality, and applicability of studies varied widely, and studies were observational. These results are consistent with those of an earlier study indicating cumulative 10-year rates of false-positive mammography results of 49% overall and as well 56% for women aged 40 to 49 years, with an overall biopsy rate of 19% (Mazzocco K. et al. 2019). In low and middle income countries, the results of these studies can be used to inform women of the likelihood of false-positive results with mammography screening.

Despite much research, the evidence for determining over-diagnosis is limited. There is no consensus definition of overdiagnosis, and there are no criteria on which to base critical appraisal on the studies. Studies are highly heterogeneous, and estimates vary depending on the analytic approach. The biased estimates were derived from three Randomized Control Trials and thirteen Case Control that shows the rate of overdiagnosis between 11% to 22% and from 0% to 54% respectively. Women who are overdiagnosed can be harmed by unnecessary procedures and treatments and by the burden of receiving a cancer diagnosis. The primary concern with overdiagnosis is the subsequent overtreatment. Because doctors currently lacks a definitive way to distinguish between a ‘‘harmless’’ cancer and a ‘‘lethal’’ one at the point of diagnosis, almost all detected cancers are treated. This can lead to physical morbidity (unnecessary surgery, radiation, chemotherapy), Psychological burden and Economic cost (increased healthcare spending on procedures that do not improve life expectance). The introduction of technology capable of detecting even smaller suspicious lesions may also lead to increased overdiagnosis. Understanding the concept of overdiagnosis is important to appropriately inform women about the benefits and harms of screening despite current limitations in determining its effect on individual women.

In studies assessing the anxiety and distress on breast screening mammography outcomes, twenty five studies supported the findings with a moderate level of evidence. In such studies, the reference standard applicability concern is considered low, the study uses validated tools (such as the Hospital Anxiety and Depression, etc.) to measure psychological impacts. In general, women with false-positive results have more anxiety and distress than those with normal results. Anxiety lessens over time for most women but persists for others, and some women with false-positive results do not attend subsequent screenings.

Five observational studies and Seven Randomize Control Trial are supported with strong level of evidence on the outcome of pains after mammograms population screening. Although women that attended mammography experienced pain, the proportion of those who do not attend subsequent screenings varies. Studies indicated that women that experienced false positive results and pains during mammography differ widely. Effort to minimize false positive results in breast cancer screening for many women focused on a combination of advanced imaging modalities and improved communication strategies to ensure that patients continue their screening regimens despite the anxiety caused by recalls.

The harms of radiation exposure from mammography screening are based on only three modeling studies with moderate quality evidence. Thus, up to one breast cancer may be induced per 1,000 women undergoing annual mammograms from ages 40 to 80 years. Such risk is doubled in women with large breasts who require increased radiation doses and in women with breast augmentation who require additional views. Radiation-induced breast cancers may be reduced fivefold for women who begin biennial screening at age 50 years rather than annually at age 40 years (Miglioretti DL. Et al. 2016). The number of deaths due to radiation-induced cancer from screening with digital mammography was estimated to be 2 to 11 per 100 000 women, depending on age and screening intervals. Reducing radiation exposure through more effective imaging modality is an important area of future research. As of 2026, there is a notable absence of published randomized controlled trials (RCTs) directly comparing the diagnostic accuracy and radiation dose of dedicated Photon-Counting Detector CT (PCD-CT) and Cone Bean Breast CT (CBBCT).

To address the two research questions above. Firstly, among women recalled after screening mammography, the outcomes following screening includes false positive rate, overdiagnosis, anxiety and distress, pains and radiation exposure. The most common outcome is a ‘‘false positive’’ where the recalled area is determined to be normal tissue, a cyst, or a benign calcification. Women who get screened annually for 10 years have over 50% chance of experiencing at least one false-positive recall, and this has been consistent with previous studies conducted by other researchers (Pace, L.E, & Keating, N.L. (2014; Marmot, M.G., et al. 2013).

Secondly, incorporating Photon-Counting Detector (PCD) Technology into clinical settings brings notable benefits compared to conventional 2D mammography and standard CBBCT, especially in enhancing diagnostic precision—particularly for women with dense breast tissue. It also enables high-resolution, three-dimensional imaging that overcomes the issue of tissue overlap, commonly referred to as the "summation effect" (O’Connell & Kawakyu-O’Connor, 2012). According to Lehman et al. (2017), the broader goal of adopting 3D imaging is to lower the "Abnormal Interpretation Rate" (AIR), which currently exceeds recommended levels among radiologists relying on traditional mammography. By offering a layered, three-dimensional perspective, PCD Technology aids in clarifying ambiguous findings caused by superimposed tissue—a major factor contributing to false-positive results in conventional 2D imaging (O’Connell & Kawakyu-O’Connor, 2012).

LIMITATIONS

Several studies from Canada and Europe on screening outcomes did not report all findings, possibly due to incomplete analyses, which may have introduced non-reporting bias. Additionally, the evaluation of post-mammography assessment outcomes failed to account for all relevant risk factors. This omission contributed to patient selection bias, an underestimation of potential harms such as over-diagnosis, and misleading efficacy estimates.

Future research assessing diagnostic accuracy and radiation dose—comparing Photon-Counting Detector Technology with conventional CBBT in breast imaging—should incorporate risk factor analysis. Integrating these factors into PCD-based studies could support the

development of personalized, high-precision imaging protocols, improving lesion detection in dense breast tissue while substantially lowering radiation exposure.

RECOMMENDATIONS

Recent clinical guidelines for breast cancer screening highlight earlier screening initiation and personalized approaches to better weigh the benefits of lower mortality against potential risks. Major recommendations from the U.S. Preventive Services Task Force (USPSTF) and the American College of Physicians suggest annual mammograms—ideally using 3D imaging—for women at average risk starting at age 40, while biennial screening remains an acceptable alternative for those aged 40 to 74. For women at higher risk, annual screening should begin between ages 30 and 35, incorporating breast MRI as an additional tool.

Women with heterogeneously or extremely dense breasts are increasingly encouraged to use supplementary techniques such as photon-counting detector systems or 3D tomosynthesis, which can reduce false positives due to tissue overlap. Healthcare providers are advised to engage patients in transparent conversations about the pros and cons, emphasizing that while screening can prevent deaths, it may also lead to unnecessary biopsies and emotional strain. Although photon-counting CT is becoming more common in general radiology, its role in routine breast screening is still under evaluation, with interest in its potential to improve diagnostic accuracy, minimize false positives and overdiagnosis, and as well lower radiation doses.

Enhancing radiologists' diagnostic skills and interpretation in breast imaging calls for a multifaceted strategy, including structured education, managing case volume, adopting new technologies, and establishing ongoing feedback. Implementing "batch reading" sessions—reviewing 50+ or more cases consecutively—can sharpen diagnostic focus and pattern recognition compared to fragmented reading throughout the day. It is also recommended that radiologists systematically review pathology results from all biopsies to learn which imaging findings correspond to true versus false positives. Regular audit reviews should be incorporated into practice to assess individual performance metrics—such as Cancer Detection Rate, Recall Rate, and Positive Predictive Value—against established benchmarks, helping identify targeted areas for improvement.

CONCLUSION

False-positive results and overdiagnosis are common and notable downsides of mammography screening, with around 10% of screenings yielding false alarms and a cumulative 10-year risk of overdiagnosis estimated between 20% and 60%. Although screening helps lower breast cancer deaths in women, it often leads to unnecessary stress, additional diagnostic procedures, and the identification of slow-growing cancers that may never cause harm. Despite these significant drawbacks, most medical guidelines continue to support screening for certain age groups—typically those aged 50 and older—because the mortality benefits from early detection are considered to outweigh the risks. Nevertheless, there is growing interest in tailoring screening approaches to individual risk factors in order to minimize these adverse effects.

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REFERENCES

American College of Radiology. (2016). ACR practice parameter for the performance of magnetic resonance imaging-guided breast interventional procedures.

BCSC, (2017). Screening Mammography Sensitivity, Specificity, & False Negative Rate. Breast Cancer Surveillance Consortium (BCSC) 2017. http://bcsc-research.org/(accessed August 21,2020).

Berg WA. (2016). Nuclear breast imaging: clinical results and future directions. J Nucl Med 2016; 57 Suppl 1:46S-52S. Doi: 10.2967/jnumed.115.157891.

Baltzer PAT, Kapetas P, et al. (2017). New diagnostic tools for breast cancer. Memo 2017; 10:175-80. Doi.10.1007/s12254-017-0341-5.

Barlow, W.E., Chi, C., Carney A., Taplin, S.H., D'Orsi, C., Cuttler, P. A., Taplin, S.H., D'Orsi, C., Cutter, G., Hendrick, R.E., & Elmore, J. G. (2004). Accuracy of screening mammography interpretation by characteristics of radiologists. *JNCI Journal* of the National Cancer Institute, 86(24),1840-1850.

Bickel H, Pinker-Domenig K. et al. (2015). Quantitative apparent diffusion coefficient as a non-invasive imaging biomarker for the differentiation of invasive breast cancer and ductal carcinoma in situ. Invest Radiol. 50:95-100.

Conti A. Duggento A. et al. (2020). Radiomics in breast cancer classification and prediction. Semin Cancer Biol; Doi: 10.1016/j.semcancer.04.002.

Coldman, A.J., Major, D., Doyle, G.P., D'yachkova, Y., Philips, N., Onysko, J., Shumak, R., Smith, N.E., & Wadden, N. (2006). Organized in breast screening programs in Canada: Effect of radiologist reading volumes on outcomes. Radiology, 238(3), 809-815.

Chetlen A, Mack J, Chan T. Breast cancer screeningcontroversies; who, when, why, and how? Clin Imaging 2016; 40:279-82. Doi: 10.1016/j. clinimag; 05.017.

Chilla GS, Tan CH, Xu C, Poh CL. (2015). Diffusion weighted magnetic resonance imaging and its recent trend-a survey. Quant Imaging Med Surg; 5:407-22. Doi: 10.3978/j.issn.2223-4292.03.1.

Cardoso F, Kyriakides S. et al. (2019). Early breast cancer: ESMO Clinical Practice Guidelines for diagnostic, treatment and follow-up. *Ann Oncol* 2019; 30:1194-220. Doi: 10.7326/M19-2125.

Crivelli P, Ledda RE, Parascandolo N, Fara A, Soro D, Conti M. (2018). A new challenge for radiologists:radiomics in breast cancer. Biomed Res Int. 6120703. Doi: 10.1155/2018/6120703.

Dai X, Xiang L, Li T, Bai Z. (2016). Cancer hallmarks, biomarkers and breast cancer molecular subtypes. J Cancer; 7:1281-94. Doi: 10.7150/jca.13141.

Dye, T.D., Bogale, S., Hobden, C., Tilahun, Y., Deressa, T., & Reeler, A. (2012). Experience of Initial Symptoms of Breast Cancer and Triggers for Action in Ethiopia. *International Journal* of Breast Cancer, 2012,1-5.

Elmore JG, Longton GM. Et al. (2015). Diagnostic concordance among pathologists interpreting breast biopsy specimens. *JAMA* 2015; 313:1122-32. Doi: 10. 1001/jama. 1405.

Gou C, Zhang C, Liu J, Tong L, Huang G. (2016). Is Tc-99m sestamibi sciintimammography useful in the prediction of neoadjuvant chemotherapy responses in breast cancer? A systematic review and meta-analysis. Nucl Med Commun 2016; 37:675-88.

Gilbert FJ, Tucker L, Young KC. (2016). Digital breast tomosynthesis (DBT): a review of the evidence for use as a screening tool. Clin Radiol 2016;71:141-50.

Gillies R, Kinahan PE, Hricak H. (2016). Radiomics: Images are more than pictures, they are Data. *Radiology*. 278:563-77. Doi: 10.1148/radio.2015151169.

Grandishar WJ, Anderson BO, Abraham J, Aft R, Agnese D, Allison KH, et al. (2020). Breast Cancer, version 3.2020, NCCN clinical practice guidelines in oncology. *J Natle Compr Canc Netw*; 18:452-78. Doi: 10.6004/jnccn.2020.0016.

Greene LR & Wilkinson D. (2015). The role of general nuclear medicine in breast cancer. J Med Radiat Sci, 62:54-65. Doi: 10.1002/jmrs.97.

Geisel J, Raghu M, Hooley R. (2017). The role of ultrasound in breast in breast cancer screening: the case for and against ultrasound. Semin Ultrasound CT MR ; 39:25-34.

Helvie MA. (2010). Digital Mammography imaging: breast tomosythesis and advanced applications. *Radiol Clin* North Am 2010;48:917-29. Doi: 10.1016/j.rcl.2010.06.009.

Iezzoni LI, Kilbridge K, Park ER. (2010). Physical access barriers to care for diagnosis and treatment of breast cancer among women with mobility impairments. *Oncol Nurs* Forum 2010;37:711-7. Doi: 10.1188/10.ONF. 711-717. Stic radiation force impulse imaging in benign and malignant breast lesions. Cureus; 9:el301.

Jayaraman J, Indiran V, Kannan K, Maduraimuthu P. (2017). AcouStic radiation force impulse imaging in benign and malignant breast lesions. Cureus; 9:el301.

Kontos M, Wilson R, Fentiman I. (2011). Digital Infrared thermal imaging (DITI) of breast lesions: sensitivity and specificity of detection of primary breast cancers. *Clin Radiol* 2011; 66:536-9. Doi:10.1016/j.crad.2011.01.009.

Lucznska E. (2017). Comparison of degree of enhancement on Contrast-Enhanced Spectral Mammography and Lesion characteristics on Mammography based on lesion histology. *European Congress on Radiology* 2017. Doi:10.1594/ecr2017/c-0831.

Liu G.Y, Lu J.S. et al. (2008). Fiberoptic ductoscopy combined with cytology testing in the patients of spontaneous nipple discharge. Breast Cancer Res Treat 2008; 108:271-7. Doi:10.1007/s10549-007-9598-4.

Mettler FA, Huda W, Yoshizumi TT, Mahesh M. (2008). Effective doses in radiology and diagnostic nuclear medicine*: Radiology*; 248:254-63.

Miglioretti, D. L., *et al*. (2015). Do mammographic technologists affect radiologists' diagnostic mammography interpretative performance? *American Journal of Roentgenology*.

Miglioretti, D.L., Gard, C.C., Carney, P.A.,Onega, T.L., Buist, D.S.M., Sickles, E.A., Kerlikowske, K., Rosenberg, R.D., Yankaskas, B.C., Geller, B.M., & Elmore, J.G. (2009). When radiologists perform best: The learning curve in screening mammogram interpretation. *Radiology*, 253(3), 632-640.

Miglioretti, D.L., Smith-Bindman, R., Abrham, L., Brenner, R.J., Carney, P.A., Bowles, E.J.A., Buist, D.S.M., & Elmore, J.G. (2007). Radiologist characteristics associated with interpretive performance of diagnostic mammography. *JNCI: Journal of the National Cancer Institute*, 99(24), 1854-1863.

Mankoff D.A, Gralow RR. (2007). The Role of FDG-PET/CT in Suspected Recurrence of Breast Cancer. Breast Disease: A Year Book Quarterl 2007; 18:251-2.

Mann RM, Balleyguier C, Baltzer PA, Bick U, Colin C, Cornford E. et al. (2015). Breast MRI: EUSOBI recommendations for women's information. Eur Radiol; 25:3669-78. Doi: 10.1007/s00330-015-3807-z.

Mazzocco K, Masiero M, Carriro MC, Pravettoni G. (2019). The role of emotions in cancer patients' decision-making. Ecancermedicalscience 2019;13-914. Doi.10.3332/ecancer.2019.914.

Rahbar H, Lee JM, Lee CI. (2020). Optimal screening in breast cancer survivors with dense breasts on mammography. *J Clin Oncol* 2020: JCO2001641. Doi: 10.1200/JCO.20.01641.

Oeffinger KC, Fontham ETH, Etzioni R, Herzig A, Michaelson JS, Shih Y-CT, et al. (2015). Breast Cancer Screening for women at average risk: 2015 guideline update from the American Cancer Society. JAMA 314:1599-614. Doi: 10.1001/jama. 2015.12783.

Poiseuil M, Coureau G. et al. (2019). Deprivation and mass screening: Survival of women diagnosed with breast cancer in France from 2008 to 2010. *Cancer Epidemiol* 2019; 60:149-55. Doi: 10.1016/j.canep. 2019.03.016.

Partridge SC, Nisaan N, Rahbar H, Kitsch AE, Sigmund EE. (2017). Diffusion-weighted breast MRI: Clinical applications and emerging techniques. *J Magn Reson Imaging*. 45:337-55. Doi: 10.1002/jmri.25479.

Siu AL, U.S. (2016). Preventive Services Task Force. Screening for breast cancer: U.S Preventive Services task force recommendation statement. *Ann Interm Med* ; 164-279-96. Doi: 7326/M15-2886.

Smetherman DH. (2013). Screening, imaging, and image-guided biopsy techniques for breast cancer. Surge *Clin North Am* 2013; 93:309-27. Doi:10.1016/j.suc.2013.01.004. 003.

Schelfout K, Van Goethem M, Kersschot E, Colpaert C, Schelfhout AM, Leyman P, et al.(2004). Contrast-enhanced MR imaging of breast lesions and effect on treatment. *Eur J Surg Oncol;* 30:501-7. Doi: 10.1016/j.eso.2004.02.

Semenza GL. (2015). The hypoxic tumor microenvironment: A driving force for breast cancer progression. Biochim Biophys Acta 2016; 1863:382-91. Doi: 10.1016/j.bbamcr. 2015.05.036.

Tran WT, Jeezak. Et al. (2019). Personalized breast cancer treatments using artificial intelligent in radiomics and pathomics. *J Med Imaging Radiat Sci*; 50:S32-41. Doi: 10.1016/jmi.2019.07.010.

Qaseem A, Snow V, Sherif K, Aronson M, Weiss KB, Owens DK. Et al. (2007). Screening mammography for women 40 to 49 years of age: a clinical practice guideline from the American College of Physicians. *Ann Intem Med* 2007;146:511-5.

Valdora F, Houssami N, Rossi F, Calabrese M, Tagliafico AS. (2018). Rapid review: Radiomics and breast cancer. Breast Cancer Res Treat 2018;169:217-29. Doi: 10.1007/s10549-018-4675-4.

Welch HG, Prorok PC. et al. (2016). Breast-Cancer Tumor Size, Overdiagnosis, and Mammography Screening Effectiveness. *N Engl J Med* 2016; 375;1438-47. Doi: 10.1056/NEJMoa1600249.

Wong, D,J., Gandomkar, Z., Lewis, S., Reed, W., Suleiman, M., Siviengphanom, S., & E. (2023). Do reader characteristics affect diagnostic efficiency in screening review. Clinical Breast Cancer, 23, e56-e67.

Waks, A.G., & Winer, E. P. (2019). Breast Cancer Treatment. *JAMA*, 321(3),288-300.

Yuan. (2026). Chinese expert consensus on endocrine therapy for breast cancer (2026 edition). Translational Breast Cancer Research.

Zhang Q, Xia Y, Suo J, Shi J, Yu J, Guo Y, et al. (2016). Sonoelastomics for Breast Tumor Classification: A Radiomics Approach with Clustering-Based Features Selection on Sonoelastography. Ultrasound Med Biol; 43:1058-69. Doi: 10.1016/j.ultrasmedbio.2016.12.016.

U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2009;151:716-26. [PMID: 19920272] doi:10.7326/0003-4819-151-10-200911170-00008.

Siegel RL, Miller KD, Fuchs HE, et al . (2022). Cancer statistics, 2022. CA *Cancer J Clin* 2022;**72**:7–33. doi:10.3322/caac.21708 Cross Ref PubMedGoogle Scholar.

Miglioretti DL, Gard CC, Carney PA, et al.*(2009).* When radiologists perform best: the learning curve in screening mammogram nterpretation. *Radiology* 2009;**253**:632–40. doi:10.1148/radiol.2533090070CrossRefPubMedGoogle Scholar.

Uzun Ozsahin D, Ikechukwu Emegano D, Uzun B, et al . *(2022).*The Systematic Review of Artificial Intelligence Applications in Breast Cancer Diagnosis. *Diagnostics (Basel)* 2022;**13**:45. doi:10.3390/diagnostics13010045 Google Scholar.

Wong DJ, Gandomkar Z, Wu W-J, et al . *(2020).* Artificial intelligence and convolution neural networks assessing mammographic images: a narrative literature review. *J Med Radiat Sci* 2020;**67**:134– doi:10.1002/jmrs.385 PubMed Google Scholar.

Ferlay J., Ervik M., Lam F., Colombet M., Mery L., Piñeros M., Znaor A., Soerjomataram I., Bray F. (2021). Global Cancer Obser-Vatory: Cancer Today. International Agency for Research on Cancer; Lyon, France: 2020. [(accessed on 9 July 2021)]. Available online: https://gco.iarc.fr/today. Google Scholar.

DeSantis C.E., Fedewa S.A., Sauer A.G., Kramer J.L., Smith R.A., Jemal A.(2015). Breast cancer statistics, 2015: Convergence of incidence rates between black and white women. CA A Cancer J. Clin. 2015;66:31–42. doi: 10.3322/caac.21320. [DOI] [PubMed] [Google Scholar.

Sharma R. (2019). Breast cancer incidence, mortality and mortality-to-incidence ratio (MIR) are associated with human development, 1990–2016: Evidence from Global Burden of Disease Study 2016. Breast Cancer. 2019;26:428–445. doi: 10.1007/s12282-018-00941-4. [DOI] [PubMed] [Google Scholar].

Vostakolaei F.A., Karim-Kos H.E., Janssen-Heijnen M.L.G., Visser O., Verbeek A.L.M., Kiemeney L. (2010). The validity of the mortality to incidence ratio as a proxy for site-specific cancer survival. Eur. J. Public Health. 2010;21:573–577. doi: 10.1093/eurpub/ckq120. [DOI] [PubMed] [Google Scholar.

Sankaranarayanan R., Swaminathan R., Brenner H., Chen K., Chia K.S., Chen J.-G., Law S.C., Ahn Y.-O., Xiang Y.B., Yeole B.B., et al. (2010). Cancer survival in Africa, Asia, and Central America: A population-based study. Lancet Oncol. 2010;11:165–173. doi: 10.1016/S1470-2045(09)70335-[DOI] [PubMed] [Google Scholar.

Ferlay J., Laversanne M., Ervik M., Lam F., Colombet M., Mery L., Piñeros M., Znaor A., Soerjomataram I., Bray F. (2020).International Agency for Research on Cancer; Lyon, France: 2020. [(accessed on 9 July 2021)]. Global Cancer Observatory: Cancer Tomorrow. Available online: https://gco.iarc.fr/tomorrow. [Google Scholar.

Porter P. (2008). Westernizing Women's Risks? Breast Cancer in Lower-Income Countries. N. Engl. J. Med. 2008;358:213–216. doi: 10.1056/NEJMp0708307. [DOI] [PubMed] [Google Scholar.

Weigelt B., Horlings H.M., Kreike B., Hayes M.M., Hauptmann M., Wessels L.F.A., De Jong D., van de Vijver M., Veer L.J.V., Peterse J.L. (2008). Refinement of breast cancer classification by molecular characterization of histological special types. J. Pathol. 2008;216:141–150. doi: 10.1002/path.2407. [DOI] [PubMed] [Google Scholar].

Tavassoli F.A. (2020). Pathology and Genetics of Tumours of the Breast and Female Genital Organs. World Hhealth Organization Classification of Tumours; Lyon, France: 2003. [Google Scholar].

Erber R., Hartmann A. (2020). Histology of Luminal Breast Cancer. Breast Care. 2020;15:327–336. doi: 10.1159/000509025. [DOI] [PMC free article] [PubMed] [Google Scholar].

Howlader N., Altekruse S.F., Li C.I., Chen V.W., Clarke C.A., Ries L.A.G., Cronin K.A. (2014). US Incidence of Breast Cancer Subtypes Defined by Joint Hormone Receptor and HER2 Status. J. Natl. Cancer Inst. 2014;106:dju055. doi: 10.1093/jnci/dju055. [DOI] [PMC free article] [PubMed] [Google Scholar.

Weigelt B., Geyer F.C., Reis-Filho J.S. (2010). Histological types of breast cancer: How special are they? Mol. Oncol. 2010;4:192–208. doi: 10.1016/j.molonc.2010.04.004. [DOI] [PMC free article] [PubMed] [Google Scholar].

Makki J. (2015). Diversity of Breast Carcinoma: Histological Subtypes and Clinical Relevance. Clin. Med. Insights Pathol. 2015;8:23–31. doi: 10.4137/CPath.S31563. [DOI] [PMC free article] [PubMed] [Google Scholar].

Ades F. (2014). Luminal B breast cancer: Molecular characterization, clinical management, and future perspectives. J. Clin. Oncol. 2014;32:2794–2803. doi: 10.1200/JCO.2013.54.1870. [DOI] [PubMed] [Google Scholar].

Cheang M.C.U., Chia S.K., Voduc D., Gao D., Leung S., Snider J., Watson M., Davies S., Bernard P.S., Parker J.S., et al.(2009). Ki67 Index, HER2 Status, and Prognosis of Patients with Luminal B Breast Cancer. J. Natl. Cancer Inst. 2009;101:736–750. doi: 10.1093/jnci/djp082. [DOI] [PMC free article] [PubMed] [Google Scholar

Raj-Kumar P.-K., Liu J., Hooke J.A., Kovatich A.J., Kvecher L., Shriver C.D., Hu H. (2019). PCA-PAM50 improves consistency between breast cancer intrinsic and clinical subtyping reclassifying a subset of luminal A tumors as luminal B. Sci. Rep. 2019;9:7956. doi: 10.1038/s41598-019-44339-4. [DOI] [PMC free article] [PubMed] [Google Scholar].

Ranjit K. Breast cancer. Lancet. 2005;365:1742. doi: 10.1016/S0140-6736(05)66547-6. [DOI] [PubMed] [Google Scholar].

Roberts S.A., Lawrence M.S., Klimczak L.J., Grimm S.A., Fargo D., Stojanov P., Kiezun A., Kryukov G., Carter S.L., Saksena G., et al. (2013). An APOBEC cytidine deaminase mutagenesis pattern is widespread in human cancers. Nat. Genet. 2013; 45:970–976. doi: 10.1038/ng.2702. [DOI] [PMC free article] [PubMed] [Google Scholar].

Plasilova M.L., Hayse B., Killelea B.K., Horowitz N.R., Chagpar A.B., Lannin D.R. (2016). Features of triple-negative breast cancer. Medicine. 2016;95:e4614. doi: 10.1097/MD.0000000000004614. [DOI] [PMC free article] [PubMed] [Google Scholar].

Newman L.A., Reis-Filho J.S., Morrow M., Carey L.A., King T.A. (2014).The 2014 Society of Surgical Oncology Susan G. Komen for the Cure Symposium: Triple-Negative Breast Cancer. Ann. Surg. Oncol. 2014;22:874–882. doi: 10.1245/s10434-014-4279-0. [DOI] [PubMed] [Google Scholar].

Pareja F. (2016). Triple-negative breast cancer: The importance of molecular and histologic subtyping, and recognition of low-grade variants. NPJ Breast Cancer. 2016;2:16036. doi: 10.1038/npjbcancer.2016.36. [DOI] [PMC free article] [PubMed] [Google Scholar].

Wetterskog D. (2012). Adenoid cystic carcinomas constitute a genomically distinct subgroup of triple-negative and basal-like breast cancers. J. Pathol. 2012;226:84–96. doi: 10.1002/path.2974. [DOI] [PubMed] [Google Scholar].

Badve S., Dabbs D.J., Schnitt S.J., Baehner F.L., Decker T., Eusebi V., Fox S., Ichihara S., Jacquemier J., Lakhani S.R., et al. (2010). Basal-like and triple-negative breast cancers: A critical review with an emphasis on the implications for pathologists and oncologists. Mod. Pathol. 2010;24:157–167. doi: 10.1038/modpathol.2010.200. [DOI] [PubMed] [Google Scholar].

Weiss A., Mac Gregor M.C., Lichtensztajn D., Yi M., Tadros A., Hortobagyi G.N., Giordano S.H., Hunt K.K., Mittendorf E.A. (2018). Validation Study of the American Joint Committee on Cancer Eighth Edition Prognostic Stage Compared with the Anatomic Stage in Breast Cancer. JAMA Oncol. 2018;4:203–209. doi: 10.1001/jamaoncol.2017.4298. [DOI] [PMC free article] [PubMed] [Google Scholar].

Stat Bite: Lifetime Probability among Females of Dying of Cancer. JNCI J. Natl. Cancer Inst. 2004;96:1311–1321. doi: 10.1093/jnci/96.11.818. [DOI] [PubMed] [Google Scholar].

Benz C.C.(2007). Impact of aging on the biology of breast cancer. Crit. Rev. Oncol. 2008;66:65–74. doi: 10.1016/j.critrevonc.2007.09.001. [DOI] [PMC free article] [PubMed] [Google Scholar].

McGuire A., Brown J.A.L., Malone C., McLaughlin R., Kerin M.J. (2015). Effects of Age on the Detection and Management of Breast Cancer. Cancers. 2015;7:908–929. doi: 10.3390/cancers7020815. [DOI] [PMC free article] [PubMed] [Google Scholar].

Collaborative Group on Hormonal Factors in Breast Cancer Familial breast cancer: Collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. Lancet. 2001;358:1389–1399. doi: 10.1016/S0140-6736(01)06524-2. [DOI] [PubMed] [Google Scholar].

Shiyanbola O.O., Arao R.F., Miglioretti D.L., Sprague B.L., Hampton J.M., Stout N.K., Kerlikowske K., Braithwaite D., Buist D.S., Egan K.M., et al.(2017). Emerging Trends in Family History of Breast Cancer and Associated Risk. Cancer Epidemiol. Biomark. Prev. 2017;26:1753–1760. doi: 10.1158/1055-9965.EPI-17-0531. [DOI] [PMC free article] [PubMed] [Google Scholar].

Baglia M.L., Tang M.-T.C., Malone K.E., Porter P., Li C.I. (2018). Family History and Risk of Second Primary Breast Cancer after In Situ Breast Carcinoma. Cancer Epidemiol. Biomark. Prev. 2018;27:315–320. doi: 10.1158/1055-9965.EPI-17-0837. [DOI] [PMC free article] [PubMed] [Google Scholar].

Brewer H.R., Jones M.E., Schoemaker M.J., Ashworth A., Swerdlow A.J. (2017). Family history and risk of breast cancer: An analysis accounting for family structure. Breast Cancer Res. Treat. 2017;165:193–200. doi: 10.1007/s10549-017-4325-2. [DOI] [PMC free article] [PubMed] [Google Scholar].

Shiovitz S., Korde L.A. (2015). Genetics of breast cancer: A topic in evolution. Ann. Oncol. 2015;26:1291–1299. doi: 10.1093/annonc/mdv022. [DOI] [PMC free article] [PubMed] [Google Scholar].

Shahbandi A., Nguyen H.D., Jackson J.G.(2020). TP53 Mutations and Outcomes in Breast Cancer: Reading beyond the Headlines. Trends Cancer. 2020;6:98–110. doi: 10.1016/j.trecan.2020.01.007. [DOI] [PMC free article] [PubMed] [Google Scholar].

Corso G., Veronesi P., Sacchini V., Galimberti V. (2018). Prognosis and outcome in CDH1-mutant lobular breast cancer. Eur. J. Cancer Prev. 2018;27:237–238. doi: 10.1097/CEJ.0000000000000405. [DOI] [PMC free article] [PubMed] [Google Scholar].

Corso G., Intra M., Trentin C., Veronesi P., Galimberti V. (2016). CDH1 germline mutations and hereditary lobular breast cancer. Fam. Cancer. 2016;15:215–219. doi: 10.1007/s10689-016-9869-5. [DOI] [PubMed] [Google Scholar].

Kechagioglou P., Papi R.M., Provatopoulou X., Kalogera E., Papadimitriou E., Grigoropoulos P., Nonni A., Zografos G., Kyriakidis D.A., Gounaris A. (2014). Tumor suppressor PTEN in breast cancer: Heterozygosity, mutations and protein expression. Anticancer. Res. 2014;34:1387–1400. [PubMed] [Google Scholar].

Hill D.A., Prossnitz E.R., Royce M., Nibbe A. (2019). Temporal trends in breast cancer survival by race and ethnicity: A population-based cohort study. PLoS ONE. 2019;14:e0224064. doi: 10.1371/journal.pone.0224064. [DOI] [PMC free article] [PubMed] [Google Scholar].

Yedjou C.G., Sims J.N., Miele L., Noubissi F., Lowe L., Fonseca D.D., Alo R.A., Payton M., Tchounwou P.B. (2019). Health and Racial Disparity in Breast Cancer. Adv. Exp. Med. Biol. 2019;1152:31–49. doi: 10.1007/978-3-030-20301-6_3. [DOI] [PMC free article] [PubMed] [Google Scholar].

American Cancer Society (2016) Breast Cancer Facts & Figures, 2015–2016. American Cancer Society; Atlanta, GA, USA: 2016. [Google Scholar].

Bernstein L. (2002). Epidemiology of Endocrine-Related Risk Factors for Breast Cancer. J. Mammary Gland. Biol. Neoplasia. 2002;7:3–15. doi: 10.1023/A:1015714305420. [DOI] [PubMed] [Google Scholar].

Albrektsen G., Heuch I., Hansen S., Kvåle G. (2004). Breast cancer risk by age at birth, time since birth and time intervals between births: Exploring interaction effects. Br. J. Cancer. 2004;92:167–175. doi: 10.1038/sj.bjc.6602302. [DOI] [PMC free article] [PubMed] [Google Scholar].

Husby A., Wohlfahrt J., Øyen N., Melbye M. (2018). Pregnancy duration and breast cancer risk. Nat. Commun. 2018;9:4255. doi: 10.1038/s41467-018-06748-3. [DOI] [PMC free article] [PubMed] [Google Scholar].

Checka C.M., Chun J.E., Schnabel F.R., Lee J., Toth H. (2012). The Relationship of Mammographic Density and Age: Implications for Breast Cancer Screening. Am. J. Roentgenol. 2012;198:W292–W295. doi: 10.2214/AJR.10.6049. [DOI] [PubMed] [Google Scholar].

Kim E.Y., Chang Y., Ahn J., Yun J., Park Y.L., Park C.H., Shin H., Ryu S. (2020). Mammographic breast density, its changes, and breast cancer risk in premenopausal and postmenopausal women. Cancer. 2020;126:4687–4696. doi: 10.1002/cncr.33138. [DOI] [PubMed] [Google Scholar].

Duffy S.W., Morrish O.W., Allgood P.C., Black R., Gillan M.G., Willsher P., Cooke J., Duncan K.A., Michell M.J., Dobson H.M., et al. (2017). Mammographic density and breast cancer risk in breast screening assessment cases and women with a family history of breast cancer. Eur. J. Cancer. 2017;88:48–56. doi: 10.1016/j.ejca.2017.10.022. [DOI] [PMC free article] [PubMed] [Google Scholar].

Chen X., Wang Q., Zhang Y., Xie Q., Tan X. (2018). Physical Activity and Risk of Breast Cancer: A Meta-Analysis of 38 Cohort Studies in 45 Study Reports. Value Health. 2018;22:104–128. doi: 10.1016/j.jval.2018.06.020. [DOI] [PubMed] [Google Scholar].

Kyu H.H., Bachman V.F., Alexander L.T., Mumford J.E., Afshin A., Estep K., Veerman L., Delwiche K., Iannarone M.L., Moyer M.L., et al. (2013). Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: Systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013. BMJ. 2016;354:i3857. doi: 10.1136/bmj.i3857. [DOI] [PMC free article] [PubMed] [Google Scholar].

Hoffinan-Goetz L. (2009). Influence of Physical Activity and Exercise on Innate Immunity. Nutr. Rev. 2009;56:S126–S130. doi: 10.1111/j.1753-4887.1998.tb01629.x. [DOI] [PubMed] [Google Scholar][Ref list].

Wang X., Hui T.-L., Wang M.-Q., Liu H., Li R.-Y., Song Z.-C. (2019). Body Mass Index at Diagnosis as a Prognostic Factor for Early-Stage Invasive Breast Cancer after Surgical Resection. Oncol. Res. Treat. 2019;42:195–201. doi: 10.1159/000496548. [DOI] [PubMed] [Google Scholar].

James F., Wootton S., Jackson A., Wiseman M., Copson E., Cutress R. (2015). Obesity in breast cancer—What is the risk factor? Eur. J. Cancer. 2015;51:705–720. doi: 10.1016/j.ejca.2015.01.057. [DOI] [PubMed] [Google Scholar].

Protani M., Coory M., Martin J. (2010). Effect of obesity on survival of women with breast cancer: Systematic review and meta-analysis. Breast Cancer Res. Treat. 2010;123:627–635. doi: 10.1007/s10549-010-0990-0. [DOI] [PubMed] [Google Scholar].

Rachdaoui N., Sarkar D.K.(2013). Effects of Alcohol on the Endocrine System. Endocrinol. Metab. Clin. N. Am. 2013;42:593–615. doi: 10.1016/j.ecl.2013.05.008. [DOI] [PMC free article] [PubMed] [Google Scholar].

Erol A., Ho A.M.-C., Winham S.J., Karpyak V.M. (2017). Sex hormones in alcohol consumption: A systematic review of evidence. Addict. Biol. 2017;24:157–169. doi: 10.1111/adb.12589. [DOI] [PMC free article] [PubMed] [Google Scholar].

Terry P.D., Rohan T.E. (2002). Cigarette smoking and the risk of breast cancer in women: A review of the literature. Cancer Epidemiol. Biomark. Prev. 2002;11:953–971. [PubMed] [Google Scholar].

Catsburg C., Miller A.B., Rohan T.E. (2014). Active cigarette smoking and risk of breast cancer. Int. J. Cancer. 2014;136:2204–2209. doi: 10.1002/ijc.29266. [DOI] [PubMed] [Google Scholar].

Jones M., Schoemaker M.J., Wright L.B., Ashworth A., Swerdlow A.J. (2017). Smoking and risk of breast cancer in the Generations Study cohort. Breast Cancer Res. 2017;19:118. doi: 10.1186/s13058-017-0908-4. [DOI] [PMC free article] [PubMed] [Google Scholar].

Misotti A.M., Gnagnarella P. (2013). Ecancermedicalscience. Ecancermedicalscience. 2013;7:365. doi: 10.3332/ecancer.2013.365. [DOI] [PMC free article] [PubMed] [Google Scholar].

Cui Y. (2006). Vitamin D, Calcium, and Breast Cancer Risk: A Review. Cancer Epidemiol. Biomark. Prev. 2006;15:1427–1437. doi: 10.1158/1055-9965.EPI-06-0075. [DOI] [PubMed] [Google Scholar].

Atoum M., Alzoughool F. (2017). Vitamin D and Breast Cancer: Latest Evidence and Future Steps. Breast Cancer: Basic Clin. Res. 2017;11:1178223417749816. doi: 10.1177/1178223417749816. [DOI] [PMC free article] [PubMed] [Google Scholar].

El-Sharkawy A., Malki A. (2020). Vitamin D Signaling in Inflammation and Cancer: Molecular Mechanisms and Therapeutic Implications. Molecules. 2020;25:3219. doi: 10.3390/molecules25143219. [DOI] [PMC free article] [PubMed] [Google Scholar].

Estébanez N., Gómez-Acebo I., Palazuelos C., Llorca J., Dierssen-Sotos T. (2018). Vitamin D exposure and Risk of Breast Cancer: A meta-analysis. Sci. Rep. 2018;8:9039. doi: 10.1038/s41598-018-27297-1. [DOI] [PMC free article] [PubMed] [Google Scholar].

Huss L., Butt S.T., Borgquist S., Elebro K., Sandsveden M., Rosendahl A., Manjer J. (2019). Vitamin D receptor expression in invasive breast tumors and breast cancer survival. Breast Cancer Res. 2019;21:84. doi: 10.1186/s13058-019-1169-1. [DOI] [PMC free article] [PubMed] [Google Scholar].

Zhou L., Chen B., Sheng L., Turner A. (2020). The effect of vitamin D supplementation on the risk of breast cancer: A trial sequential meta-analysis. Breast Cancer Res. Treat. 2020;182:1–8. doi: 10.1007/s10549-020-05669-4. [DOI] [PubMed] [Google Scholar.

Al-Naggar R.A., Anil S. (2016). Artificial Light at Night and Cancer: Global Study. Asian Pac. J. Cancer Prev. 2016;17:4661–4664. doi: 10.22034/APJCP.2016.17.10.4661. [DOI] [PMC free article] [PubMed] [Google Scholar].

Johns L.E., Jones M., Schoemaker M., McFadden E., Ashworth A., Swerdlow A. (2018). Domestic light at night and breast cancer risk: A prospective analysis of 105,000 UK women in the Generations Study. Br. J. Cancer. 2018;118:600–606. doi: 10.1038/bjc.2017.359. [DOI] [PMC free article] [PubMed] [Google Scholar].

Myers, E.R. · Moorman, P. · Gierisch, J.M. (2015). Benefits and harms of breast Cancer screening: a systematic review JAMA. 2015; 314:1615-1634 Crossref Scopus (465) PubMed Google Scholar.

Sankatsing, V.D.V. · van Ravesteyn, N.T. · Heijnsdijk, E.A.M. (2017). The effect of population-based mammography screening in Dutch municipalities on breast cancer mortality: 20 years of follow-up Int. J. Cancer. 2017; 141:671-677 Crossref Scopus (55) PubMed Google Scholar.

World Health Organisation.*(2002). International agency for research on cancer. breast cancer screening*. WHO: International Agency for Research on Cancer, 2002.Google Scholar.

Brodersen J, Siersma VD. *(2013).* Long-Term psychosocial consequences of false-positive screening mammography. *Ann Fam Med* 2013;**11**:106–15. doi:10.1370/afm.1466 Abstract/FREE Full TextGoogle Scholar.

Elmore JG, Miglioretti DL, Reisch LM, et al. *(2002).* Screening mammograms by community radiologists: variability in false-positive rates. *J Natl Cancer Inst* 2002;**94**:1373–80. doi:10.1093/jnci/94.18.1373 CrossRefPubMedWeb of ScienceGoogle Scholar.

Barratt A, Howard K, Irwig L, *et al*. Model of outcomes of screening mammography: information to support informed choices. *BMJ* 2005;**330**:936. doi:10.1136/bmj.38398.469479.8F Google Scholar.

Castells X, Molins E,Macià F.(2006). Cumulative false positive recall rate and association with participant related factors in a population based breast cancer screening programme. *J Epidemiol Community Health* 2006;**60**:316–21. doi:10.1136/jech.2005.042119 Abstract/FREE Full TextGoogle Scholar.

Roman M, Hubbard RA, Sebuodegard S, et al. *(2013).* The cumulative risk of false-positive results in the Norwegian breast cancer screening program: updated results. *Cancer* 2013;**119**:3952–8. doi:10.1002/cncr.28320 CrossRefPubMedGoogle Scholar.

Hubbard RA, Kerlikowske K, Flowers CI, Yankaskas BC, Zhu W, Miglioretti DL. (2011). Cumulative probability of false-positive recall or biopsy recommendation after 10 years of screening mammography: a cohort study. *Ann Intern Med*. 2011;155:481-92. [PMID: 22007042] doi:10.7326/0003-4819-155-8-201110180-00004.

Kerlikowske K, Zhu W, Hubbard RA, Geller B, Dittus K, Braithwaite D, et al. (2013). Breast Cancer Surveillance Consortium. Outcomes of screening mammography by frequency, breast density, and postmenopausal hormone therapy. *JAMA Intern Med*. 2013;173:807-16. [PMID: 23552817] doi:10.1001/jamainternmed.2013.307.

Christiansen CL, Wang F, Barton MB, et al. (2013). Predicting the cumulative risk of false-positive mammograms. J Natl Cancer Inst 92 (20): 1657-66, 2000. [PubMed].

Kerlikowske K, Zhu W, Hubbard RA, et al.: Outcomes of screening mammography by frequency, breast density, and postmenopausal hormone therapy. JAMA Intern Med 173 (9): 807-16, 2013. [PMC free article] [PubMed].

Jørgensen KJ, Gøtzsche PC, Kalager M, et al. (2017). Breast Cancer Screening in Denmark: A Cohort Study of Tumor Size and Overdiagnosis. *Ann Intern Med* 166 (5): 313-323, 2017. [PubMed].

Autier P, Boniol M, Koechlin A, et al. (2017). Effectiveness of and overdiagnosis from mammography screening in the Netherlands: population based study. *BMJ* 359: j5224, 2017. [PMC free article] [PubMed].

Harding C, Pompei F, Burmistrov D, et al. (2015). Breast Cancer Screening, Incidence, and Mortality Across US Counties. *JAMA Intern* Med 175 (9): 1483-9, 2015. [PubMed].

Miller AB, Wall C, Baines CJ, et al.: Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study: randomised screening trial. BMJ 348: g366, 2014. [PMC free article] [PubMed].

Marmot MG, Altman DG, Cameron DA, Dewar JA, Thompson SG, Wilcox M. (2013). The benefits and harms of breast cancer screening: an independent review. *Br J Cancer*. 2013;108:2205-40. [PMID: 23744281] doi:10.1038/bjc.2013.177.

Independent UK Panel on Breast Cancer Screening. (2012). The benefits and harms of breast cancer screening: an independent review. Lancet. 2012;380:1778-86. [PMID: 23117178] doi:10.1016/S0140-6736 (12)61611-0.

Miller AB, To T, Baines CJ, Wall C. (2002). The Canadian National Breast Screening Study-1: breast cancer mortality after 11 to 16 years of follow-up. A randomized screening trial of mammography in women age 40 to 49 years. *Ann Intern Med*. 2002;137:305-12. [PMID: 12204013] doi:10.7326/0003-4819-137-5_Part_1-200209030-00005.

Puliti D, Duffy SW, Miccinesi G, de Koning H, Lynge E, Zappa M, et al. (2012). EUROSCREEN Working Group. Overdiagnosis in mammographic screening for breast cancer in Europe: a literature review. *J Med Screen*. 2012;19 Suppl 1:42-56. [PMID: 22972810].

Brett J, Bankhead C, Henderson B, Watson E, Austoker J. (2005). The psychological impact of mammographic screening. A systematic review. Psychooncology. 2005;14:917-38. [PMID: 15786514]

Brewer NT, Salz T, Lillie SE. (2007). Systematic review: the long-term effects of false-positive mammograms. *Ann Intern Med*. 2007;146: 502-10. [PMID: 17404352] doi:10.7326/0003-4819-146-7-200704030 -00006.

Hafslund B, Nortvedt MW. (2009). Mammography screening from the perspective of quality of life: a review of the literature. Scand J Caring Sci. 2009;23:539-48. [PMID: 19170959] doi:10.1111/j.1471-6712 .2008.00634.

Hislop TG, Harris SR, Jackson J, Thorne SE, Rousseau EJ, Coldman AJ, et al. (2002). Satisfaction and anxiety for women during investigation of an abnormal screening mammogram. Breast Cancer Res Treat. 2002;76:245-54. [PMID: 12462385].

Brett J, Austoker J. (2001). 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;23:292-300. [PMID: 11873891]

Bond M, Pavey T, Welch K, Cooper C, Garside R, Dean S, et al. (2013). Psychological consequences of false-positive screening mammograms in the UK. Evid Based Med. 2013;18:54-61. [PMID: 22859786] doi:10.1136/eb-2012-100608

Gibson CJ, Weiss J, Goodrich M, Onega T. (2009). False-positive mammography and depressed mood in a screening population: findings from the New Hampshire Mammography Network. *J Public Health (Oxf). 2009;31:554-60. [PMID: 19574274] doi:10.1093/pubmed /fdp064*

Keyzer-Dekker CM, De Vries J, van Esch L, Ernst MF, Nieuwenhuijzen GA, Roukema JA, et al. (2012). Anxiety after an abnormal screening mammogram is a serious problem. Breast. 2012;21:83-8. [PMID: 21924905] doi:10.1016/j.breast.2011.08.137

Brodersen J, Siersma VD. (2013). Long-term psychosocial consequences of false-positive screening mammography. *Ann Fam Med*. 2013;11: 106-15. [PMID: 23508596] doi:10.1370/afm.1466

Tosteson AN, Fryback DG, Hammond CS, Hanna LG, Grove MR, Brown M, et al. (2014). Consequences of false-positive screening mammograms. *JAMA Intern Med*. 2014;174:954-61. [PMID: 24756610] doi: 10.1001/jamainternmed.2014.981

Espasa R, Murta-Nascimento C, Baye´ s R, Sala M, Casamitjana M, Macia` F, et al. (2012). The psychological impact of a false-positive screening mammogram in Barcelona. *J Cancer Educ*. 2012;27:780-5. [PMID: 22477233] doi:10.1007/s13187-012-0349-9

Schou Bredal I, Kåresen R, Skaane P, Engelstad KS, Ekeberg Ø (2013). Recall mammography and psychological distress. Eur J Cancer. 2013;49:805-11. [PMID: 23021930] doi:10.1016/j.ejca.2012.09.001

Hafslund B, Espehaug B, Nortvedt MW. (2012). Effects of false-positive results in a breast screening program on anxiety, depression and health-related quality of life. *Cancer Nurs*. 2012;35:E26-34. [PMID: 22067696] doi:10.1097/NCC.0b013e3182341ddb

Fitzpatrick P, Fleming P, O'Neill S, Kiernan D, Mooney T. (2011). Falsepositive mammographic screening: factors influencing reattendance over a decade of screening. *J Med Screen*. 2011;18: 30-3. [PMID: 21536814] doi:10.1258/jms.2010.010104

Klompenhouwer EG, Duijm LE, Voogd AC, den Heeten GJ, Strobbe LJ, Louwman MW, et al. (2014). Re-attendance at biennial screening mammography following a repeated false positive recall. Breast Cancer Res Treat. 2014;145:429-37. [PMID: 24748569] doi:10.1007 /s10549-014-2959-x

Maxwell AJ, Beattie C, Lavelle J, Lyburn I, Sinnatamby R, Garnett S, et al. (2013). The effect of false positive breast screening examinations on subsequent attendance: retrospective cohort study. J Med Screen. 2013;20:91-8. [PMID: 24009091] doi:10.1177/0969141313499147.

Sandin B, Chorot P, Valiente RM, et al. (2002). Adverse psychological effects in women attending a second-stage breast cancer screening. J Psychosom Res 52 (5): 303-9, 2002. [PubMed].

Armstrong K, Moye E, Williams S, Berlin JA, Reynolds EE. (2007). Screening mammography in women 40 to 49 years of age: a systematic review for the American College of Physicians. *Ann Intern Med*. 2007;146:516-26. [PMID: 17404354] doi:10.7326/0003-4819-146-7 -200704030-00008.

Whelehan P, Evans A, Wells M, Macgillivray S. (2013). The effect of mammography pain on repeat participation in breast cancer screening: a systematic review. Breast. 2013;22:389-94. [PMID: 23541681] doi:10.1016/j.breast.2013.03.003.

Miller D, Livingstone V, Herbison P. (2008). Interventions for relieving the pain and discomfort of screening mammography. Cochrane Database Syst Rev. 2008:CD002942. [PMID: 18254010] doi:10.1002 /14651858.CD002942.pub2.

Miglioretti DL, Lange J, van den Broek JJ, et al. (2016). Radiation-Induced Breast Cancer Incidence and Mortality From Digital Mammography Screening: A Modeling Study. Ann Intern Med 164 (4): 205-14, 2016. [PMC free article] [PubMed].

Hendrick RE. (2010). Radiation doses and cancer risks from breast imaging studies. Radiology. 2010;257:246-53. [PMID: 20736332] doi:10 .1148/radiol.10100570.

Yaffe MJ, Mainprize JG. (2011). Risk of radiation-induced breast cancer from mammographic screening. Radiology. 2011;258:98-105. [PMID: 21081671] doi:10.1148/radiol.10100655.

Pisano, E.D., et al. (2005). Diagnostic Performance of Digital versus Film Mammography for Breast-Cancer Screening. *New England Journal of Medicine*, 353 (17), 1773-1783.

Sechopoulos, I. (2013). A review of breast tomosynthesis. Medical Physics, 40(1)

Skaane, P., et al. (2013). Comparison of digital mammography alone and digital mammography plus tomosynthesis in a population-based screening program. *Radiology*, 267(1), 47-56.

Vedantham, S., et al. (2015). Dedicated Cone-Beam Breast CT: Performance Evaluation of a Prototype Clinical System. Scientific Reports, 5, 12643.

Skaane, P., et al. (2013). Comparison of digital mammography alone and digital mammography plus tomosynthsies. *Radiology*.

Sechopoulos, I. (2013). A review of breast tomosynthesis. Part II. *Medical Physics*.

Friedewald, S. M., et al. (2014). Breast cancer screening using tomosynthesis in combination with digital mammography. *JAMA*.

Zuckerman, S. P., et al. (2016). Implementation of synthesized two-dimensional mammography in a population-based screening program. *Radiology*.

Yun, G., Kim, S. M., Yun, B.L., Ahn, H.S., & Jang, M. (2019). Reliability of automated versus handheld breast ultrasound examinations of suspicious breast masses. Ultrasonography, 38(3), 264-271.

Iacob, R., Iacob, E.R., Stoicescu, E.R., et al. (2024). Evaluating the Role of Breast Cancer in Low- and Middle-Income Countries: A Comprehensive Narrative Review. Bioengineering, 11(3), 262.

Catalono, O., Fusco, R., De Muzio, F., et al. (2023). Recent Advances in Ultrasound Breast Imaging: From Industry to Clinical Practice. Diagnostics, 13(5), 980.

Brem, R.F., Lenihan, M.J., Lieberman, J., & Torrente, J. (2015). Screening Breast Ultrasound: Past, Present, and Future. American Journal of Roentgenology, 204(2), 234-240.

Kriege M, Brekelmans CT, Boetes C, et al. (2004). Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. N Engl J Med. 2004;351:427-437. Doi:10.1056/NEJMoa031759. [DOI] [PubMed][Google Scholar].

Tabar L, Yen MF, Vitak B, Chen HH, Smith RA, Duffy SW. (2003). Mammography service screening and mortality in breast cancer patients: 20-years follow-up. Lancet. 2003; 361 (9363):1405-10.

Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. (2018). Global cancer statistics 2018:GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA *Cancer J Clin*. 2018;68(6):394-424.

Vercher-Conejero J.L., Pelegri-Martinez L., Lopez-Aznar D., Cozar-Santiago M.D.P. (2015). Positron Emission Tomography in Breast Cancer. Diagnostics. 2015;5:61-83. Doi:10.3390/diagnostics5010061. [DOI] [PMC free article] [Pubmed] [Google Scholar].

Chen CJ. Lee BF, Yao WJ, et al. (2009). A false positive F-FDG PET/CT scan caused by breast silicone injection. *Korean J Radiol* 2009; 10:194???196. [PubMed] [Google Scholar].

Yanai, A., Itoh, M., Hirakawa, H., Yanai, K. et al. (2018). Newly Developed Positron Emission Mammography (PEM) Device for the Detection of Small Breast Cancer. Tohoku J. Exp. Med: 245,13-19. [Google Scholar] [CrossRef].

Lee, K. (2011). Optical mammography: Diffuse optical imaging of breast cancer. *World Journal of Clinical Oncology*, 2(1), 64.

Poplack, S.P., Park, E-Y., & Ferrara, K.W. (2023). Optical Breast Imaging: A Review of Physical Principles, Technologies, and Clinical Applications. *Journal of Breast Imaging*, 5,520-537.

Kakileti, S.T; Manjunath, G; Madhu, H; Ramprakash, H.V. (2017). Advances in Breast Thermography. In New Perspectives in Breast Imaging, IntechOpen: London, UK; ISBN 978-953-51-3558-6. [Google Scholar].

Lee, K., et al. (2012). Thermography as a screening and diagnostic tool: a systematic review. The New Zealand Medical Journal.

Food and Drug Administration (FDA). (2019). Thermography Machines Are Not a Replacement for Mammograms: FDA Safety Communication.

Molina Healthcare. (2013). Thermography for the Detection of Breast Lesions (MCG-127). Clinical Policy Review.

UCHealth. (2022). Thermography is not FDA-approved as a screening tool for breast cancer. [interview with Dr. Olga Mengin, Harvard-trained breast radiologist].

Covington, M.F., Salmon, S., Weaver, B.D., & Fajardo, L, L. (2024). State-of-the-art for contrast-enhanced mammography. *Bristish Journal of Radiology*, 97(1156), 695-704.

Moffa, G., Galati, F., Maroncelli, R., Rizzo, V., Cicciarelli, F., Pasculli, M., & Pediconi, F. (2023). Diagnostic performance of contrast-enhanced digital mammography versus conventional imaging in women with dense breasts. Diagnostics, 13(15), 2520.

Tari, (2025). Contrast-enhanced mammography in high-dense breasts: a narrative review. Translational Breast Cancer Research.

Barone, A. et al. (2024). ‘‘Evolution of Nuclear Medicine in Breast Cancer: From Scientimammography to Molecular Breast Imaging’’. Journal of Clinical Medicine, 13(4), 1102.

Jadvar, H. (2024). ‘‘Molecular Imaging of Breast Cancer: A Comprehensive Review’’. *American Journal of Roentgenology,* 222(2),145-158.

Nawaz, A. et al. (2023). ‘‘Diagnostic Accuracy of Scintimammography in the Evaluation of Breast Masses’’. Nuclear Medicine Communications, (44(8), 612-619.

BCBSM Medical Policy. (2026). Breast Elastography-Ultrasound or Magnetic Resonance. Blue Cross Blue Shield of Michigan. [Medical Policy Statement].

PMC (PubMed Central). (2026, March). Establishing an evidence-based modern breast MRI program. PMC12900033.

Slyyir Medical Journal. (2026). Differential diagnostic performance of acoustic radiation force implse imaging in small (≤20 mm) breast cancers.

Taylor & Francis. (2025, January). Computational predictions of magnetic resonance acoustic radiation force imaging for breast cancer.

Lee, S.H., Shin, H.J., & Moon, W. K. (2021). Diffusion-Weighted Magnetic Resonance Imaging of the breast: Standardization of image acquision and interpretation. Korean Journal of Radiology, 22(1), 9.

Lo Gullo, R., Partidge, S. C., Shine, H.J., Takur, S.B., & Pinker, K. (2024). Update on DWI for breast cancer diagnosis and treatment monitoring. *American Journal of Roentgenology*, 222.

Mendez, A.M., Fang, L.K., Meriwether, C.H., Batasin, S.J.,Loubrie, S., Rodriguez-Soto, A.E., & Rakow-Penner, R.A. (2022). Diffusion breast MRI: Current standard and emerging techniques. *Frontiers in Oncology*, 12.

Partridge, S.C., & Amornsiripanitch, N. (2017). DWI in the assessment of breast lesions. Topics in Magnetic Resonance Imaging, 26(5), 201-209.

Bahl, M., Baker, J.A., Kinsey, E. N., & Ghate, S.V. (2015). Ductoscopy: A review of the literature and future directions. *Journal of Breast Imaging*, 1(1).

Hery, C., Ferlay, J., Boniol, M., & Autier, P. (2011). Quantification of the risk of breast cancer associated with ductal lavage findings: A meta-analysis. Breast Cancer Research and Treatment, 126(1),1-10.

Khan, S.A., Wiley, E.L., Rodringues, N., Baird, C., Ramakrishnan, R., Nayar, R.,… & Morrow, M. (2004). Ductal lavage findings in women with known breast cancer undergoing modified radical mastectomy. Cancer, 100(9), 1757-1763.

Moncrief, R.M., Nayar, R., Diaz, L.K., Staradub, V.L., Morrow, M., & Khan, S.A. (2005). A comparison of ductal lavage and nipple aspiration for the grade of cytology and immunoreactivity for p53, HER2/neu, and cyclin D1. Cancer, 103(9), 1773-1779.

Waaijer, L., Van Diest, P.J., Verkooijen, H.M., Koning, S.G., & Witkamp, A.J. (2016). The value of ductoscopy in patients with pathological nipple discharge: A systematic review. *European Journal of Surgical Oncology* (EJSO), 42(5), 629-642.

Li, X., et al. (2024). Radiomics analysis combining gray-scale ultrasound and mammography for differentiating breast adenosis from invasive ductal carcinoma. Frontiers in Oncology, 14.

PMC. (2026). Intergrating deep learning and radiomics for precise and radiomics for precise identification of luminal A/B breast cancer subtypes on dynamic contrast-enhanced MRI. PMC12958541.

Preprints.org. (2026). Potential of radiomics to improve diagnostic accuracy of mammograms and personalize patient management in breast cancer. Preprints 202601.0182.

Li, S., Qu, F., Yang, Y., Wang, L., Shen, J., & Shao, Z. (2020). Value of Stereotactic 11-gauge vacuum-assisted breast biopsy in non-palpable suspicious calcifications: An eight-year single institution experience with 587 patients. Gland Surgery, 9(5), 1258-1266.

Pyo, J.-S., Jung, J., Lee, S.G., Kim, N.-Y., &Kang, D.-W. (2020). Diagnostic accuracy of fine-needle aspiration cytology and core-needle biopsy in the assessment of the axillary lymph nodes in breast cancer – meta-analysis. Diagnostics, 10(9), 717.

Tikku, G., & Umap, P. (2015). Comparative study of core needle biopsy and fine needle aspiration cytology in palpable breast lumps: Scenario in developing nations. Turkisk Journal of Pathology.

AuntMinnieEurope. (2026). Photon-counting CT excels in cancer imaging. Clinical news report on recent oncology imaging advancements.

PMC (Pubmed Central). (2026). Photon-counting detector CT in oncology: a new era of cancer imaging. PMC12824093.

Joensuu H, Lehtimäki T, Holli K, et al. (2004). Risk for distant recurrence of breast cancer detected by mammography screening or other methods. *JAMA* 292 (9): 1064-73, 2004. [PubMed].

Shen Y, Yang Y, Inoue LY, et al. (2005). Role of detection method in predicting breast cancer survival: analysis of randomized screening trials. *J Natl Cancer* Inst 97 (16): 1195-203, 2005. [PubMed].

Wishart GC, Greenberg DC, Britton PD, et al. (2008). Screen-detected vs symptomatic breast cancer: is improved survival due to stage migration alone? Br J Cancer 98 (11): 1741-4, 2008. [PMC free article] [PubMed].

AJMC. (2026). Aligning the Stars: Quality Metrics Must Evolve From Screening Rate to Diagnostic Resolution. *American Journal of Managed Care*.

Frontiers in Public Health. (2025). Developing and validating key performance indicators for breast cancer screening programs: a literature review and Delphi survey. Frontiers.

Newell, M.S., et al. (2025). ACR BI-RADS. *American College of Radiology*. Reston, VA. Porter PL, El-Bastawissi AY, Mandelson MT, et al. (2020). Breast tumor characteristics as predictors of mammographic detection: comparison of interval- and screen-detected cancers. J Natl Cancer Inst 91 (23): 2020-8. [PubMed].

Niraula S, Biswanger N, Hu P, et al. (2020). Incidence, Characteristics, and Outcomes of Interval Breast Cancers Compared With Screening-Detected Breast Cancers. JAMA Netw Open 3 (9): e2018179, 2020. [PMC free article] [PubMed].

Sprague, B.L., Coley, R.Y., et al. (2023). Digital Tomosynthesis versus Digital Mammography Screening Performance on Successive Screening Rounds from the Breast Cancer Surveillance Consortium. Radiology, 307, e223142. [Doi] [PubMed] [Google Scholar].

PMC (2026). Beyond mammography Superior performance of ultrasound in early-onset breast cancer….

PMC (2026, Jan). Agreement Among Breast Cancer Screening Modalities in Breast Density Assessment and Cancer Risk Prediction. *Journal of Clinical Medicine*.

Annals of Internal Medicine (2026). Screening for Breast Cancer in Asymptomatic, Average-Risk Adult Females: A Systematic Review for the U.S. Preventive Services Task Force.

UCLA Health (2026). Imaging Modalities: Specificity and Sensitivity Benchmarks in High-Risk Populations.

Grabler P. Sighoko D, Wang L, Allgood K, Ansell D. (2017). Recall and cancer detection rates for screening mammography: finding the sweet spot. *AJR Am J Roentgenol*; 208(1):208-213. Doi: 10.2214/AJR.15.15987. [PubMed] [Google Scholar].

Lowry, K.P.et al. (2020). Screening performance of digital breast tomosynthesis vs digital mammography in community practice by patient age, screening round, and breast density. *JAMA New*. Open3, e2011792 92020). [Doi] [PubMed] [Google Scholar].

Yoon, J.H. et al. (2023). Standalone AI for breast cancer detection at screening digital mammography and digital breast tomosynthesis: a systematic review and meta-analysis. Radiology307, e222639. [Doi] [PubMed] [Google Scholar].

Soren R. Christiansen, Philippe Autier, Henrik Stovering. (2022). *European Journal of Public Health*, Volume 32, Issue 4, August, Pages 630-635.

World Health Organization (2026, April). Breast Cancer Fact Sheet.

ClinicaTrials.gov (2026). NCT05036096: Cone Beam Breast CT for Breast Cancer Screening. (Ongoing study focused on CBBCT efficacy; notably lacks a PCD-CT comparison arm).

Lachance, C.C., & Horton, J. (2024). ‘‘Photon-Counting CT: High Resolution, Less Radiation.’’ *Canadian Journal of Health Technologies*. (Discusses potential dose benefits over conventional CT/CBCT but identifies the lack of large-scale comparative RCTs as a primary limitation).

Pace, L.E., & Keating, N.L. (2014). A Systematic Assessment of the Benefits and Risks to Guide Breast Cancer Screening Decisions. *JAMA*.

Marmot, M.G., et al. (2013). The benefits and harms of breast cancer screening: an independent review. *British Journal of Cancer*.

Journal of Clinical Oncology (2026): Genomic assay utility in Node-Positive (N1) Disease. Discusses the reduction of chemotherapy in postmenpausal Stage 2 patients. https://www.verywellhealth.com/stages-of-breast-cancer-8362458).