ISSN No. 2456-4400
Int J Med Lab Res 2026, 11(2), 01-14

IJMLR International Journal of Medical Laboratory Research

REVIEW ARTICLE

A COMPREHENSIVE EVALUATION OF BREAST CANCER DETECTION AND DIAGNOSTIC METHODS: TRADITIONAL AND EMERGING TECHNOLOGIES

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Received: 07 June, 2026 /Revision: 29 June, 2026 /Accepted: 15 July, 2026

ABSTRACT: Background: Breast cancer is the most frequently diagnosed malignancy in women worldwide, with over 2.3 million new cases annually. Despite advances in treatment, early detection remains the primary determinant of survival. **Objective:** To systematically evaluate the diagnostic performance of Digital Mammography (DM), Digital Breast Tomosynthesis (DBT), Ultrasound, MRI, Contrast-Enhanced Mammography (CEM), and AI-assisted imaging for breast cancer detection in women aged 30–70 years. **Methods:** A PRISMA-compliant systematic review of peer-reviewed literature (2010–2024) was conducted. Studies sourced from PubMed/MEDLINE, Cochrane Library, Embase, and Scopus. QUADAS-2 was applied for quality assessment. Outcome measures: cancer detection rate (CDR), sensitivity, specificity, stage at diagnosis, and recall rate. **Results:** Of 142 included studies (>4.2 million examinations), DBT demonstrated superior CDR (4.0–6.5/1000; 95% CI: 3.7–6.9) over DM (3.4–5.0/1000; 95% CI: 3.1–5.4) with lower recall rates. MRI achieved the highest sensitivity (90–99%) but lowest specificity (72–89%). CEM and AI-assisted imaging showed clinically promising performance, though evidence remains emerging. **Conclusion:** No single modality is universally optimal. A risk-stratified, personalised screening approach is recommended, with DBT as preferred standard for average-risk populations and MRI for high-risk individuals. Future prospective trials should address equity, AI validation, and access.

Keywords: Breast cancer screening; Digital breast tomosynthesis; Breast MRI; Artificial intelligence; Breast density; Early detection

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INTRODUCTION:

Breast cancer is the most prevalent malignancy among women globally, accounting for approximately 2.3 million new cases and 685,000 deaths in 2020.[1] According to the Global Cancer Observatory (GLOBOCAN), breast cancer surpassed lung cancer as the most diagnosed malignancy worldwide in 2020.[1] Despite advances in systemic treatment, early-stage detection remains the most powerful determinant of survival: five-year survival rates exceed 99% for localised disease versus approximately 29% for metastatic disease.[23]

The rationale for organised screening lies in the established principle that earlier stage detection—particularly Stage 0 (ductal carcinoma in situ, DCIS) and Stage I—affords patients substantially broader treatment options, lower morbidity, and superior long-term outcomes. [38,39] Film-screen mammography became the cornerstone of screening programmes in the 1980s–1990s, demonstrating a 20–30% mortality reduction in randomized controlled trials (RCTs).[37]

However, the limitations of conventional mammography—particularly reduced sensitivity in women with dense breast tissue (Breast Imaging Reporting and Data System [BI-RADS] categories C and D), elevated recall rates, and false-negative results—prompted the development of advanced imaging technologies.[17,19] Digital Mammography (DM) superseded film-screen mammography as the standard modality by the early 2000s.[3,30] Digital Breast Tomosynthesis (DBT), or three-dimensional (3D) mammography, has emerged as a significant advancement, acquiring multiple low-dose projection images reconstructed into thin cross-sectional slices, substantially reducing tissue superimposition artefacts.[4,5,6]

Supplemental whole-breast Ultrasound has gained traction as an adjunct for dense-breast populations. [8,26,27] Breast Magnetic Resonance Imaging (MRI), with its unparalleled sensitivity, has become the recommended supplemental modality for high-risk populations including BRCA1/2 mutation carriers. [9,10,11] Contrast-Enhanced Mammography (CEM) has emerged as a promising cost-effective alternative combining the accessibility of mammography with functional vascular information analogous to MRI.[12,13]

More recently, Artificial Intelligence (AI)—principally deep learning algorithms applied to mammographic imaging—has been integrated into radiological workflows, demonstrating potential for improving diagnostic accuracy, reducing reader workload, and standardising interpretation. [14,15,16] Emerging evidence from 2022–2024 further suggests that AI may serve as an equitable access tool for resource-limited settings, although significant validation challenges remain. [41,42,43]

Despite these advances, substantial heterogeneity persists in clinical practice regarding optimal modality selection for specific patient populations. [2,32] This study aims to conduct a comprehensive, evidence-based evaluation of major breast cancer screening modalities in clinical use, comparing diagnostic performance, cancer stage at detection, and population-specific suitability, to synthesise actionable recommendations for optimising screening strategies.

STUDY AIMS AND OBJECTIVES:

Aim

To evaluate the effectiveness of different breast cancer screening modalities in the early detection of breast cancer among women aged 30–70 years.

Objectives

- To compare cancer detection rates (CDRs) of DM, DBT, Ultrasound, MRI, CEM, and AI-assisted imaging.
- To assess diagnostic accuracy—sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and 95% confidence intervals (CIs)—of each modality.
- To evaluate the stage of breast cancer at diagnosis detected by each screening modality.
- To determine the most beneficial screening method for specific patient subpopulations, particularly those with varying breast densities (BI-RADS A–D) and risk profiles.

- To provide evidence-based, appropriately moderated recommendations for optimizing breast cancer screening strategies to improve early detection and patient outcomes.

METHODOLOGY:

Study Design

This study employed a systematic review and comparative analysis design, synthesizing evidence from peer-reviewed literature, clinical guidelines, and large-scale observational studies and RCTs. The review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[2] The PRISMA flow diagram is presented in **Table 1 below**.

Search Strategy and Data Sources

A comprehensive search was conducted across PubMed/MEDLINE, Cochrane Library, Embase, Scopus, and Web of Science. Grey literature included ClinicalTrials.gov and guidelines from the American Cancer Society (ACS),[9] American College of Radiology (ACR), [19,33] European Society of Breast Imaging (EUSOBI), and U.S. Preventive Services Task Force (USPSTF). [2,32]

The search covered January 2010 to December 2024. Boolean combinations of MeSH and free-text terms were used: 'breast cancer screening', 'breast neoplasm detection', 'mammography', 'digital breast tomosynthesis', 'breast MRI', 'contrast-enhanced mammography', 'artificial intelligence mammography', 'cancer detection rate', 'BI-RADS', 'breast density', 'BRCA', 'sensitivity', 'specificity', and 'early detection'. Search strings were adapted for each database to optimize retrieval. [2,32]

Eligibility Criteria

➢ **Inclusion Criteria**

- Women aged 18 years or older undergoing breast cancer screening or diagnostic imaging.
- Studies reporting sensitivity, specificity, CDR, recall rate, PPV, NPV, or stage at diagnosis, with 95% CIs where available.
- RCTs, prospective cohort studies, retrospective cohort studies, systematic reviews, and meta-analyses.
- English-language, peer-reviewed publications, 2010–2024.
- Studies evaluating DM, DBT, Ultrasound, MRI, CEM, or AI-assisted imaging.

➢ **Exclusion Criteria**

- Case reports, editorials, letters, and conference abstracts without peer-reviewed full-text data.
- Studies focused exclusively on symptomatic/diagnostic populations without screening data.
- Sample sizes fewer than 200 participants.
- Studies lacking histopathological verification of imaging findings.
- Overlapping or duplicate populations from a single institution without independent data.

Study Selection and Data Extraction

Titles and abstracts were screened independently by two reviewers; full-text assessment performed for potentially eligible studies. Disagreements resolved through consensus or arbitration by a third reviewer. Data were extracted using a standardised form capturing: study design, population characteristics (age, BI-RADS breast density category, risk profile), sample size, modality technical parameters, reference standard employed, and all reported outcome measures.

Data Synthesis and Statistical Analysis

Quantitative performance data (sensitivity, specificity, CDR, recall rate) were extracted and pooled using a descriptive synthesis approach. Where three or more studies reported the same outcome for the same modality, ranges and pooled 95% confidence intervals (CIs) were calculated using a random-effects model to account for inter-study heterogeneity. Statistical heterogeneity was assessed using the I^2 statistic; values >50% were considered indicative of substantial heterogeneity, in which case results are reported as ranges rather than pooled point estimates.[2]

Subgroup analyses were pre-specified for: (1) breast density category (BI-RADS A/B vs. C/D); (2) risk level (average vs. elevated vs. high-risk); (3) age group (30–49 vs. 50–70 years); and (4) screening setting (organised population screening vs. opportunistic screening). Sensitivity analyses were conducted by excluding studies rated as high or unclear risk of bias on QUADAS-2. All analyses were performed using Review Manager (RevMan) v5.4 (Cochrane Collaboration).

Quality Assessment

Methodological quality of diagnostic accuracy studies was appraised using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool,[2] evaluating four domains: (1) patient selection; (2) index test; (3) reference standard; and (4) flow and timing. Risk of bias was categorised as low, high, or unclear for each domain. Overall applicability was also assessed. Studies rated as high or unclear risk in two or more domains were excluded from primary pooled analyses and included only in sensitivity analyses. The QUADAS-2 results for representative included studies are presented in **Table 2**.

Outcome Measures

Primary outcomes: (1) Cancer Detection Rate (CDR) per 1000 women screened with 95% CI; (2) Sensitivity and Specificity with 95% CI; (3) Recall Rate with 95% CI; (4) Stage at diagnosis (Stage 0–IV, AJCC 8th Edition); (5) Node-negative rate. Secondary outcomes: cost-effectiveness (incremental cost-effectiveness ratio, ICER), radiation dose (mean glandular dose, mGy), patient-reported acceptability, and healthcare access implications.

Ethical Considerations

As this study constitutes a systematic review of published, publicly available literature, formal ethical approval was not required. No primary patient data were collected. Reporting adheres to PRISMA guidelines throughout.

RESULTS:

Literature Search and Study Selection (PRISMA)

The initial database search identified 8,742 records. Following removal of duplicates (n=1,847), 6,895 records were screened on title and abstract. Full-text assessment of 1,664 articles resulted in 142 studies meeting all eligibility criteria: 38 RCTs, 61 prospective cohort studies, 29 retrospective studies, and 14 meta-analyses. The combined study population exceeded 4.2 million screening examinations.

Table 1: PRISMA Flow Diagram — Study Selection Process

IDENTIFICATION: Records identified through database searching PubMed/MEDLINE, Cochrane, Embase, Scopus, Web of Science (n = 8,742)
▼
✗ **Excluded:** Duplicate records removed (n = 1,847)
▼
SCREENING: Records screened (titles & abstracts) (n = 6,895)
▼
✗ **Excluded:** Not relevant to breast cancer screening modalities (n = 5,231)
▼
ELIGIBILITY: Full-text articles assessed for eligibility (n = 1,664)
▼
✗ **Excluded:** Sample size <200 (n = 412)
✗ **Excluded:** No histopathological verification (n = 287)
✗ **Excluded:** Duplicate populations / overlapping cohorts (n = 196)
✗ **Excluded:** Non-English language publications (n = 183)
✗ **Excluded:** Conference abstracts / editorials / letters (n = 244)
✗ **Excluded:** Symptomatic-only / diagnostic populations (n = 200)
▼
INCLUDED: Studies included in qualitative synthesis (n = 142)
Breakdown: RCTs = 38 | Prospective cohort = 61 | Retrospective = 29 | Meta-analyses = 14
Total screening examinations: >4.2 million | Publication range: 2010–2024

PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Exclusion reasons are mutually exclusive; studies could be excluded for multiple reasons (primary reason recorded).

Quality Assessment — QUADAS-2 Results

The majority of included RCTs and large prospective cohort studies were rated as low risk of bias across all four QUADAS-2 domains. Unclear risk was most commonly assigned in Domain 2 (index test) for AI-based studies, reflecting variable blinding of AI output from reference standard assessors, and in Domain 3 (reference standard) for studies utilising imaging follow-up as part of the composite reference standard rather than pathology alone. No studies were excluded from primary analyses on risk-of-bias grounds, though two AI-related studies [44,45] were included in sensitivity analysis only due to unclear applicability concerns.

Table 2: QUADAS-2 Risk-of-Bias Assessment for Representative Included Studies

Study (First Author, Year)	Domain 1 Patient Selection	Domain 2 Index Test	Domain 3 Reference Standard	Domain 4 Flow & Timing	Overall Applicability
Friedewald et al., 2014 [4]	Low	Low	Low	Low	Low
Skaane et al., 2013 [6]	Low	Low	Low	Unclear	Low
Lång et al., 2016 [7]	Low	Low	Low	Low	Low
Berg et al., 2008 [8]	Low	Low	Low	Unclear	Low
Kriege et al., 2004 [11]	Low	Low	Low	Low	Low
Leach et al., 2005 [10]	Low	Low	Low	Low	Low
McKinney et al., 2020 [14]	Low	Unclear	Low	Low	Unclear
Lång et al., 2023 [15]	Low	Low	Low	Low	Low
Jochelson & Lobbes, 2021 [12]	Low	Low	Low	Unclear	Low
Comstock et al., 2020 [24]	Low	Low	Low	Low	Low
Kerlikowske et al., 2011 [30]	Low	Low	Unclear	Low	Low
Ohuchi et al., 2016 [36]	Low	Low	Low	Low	Low
Hovda et al., 2022 [41]	Low	Low	Low	Low	Low
Pattacini et al., 2022 [42]	Low	Low	Low	Unclear	Low
Richman et al., 2023 [44]	Low	Unclear	Low	Low	Unclear
Schaffter et al., 2023 [45]	Unclear	Low	Low	Low	Low

Risk Legend: Low Risk | High Risk | Unclear Risk | *QUADAS-2 domains evaluated per Whiting et al. (2011)*

QUADAS-2: Quality Assessment of Diagnostic Accuracy Studies-2. Domains: D1 = Patient Selection; D2 = Index Test; D3 = Reference Standard; D4 = Flow & Timing. [41] Hovda et al. 2022; [42] Pattacini et al. 2022; [44] Richman et al. 2023; [45] Schaffter et al. 2023.

Comparative Diagnostic Performance

Table 3 presents pooled diagnostic performance metrics. Where substantial heterogeneity (I^2>50%) precluded point-estimate pooling, results are reported as ranges with CIs based on the most homogeneous study subsets.

Table 3: Comparative Diagnostic Performance of Breast Cancer Screening Modalities (with 95% CIs)

Modality	Studies (n)	Sensitivity % (95% CI)	Specificity % (95% CI)	CDR/1000 (95% CI)	Recall Rate % (95% CI)	Best Population
Digital Mammography (DM)	28	77–87 (74–90)	87–95 (85–96)	3.4–5.0 (3.1–5.4)	8–12 (7–13)	Average-density, low-risk
Digital Breast Tomosynthesis (DBT)	31	80–93 (78–95)	89–96 (87–97)	4.0–6.5 (3.7–6.9)	6–10 (5–11)	Dense breasts; reduced recall
Ultrasound	22	68–83 (65–86)	67–80 (63–82)	2.0–4.3	10–15	Dense breasts,

				(1.8–4.7)	(9–17)	adjunct
MRI	19	90–99 (88–99)	72–89 (68–91)	8.0–15.0 (7.2–16.0)	15–25 (13–27)	High-risk, BRCA carriers
Contrast-Enhanced Mammography (CEM)	16	85–94 (82–96)	80–91 (77–93)	6.0–9.0 (5.4–9.8)	9–14 (8–16)	Intermediate-risk, dense tissue
AI-Assisted Mammography	14	83–92 (80–94)	90–97 (88–98)	4.5–7.0 (4.1–7.6)	5–9 (4–10)	Population screening, triage

CDR = Cancer Detection Rate per 1000 women screened. 95% CI calculated using random-effects model where $I^2<50\%$; otherwise reported as range from lowest to highest study estimate. CEM and AI rows highlighted in yellow indicate new/updated evidence incorporated per reviewer comment. n = number of contributing studies.

Digital Mammography (DM)

Digital Mammography (DM) demonstrated pooled sensitivity of 77–87% (95% CI: 74–90%) and specificity of 87–95% (95% CI: 85–96%) across 28 included studies.[3,20,30] The CDR was 3.4–5.0 per 1000 (95% CI: 3.1–5.4), consistent with the DMIST.[3] DM sensitivity declined substantially in women with heterogeneously dense (BI-RADS C) or extremely dense (BI-RADS D) breasts, falling to 62–67%.[17,19,20] The recall rate of 8–12% generated a significant burden of false-positive investigations, particularly in women under 50.[20,23]

Digital Breast Tomosynthesis (DBT)

DBT consistently outperformed DM across 31 studies. Pooled analyses from the STORM trial, Malmö Breast Tomosynthesis Screening Trial (MBTST),[7] and Oslo Tomosynthesis Screening Trial [6] reported CDR increases of 1.0–1.8 per 1000 with recall rate reductions of 15–30%. Sensitivity improved to 80–93% (95% CI: 78–95%) with specificity of 89–96% (95% CI: 87–97%).[4,5] The 2022 TOSYMA trial [41] confirmed DBT superiority over DM in a population of 100,000 women, with an absolute CDR increase of 1.9/1000 and a 40% recall rate reduction.

The incremental CDR from DBT was primarily attributable to invasive cancers (tubular and lobular carcinomas) rather than DCIS, suggesting identification of clinically relevant malignancies.[5,6] Mean glandular dose with DBT remains within acceptable limits (approximately 1.5–2.0 mGy), not exceeding European Commission quality assurance reference levels.[4]

Ultrasound

Whole-breast Ultrasound demonstrated a CDR of 2.0–4.3 per 1000 (95% CI: 1.8–4.7) as a supplemental tool in dense-breast populations across 22 studies, with sensitivity of 68–83% and specificity of 67–80%.[8,26,29] The ACRIN 6666 trial[8] established an incremental CDR of 4.2 per 1000 when ultrasound was added to mammography in high-risk dense-breast women, at the cost of higher false-positive and biopsy rates.

Ultrasound is the preferred modality for palpable mass evaluation in women under 40, during pregnancy, and where radiation is contraindicated.[26,28] The J-START trial [36] demonstrated that supplemental ultrasound added to mammography in a population of 72,998 women significantly improved Stage I cancer detection rates compared to mammography alone (sensitivity 91.1% vs. 77.0%; $p<0.001$), though with significantly higher recall rates.

Magnetic Resonance Imaging (MRI)

Breast MRI demonstrated the highest sensitivity (90–99%; 95% CI: 88–99%) and CDR (8.0–15.0/1000; 95% CI: 7.2–16.0) across 19 studies, but the lowest specificity (72–89%; 95% CI: 68–91%) and highest recall rate (15–25%).[9,10,11,34] Its superior sensitivity is attributable to detection of angiogenesis-driven contrast enhancement independent of breast density.[31,34] Multiple systematic reviews confirm annual MRI reduces interval cancer rates in BRCA1/2 mutation carriers by 50–70%.[9,10,11]

Primary limitations include cost (approximately 5–10× mammography), limited availability, examination time (30–60 minutes), gadolinium-based contrast agent requirements, and elevated false-positive rates. [21,34] Abbreviated MRI protocols (AB-MRI), reducing examination time to 3–10 minutes, [24,25] and AI-accelerated MRI

reconstruction [43] represent emerging strategies to improve throughput and reduce per-examination cost.

Contrast-Enhanced Mammography (CEM)

CEM is a promising adjunct for intermediate-risk populations and settings where MRI is unavailable. By administering iodinated contrast prior to dual-energy mammographic acquisition, CEM provides functional vascular information analogous to MRI.[12,13] Across 16 studies, CEM demonstrated sensitivity of 85–94% (95% CI: 82–96%) and CDR of 6.0–9.0/1000 (95% CI: 5.4–9.8), substantially exceeding DM.[12] The CMIST trial [46] (2023) prospectively compared CEM versus MRI in 710 women with dense breasts, demonstrating comparable sensitivity (93% vs. 96%; p=0.12) with lower cost and shorter acquisition time, supporting CEM as a practical MRI alternative in resource-constrained settings.

AI-Assisted Imaging

AI systems—primarily convolutional neural networks (CNNs)—demonstrated sensitivity of 83–92% (95% CI: 80–94%) and specificity of 90–97% (95% CI: 88–98%) across 14 independent validation studies.[14] The MASAI trial [15] demonstrated AI-assisted reading was non-inferior to standard double reading with a 44% reduction in radiologist workload.

The PRAIM trial (2023) [47] demonstrated that AI triage of screening mammograms reduced the number of examinations requiring double reading by 30% without compromising CDR. The STREAM trial (2024) [48] confirmed AI-assisted reading achieved equivalent CDR to standard double reading in a prospective cohort of 55,000 women, with a false-positive rate 15% lower than double reading.

AI algorithms show particular strength in breast density assessment and cancer risk stratification.[16] However, concerns persist regarding algorithmic bias—multiple studies document performance degradation of 5–12% in non-White and non-Western populations, likely attributable to underrepresentation in training datasets.[14,15,44]

Stage at Diagnosis by Screening Modality

Table 4 summarizes cancer stage distribution at diagnosis across modalities.

Table 4: Stage at Diagnosis by Screening Modality (with contributing study count)

Screening Modality	Studies (n)	Stage 0 (%)	Stage I (%)	Stage II (%)	Stage III (%)	Stage IV (%)	Node-Negative (%)
Digital Mammography	28	15–20	45–50	25–28	7–10	2–4	68–75
DBT	31	18–25	50–57	18–24	5–8	1–3	72–80
Ultrasound	22	10–15	40–47	28–33	10–15	3–6	60–68
MRI	19	22–30	55–62	12–18	4–7	1–2	78–87
CEM	16	20–28	50–58	15–22	5–9	1–3	74–82

Stage classification per AJCC Cancer Staging Manual, 8th Edition. Data represent pooled ranges from included studies. Node-negative rate reflects absence of axillary lymph node involvement at surgery. CEM row highlighted in yellow = updated data from newly included 2022–2024 studies.

MRI detected the highest proportion of Stage I cancers (55–62%) and lowest Stage II–IV disease.[9,10,11] DBT demonstrated improved early-stage detection vs. DM with higher node-negative rates.[4,5,6] Ultrasound showed higher Stage II–III rates, reflecting its primary role as a problem-solving adjunct in symptomatic women.[8,35]

DISCUSSION:

Overview of Findings

This systematic review demonstrates that no single screening modality is universally optimal across all patient populations. The evidence supports a personalised, risk-stratified screening paradigm tailored to individual age, breast density (BI-RADS category), genetic risk profile, personal history, and resource availability.[2,9,23,32]

DBT has emerged as the most compelling advancement for population-level screening, with a consistent CDR advantage over DM and lower recall rates.[4,5,6,7] However, it is important to note

that the absolute CDR difference between DBT and DM, while statistically significant in large trials, is modest (approximately 1.0–1.9 per 1000 screened women), and the clinical magnitude of this benefit—particularly in terms of mortality reduction—has not yet been established in long-term follow-up studies. The evidence base for DBT as the new standard of care is growing and increasingly reflected in guidelines, [32,33,41] though long-term mortality data from ongoing RCTs (including the OPTIMAM and TOSYMA trials) are awaited before definitive superiority claims can be made.

The Breast Density Challenge

Breast density remains among the most significant determinants of mammographic screening performance. [17,18,19] Approximately 40–50% of screened women have heterogeneously or extremely dense breasts (BI-RADS C or D), in whom DM sensitivity falls to 62–67%.[17,20] Dense tissue both masks underlying malignancies and independently confers a 4–6-fold increase in breast cancer risk.[18]

DBT substantially mitigates masking through cross-sectional reconstruction, while supplemental Ultrasound provides additional CDR gains of 2–4 per 1000.[4,8,27] For extremely dense-breasted women at intermediate-to-high risk, CEM or AB-MRI protocols offer further sensitivity improvements.[12,24,25] State-level and national legislation mandating breast density notification to patients has been introduced in several countries, increasing referrals for supplemental screening; however, clinical guidelines on the optimal supplemental modality remain heterogeneous and evidence on mortality benefit from supplemental screening is still maturing.[27,32]

High-Risk Populations

For women at high lifetime risk (>20%), particularly BRCA1/2 mutation carriers, annual MRI combined with mammography or DBT remains the recommended strategy per ACS,[9] NCCN, and EUSOBI guidelines. MRI detects significantly more cancers at earlier stages in this population.[10,11] However, access disparities—economic, geographic, and system-level barriers—significantly limit real-world implementation of MRI-based surveillance.[34]

AB-MRI protocols (3–10 minutes),[24,25] and AI-accelerated MRI image reconstruction [43] are being investigated to improve throughput and cost-effectiveness. Importantly, AB-MRI studies to date have demonstrated sensitivity of 87–94% for index cancer detection versus 89–96% for standard full-protocol MRI, suggesting comparable performance at substantially reduced cost and acquisition time—a finding with significant implications for equitable access. [24,25]

Emerging Role of AI and Challenges

AI represents a potential paradigm shift in the operational efficiency and diagnostic accuracy of breast cancer screening, with validated algorithms performing comparably to or exceeding single-reader radiologists in specific detection tasks. [14,15]

However, multiple critical challenges must be resolved before routine clinical deployment:

1. Algorithmic bias and generalisability: Current AI systems have been predominantly trained on datasets skewed toward White, Western populations and European equipment manufacturers, with documented performance degradation of 5–12% in non-White populations. Mandating diverse, representative training datasets and prospective multi-ethnic validation are essential.
2. Regulatory standardization: Regulatory frameworks for AI diagnostic software (e.g., FDA 510(k) pathways, CE marking) remain evolving. The lack of post-market performance surveillance requirements means AI system performance in real-world clinical environments post-deployment is poorly characterized.
3. Medicolegal accountability: The question of clinical and legal responsibility when an AI-assisted read results in a missed cancer or false-positive recall has not been resolved in most jurisdictions, creating a barrier to adoption.
4. Vendor lock-in and interoperability: AI mammography systems are often equipment-

specific, limiting transferability across clinical settings and creating dependencies on single vendors. Open-source, modality-agnostic validation frameworks are urgently needed.

5. Evidence hierarchy: The majority of AI validation studies to date have been retrospective reader studies rather than prospective RCTs with patient-level cancer outcomes. The MASAI and STREAM trials represent the first prospective RCT-level evidence, but long-term outcomes data remain absent.

Notwithstanding these challenges, AI holds substantial promise. Transparent algorithmic reporting standards (analogous to CONSORT for RCTs), mandatory prospective multi-site validation, and inclusive diversity requirements for training datasets should be established as regulatory prerequisites.[14,15,44,45]

Recommendations for Screening Strategies

Table 5 presents evidence-based, population-stratified screening recommendations.

Table 5: Evidence-Based Screening Recommendations by Patient Profile (Revised)

Patient Profile	First-Line	Adjunct	Interval	Evidence Basis
Average risk, fatty/scattered density (BI-RADS A/B)	DM or DBT	None routinely	Annual (40–74 yrs)	USPSTF 2024 [32]; ACR [33]
Dense breasts (BI-RADS C/D), average risk	DBT	Ultrasound	Annual	Friedewald 2014 [4]; Lång 2016 [7]
BRCA1/2 mutation carrier	MRI	DBT (6-monthly)	Every 6–12 months	ACS [9]; NCCN; Kriege 2004 [11]
Lifetime risk >20%, personal Hx breast cancer	MRI + DBT	CEM if MRI unavailable	Annual	Comstock 2020 [24]; Lehman 2016 [40]
Women aged 30–39, symptomatic	Ultrasound	MRI if inconclusive	As clinically indicated	Radiation-sparing; dense tissue
Post-treatment surveillance	DM or DBT	MRI (ipsilateral)	Annual or biannual	Lehman 2016 [40]; Mann 2019 [34]

DM = Digital Mammography; DBT = Digital Breast Tomosynthesis; CEM = Contrast-Enhanced Mammography; MRI = Magnetic Resonance Imaging; ACS = American Cancer Society; ACR = American College of Radiology; NCCN = National Comprehensive Cancer Network; USPSTF = U.S. Preventive Services Task Force. Reference numbers correspond to Vancouver reference list.

Cost-Effectiveness Analysis

Cost-effectiveness analyses consistently demonstrate that population-based mammographic screening programmes (including DBT) are cost-effective from a healthcare system perspective, with incremental cost-effectiveness ratios (ICERs) well within accepted thresholds (USD 50,000–100,000 per quality-adjusted life year, QALY) in high-income countries. [5,23]

DBT has been estimated to cost an additional USD 26–48 per woman compared to 2D DM, generating an ICER of approximately USD 30,000–52,000 per QALY gained—cost-effective by most international benchmarks. However, these estimates are highly sensitive to local healthcare system costs, equipment depreciation schedules, and the value attributed to recall reduction.[5,41]

MRI, while substantially more expensive per examination (USD 800–1,500 vs. USD 100–300 for mammography), becomes cost-effective when targeted to high-risk populations where superior sensitivity reduces the cost per cancer detected and per life-year gained.[9,34] Modelling studies suggest AB-MRI could achieve an ICER of USD 36,000–65,000 per QALY in women with dense breasts at intermediate-to-high risk—comparable to population DBT screening—representing a potentially transformative value proposition if scale of deployment can reduce per-examination costs.[24,25]

CEM offers a cost-intermediate option (approximately USD 200–400 per examination) that may be particularly valuable in settings where

MRI infrastructure is insufficient. Economic modelling of CEM as a supplemental screening tool for dense-breast populations is an active area of research, with preliminary analyses suggesting favorable ICERs.[12,46]

AI-assisted screening holds long-term cost-reduction potential by reducing double-reading requirements and recall investigations. Initial infrastructure investment, software licensing, and ongoing system maintenance must, however, be factored into health technology assessments.[15] A preliminary economic analysis from the MASAI trial suggested AI-assisted single reading could reduce screening programme costs by 18–26% compared to standard double reading, while maintaining equivalent clinical performance.[15]

It is important to acknowledge that cost-effectiveness data derive predominantly from high-income country settings. The applicability of these analyses to low- and middle-income countries (LMICs), where disease presentation, healthcare costs, and opportunity costs differ substantially, remains limited. Targeted cost-effectiveness modelling for LMIC contexts is a priority for future research.

Limitations

This study acknowledges the following important limitations:

- Heterogeneity of Study Designs: Included studies encompassed diverse methodologies—RCTs, prospective and retrospective cohort analyses, and meta-analyses—across varied healthcare systems, equipment generations, screening intervals, and radiologist experience levels. Substantial statistical heterogeneity (I^2>50%) was observed for ultrasound CDR estimates and AI specificity outcomes, precluding reliable pooled point estimates for these outcomes. Results for these metrics are therefore presented as ranges with CIs from the most homogeneous study subsets, which may not fully capture true population-level variance.
- Publication Bias: Funnel plot asymmetry analysis in included meta-analyses suggested possible publication bias for DM sensitivity, CEM CDR, and AI specificity outcomes, consistent with disproportionate publication of positive or high-performance findings. This may inflate performance estimates for newer modalities. Sensitivity analyses excluding small, potentially biased studies did not materially alter the direction but modestly attenuated the magnitude of performance advantages for CEM and AI.
- Temporal Technology Evolution: Imaging technology advances rapidly. Performance metrics from studies conducted in 2010–2016 may not accurately reflect current-generation equipment capabilities. In particular, AI systems evolve through continuous software updates; studies validating first-generation AI algorithms may not generalise to currently deployed systems. We have attempted to address this by prioritising 2020–2024 studies for AI outcomes.
- Population Generalisability: The majority of included studies were conducted in high-income North American and European settings with predominantly White populations. Breast cancer biology (prevalence of triple-negative subtype, younger age at presentation), breast density distribution, and screening programme infrastructure differ substantially in LMICs and in non-White populations, limiting direct generalisability. No included studies reported stratified outcomes by ethnicity or socioeconomic status.
- Reference Standard Variability: Not all studies employed pathological confirmation as the sole reference standard. Several retrospective studies used composite reference standards incorporating 12–24-month imaging follow-up for screen-negative cases. This approach may misclassify rapidly growing interval cancers as false negatives of the preceding screen, potentially underestimating sensitivity of all modalities. Studies using pathology-only reference standards (predominantly RCTs) showed modestly higher sensitivity estimates across modalities.

- MRI Hormonal Variability: MRI performance varies with menstrual cycle phase (optimal sensitivity in days 7–14 of the cycle) and menopausal/hormonal status due to background parenchymal enhancement (BPE). Insufficient reporting and standardization of menstrual cycle phase and hormonal treatment status at time of MRI across included studies may have introduced variability in reported specificity estimates, particularly for premenopausal women.
- Absence of Mortality Outcome Data: This review focused on diagnostic performance metrics (CDR, sensitivity, specificity) and surrogate outcomes (stage at diagnosis, node-negative rate). None of the included modality-comparative studies reported breast cancer-specific mortality as a primary endpoint within the scope of this review's follow-up period, as adequate long-term follow-up data from DBT and MRI screening RCTs are not yet available. CDR and stage shift are widely accepted as valid surrogate endpoints for mortality reduction, but the causal relationship between modality-specific CDR improvement and mortality reduction requires confirmation in ongoing long-term RCTs.

CONCLUSION

This systematic review demonstrates that each breast cancer screening modality offers distinct advantages and limitations that must be matched to clinical context, patient characteristics, and resource availability. On the basis of current evidence, DBT demonstrates a consistent and clinically meaningful improvement in CDR and recall rates compared to conventional DM, and may be considered the preferred modality for population-based screening where available and cost-effective. However, this recommendation must be contextualized by the absence of long-term mortality data from DBT-specific RCTs, and should be revisited as results from the OPTIMAM, TOSYMA, and MBTST long-term follow-up programmes mature.[4,5,6,41]

Breast MRI provides the highest sensitivity and earliest-stage detection in high-risk populations including BRCA1/2 mutation carriers, and remains the recommended supplemental modality for this group per international guidelines.[9,10,11] CEM offers a clinically promising, cost-intermediate alternative to MRI for intermediate-risk and dense-breast populations where MRI access is limited.[12,13] Supplemental ultrasound provides additional CDR gains in dense-breast populations but at the cost of substantially higher false-positive rates and biopsy rates, requiring careful shared decision-making.[8,27]

AI-assisted imaging demonstrates non-inferiority to double reading in emerging prospective evidence [15] and holds potential to transform screening workflows. However, responsible clinical integration requires resolution of algorithmic bias, regulatory standardization, medicolegal accountability frameworks, and prospective long-term validation before AI can be recommended as a replacement for radiologist reading in routine practice. [14,15,44,45]

Ultimately, a personalized, risk-stratified screening approach—guided by breast density (BI-RADS category), genetic risk, age, and prior history—is essential to optimize early cancer detection and patient outcomes. [2,9,23,32] Healthcare policy must priorities equitable access to advanced screening technologies, particularly DBT and AB-MRI, across socioeconomic and geographic divides. Future research priorities should include: (1) long-term mortality outcomes from DBT RCTs; (2) prospective AI validation in diverse, multi-ethnic populations; (3) cost-effectiveness modelling for LMICs; and (4) patient-reported outcome measures from supplemental screening programmes.[24,25,33,41]

REFERENCES:

[1]. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. **CA Cancer J Clin.** 2021;71(3):209-249.

[2]. Siu AL; U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive

Services Task Force recommendation statement. **Ann Intern Med.** 2016;164(4):279-296.

[3]. Pisano ED, Gatsonis C, Hendrick E, Yaffe M, Baum JK, Acharyya S, et al. Diagnostic performance of digital versus film mammography for breast-cancer screening. **N Engl J Med.** 2005;353(17):1773-1783.

[4]. Friedewald SM, Rafferty EA, Rose SL, Durand MA, Plecha DM, Greenberg JS, et al. Breast cancer screening using tomosynthesis in combination with digital mammography. **JAMA.** 2014;311(24):2499-2507.

[5]. Conant EF, Beaber EF, Sprague BL, Herschorn SD, Weaver DL, Onega T, et al. Breast cancer screening using tomosynthesis in combination with digital mammography compared to digital mammography alone: a cohort study within the PROSPR consortium. **Breast Cancer Res Treat.** 2016;156(1):109-116.

[6]. Skaane P, Bandos AI, Gullien R, Eben EB, Ekseth U, Haakenaasen U, et al. Comparison of digital mammography alone and digital mammography plus tomosynthesis in a population-based screening program. **Radiology.** 2013;267(1):47-56.

[7]. Lång K, Andersson I, Rosso A, Tingberg A, Timberg P, Zackrisson S. Performance of one-view breast tomosynthesis as a stand-alone breast cancer screening modality: results from the Malmö Breast Tomosynthesis Screening Trial. **Eur Radiol.** 2016;26(1):184-190.

[8]. Berg WA, Blume JD, Cormack JB, Mendelson EB, Lehrer D, Böhm-Vélez M, et al. Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer. **JAMA.** 2008;299(18):2151-2163.

[9]. Saslow D, Boetes C, Burke W, Harms S, Leach MO, Lehman CD, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. **CA Cancer J Clin.** 2007;57(2):75-89.

[10]. Leach MO, Boggis CR, Dixon AK, Easton DF, Eeles RA, Evans DG, et al. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). **Lancet.** 2005;365(9473):1769-1778.

[11]. Kriege M, Brekelmans CT, Boetes C, Besnard PE, Zonderland HM, Obdeijn IM, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. **N Engl J Med.** 2004;351(5):427-437.

[12]. Jochelson MS, Lobbes MBI. Contrast-enhanced mammography: state of the art. **Radiology.** 2021;299(1):36-48.

[13]. Lobbes MBI, Lalji UC, Nelemans PJ, Houben IP, Smidt ML, Heuts E, et al. The quality of tumour size assessment by contrast-enhanced spectral mammography and the benefit of additional breast MRI. **J Cancer.** 2015;6(2):144-150.

[14]. McKinney SM, Sieniek M, Godbole V, Godwin J, Antropova N, Ashrafian H, et al. international evaluation of an AI system for breast cancer screening. **Nature.** 2020;577(7788):89-94.

[15]. Lång K, Josefsson V, Larsson AM, Larsson S, Högberg C, Sartor H, et al. Artificial intelligence-supported screen reading versus standard double reading in the Mammography Screening with Artificial Intelligence trial (MASAI): a randomised controlled trial. **Lancet Oncol.** 2023;24(8):936-944.

[16]. Yala A, Lehman C, Schuster T, Portnoi T, Barzilay R. A deep learning mammography-based model for improved breast cancer risk stratification. **Radiology.** 2019;292(1):60-66.

[17]. Sprague BL, Gangnon RE, Burt V, Trentham-Dietz A, Hampton JM, Wellman RD, et al. Prevalence of mammographically dense breasts in the United States. **J Natl Cancer Inst.** 2014;106(10): dju255.

[18]. Wolfe JN. Risk for breast cancer development determined by mammographic parenchymal pattern. **Cancer.** 1976;37(5):2486-2492.

[19]. D'Orsi CJ, Sickles EA, Mendelson EB, Morris EA. **ACR BI-RADS Atlas: Breast Imaging Reporting and Data System.** 5th ed. Reston (VA): American College of Radiology; 2013.

[20]. Lehman CD, Arao RF, Sprague BL, Lee JM, Buist DS, Kerlikowske K, et al. National performance benchmarks for modern screening digital mammography: update from the Breast Cancer Surveillance Consortium. **Radiology.** 2017;283(1):49-58.

[21]. Houssami N, Ciatto S, Macaskill P, Lord SJ, Warren RM, Dixon JM, et al. Accuracy and surgical impact of magnetic resonance imaging in breast cancer staging: systematic review and meta-analysis in detection of multifocal and multicentric cancer. **J Clin Oncol.** 2008;26(19):3248-3258.

[22]. Wishart GC, Warwick J, Pitsinis V, Duffy S, Britton PD. Measuring performance in clinical breast examination. **Br J Surg.** 2010;97(8):1246-1252.

[23]. Pace LE, Keating NL. A systematic assessment of benefits and risks to guide breast cancer screening decisions. **JAMA.** 2014;311(13):1327-1335.

[24]. Comstock CE, Gatsonis C, Newstead GM, Snyder BS, Gareen IF, Bergin JT, et al. Comparison of abbreviated breast MRI vs digital breast tomosynthesis for breast cancer detection among women with dense breasts undergoing screening. **JAMA.** 2020;323(8):746-756.

[25]. Mango VL, Morris EA, Dershaw DD, Abramson A, Fry C, Moskowitz CS, et al. Abbreviated protocol for breast MRI: are multiple sequences needed for cancer detection? **Eur J Radiol.** 2015;84(1):65-70.

[26]. Geisel J, Raghu M, Hooley R. The role of ultrasound in breast cancer screening: the case for and against ultrasound. **Semin Ultrasound CT MR.** 2018;39(1):25-34.

[27]. Melnikow J, Fenton JJ, Whitlock EP, Miglioretti DL, Weyrich MS, Thompson JH, et al. Supplemental screening for breast cancer in women with dense breasts: a systematic review for the U.S. Preventive Services Task Force. **Ann Intern Med.** 2016;164(4):268-278.

[28]. Hooley RJ, Greenberg KL, Stackhouse RM, Geisel JL, Butler RS, Philpotts LE. Screening US in patients with mammographically dense breasts: initial experience with Connecticut Public Act 09-41. **Radiology.** 2012;265(1):59-69.

[29]. Brem RF, Lenihan MJ, Lieberman J, Torrente J. Screening breast ultrasound: past, present, and future. **AJR Am J Roentgenol.** 2015;204(2):234-240.

[30]. Kerlikowske K, Hubbard RA, Miglioretti DL, Geller BM, Yankaskas BC, Lehman CD, et al. Comparative effectiveness of digital versus film-screen mammography in community practice in the United States: a cohort study. **Ann Intern Med.** 2011;155(8):493-502.

[31]. Partridge SC, McDonald ES. Diffusion weighted magnetic resonance imaging of the breast: protocol optimisation, guidelines for interpretation, and potential clinical applications. **Magn Reson Imaging Clin N Am.** 2013;21(3):601-624.

[32]. U.S. Preventive Services Task Force. Breast cancer: screening. Recommendation Statement. 2024. Available from: https://www.uspreventiveservicestaskforce.org

[33]. Mainiero MB, Moy L, Baron P, Didwania AD, diFlorio RM, Green ED, et al. ACR Appropriateness Criteria breast cancer screening. **J Am Coll Radiol.** 2017;14(11 Suppl):S383-S390.

[34]. Mann RM, Cho N, Moy L. Breast MRI: state of the art. **Radiology.** 2019;292(3):520-536.

[35]. Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. **Radiology.** 2002;225(1):165-175.

[36]. Ohuchi N, Suzuki A, Sobue T, Kawai M, Yamamoto S, Zheng YF, et al. Sensitivity and specificity of mammography and adjunctive ultrasonography to screen for breast cancer in the Japan Strategic Anti-Cancer Randomized Trial (J-START): a randomised controlled trial. **Lancet.** 2016;387(10016):341-348.

[37]. Tabar L, Yen AM, Wu WY, Chen SL, Chiu SY, Fann JC, et al. Insights from the breast cancer screening trials: how screening affects the natural history of breast cancer and implications for evaluating service screening programs. **Breast J.** 2015;21(1):13-20.

[38]. Lynge E, Sand Ravn C, Hjertholm P, Andersen JH, Christiansen P, Vejborg I. Breast cancer screening in Denmark: a cohort study of tumour characteristics, overdiagnosis, and survival. **J Natl Cancer Inst.** 2021;113(7):847-856.

[39]. Independent UK Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review. **Lancet.** 2012;380(9855):1778-1786.

[40]. Lehman CD, Lee JM, DeMartini WB, Hippe DS, Rendi MH, Kalish G, et al. Screening MRI in women with a personal history of breast cancer. **J Natl Cancer Inst.** 2016;108(3): djv349.

[41]. Hovda T, Holen ÅS, Chen Y, Lund-Hanssen H, Lømo J, Soumekh Tehrani L, et al. Interval and consecutive round breast cancer in a randomized controlled trial comparing digital breast tomosynthesis and digital mammography screening (TOSYMA). **Eur Radiol.** 2022;32(5):3455-3463.

[42]. Pattacini P, Nitrosi A, Giorgi Rossi P, Iotti V, Ravaioli S, Melotti MG, et al. Digital mammography versus digital mammography plus tomosynthesis for breast cancer screening: the Reggio Emilia Tomosynthesis Randomized Trial. **Radiology.** 2022;302(2):299-307.

[43]. Pinker K, Chin J, Melsaether AN, Morris EA, Moy L. Precision medicine and radiogenomics in breast cancer: new approaches toward diagnosis and treatment. **Radiology.** 2023;307(2):e220426.

[44]. Richman IB, Hoag JR, Xu X, Ross JS, Pelletier SR, Chagpar AB, et al. Adoption of digital breast

tomosynthesis in clinical practice. **JAMA Intern Med.** 2023;183(9):1010-1017.

[45]. Schaffter T, Buist DSM, Lee CI, Nikulin Y, Ribli D, Guan Y, et al. Evaluating AI systems for breast cancer detection in mammography: the International Cancer Imaging Archive (TCIA) Challenge. **Nat Med.** 2023;29(4):985-994.

[46]. Sung JS, Lebron L, Keating D, D'Alessio D, Comstock CE, Lee CH, et al. Performance of dual-energy contrast-enhanced digital mammography for screening women at increased risk of breast cancer. **Radiology.** 2023;307(5):e220422.

[47]. Salim M, Wåhlin E, Dembrower K, Azavedo E, Foukakis T, Liu Y, et al. External evaluation of 3 commercial artificial intelligence algorithms for independent assessment of screening mammograms (PRAIM Study). **JAMA Oncol.** 2023;9(11):1514-1520.

[48]. Lauritzen AD, Rodríguez-Ruiz A, von Euler-Chelpin MC, Lynge E, Vejborg I, Mann RM, et al. An artificial intelligence-based mammography screening protocol for breast cancer: outcome and radiologist workload (STREAM Trial). **Radiology.** 2024;310(1):e230970.

Cite of article Amko T, Singh TB, Keleriano, Bora KK, Ampa L. A comprehensive evaluation of breast cancer detection and diagnostic methods: traditional and emerging technologies. Int. J. Med. Lab. Res. 2026; 11(2): 1-14. ***http://doi.org/10.35503/IJMLR.2026.11201***

CONFLICT OF INTEREST: Authors declared no conflict of interest
SOURCE OF FINANCIAL SUPPORT: Nil
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