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Contemporary Approaches to Breast Cancer Management: An Evidence Synthesis Guiding Clinical Practice and Patient Care.

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Original Research Article

Abstract

Background: Breast cancer remains the most frequently diagnosed cancer globally, though its management varies significantly across regions. This systematic review integrates recent evidence across six domains to delineate best practices for comprehensive care.

Method: A systematic literature search was conducted across MEDLINE, Embase, Cochrane Library, Web of Science, and CINAHL (2010–2024), in line with PRISMA 2020 reporting standards. Eligible studies were screened by two reviewers. Quality was assessed using validated tools appropriate to study design, including Cochrane RoB 2.0, Newcastle-Ottawa Scale, AMSTAR-2, and AGREE II. Evidence was synthesized narratively and appraised using the GRADE framework.

Results: Key advances include the application of molecular profiling in tailoring therapy, treatment de-intensification for selected low-risk groups, escalation for aggressive subtypes, and improved multidisciplinary decision-making. Hypofractionated radiotherapy has shown comparable efficacy with reduced side effects, while genomic testing helps identify patients who can safely avoid chemotherapy. Targeted therapies have substantially improved outcomes in specific subgroups. Unique strategies are needed for elderly, male, and pregnant patients, and oligometastatic disease is increasingly approached with curative intent.

Conclusion: Precision medicine has redefined breast cancer treatment, emphasizing individualized and integrated multidisciplinary strategies. Implementation frameworks that minimize disparities and maximize both survival and quality of life outcomes are necessary to put this evidence into practice.

Keywords: Breast neoplasms; evidence-based oncology; multidisciplinary care; precision medicine; adjuvant therapy; clinical guidelines; patient-centered care.

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INTRODUCTION

The treatment of breast cancer has changed significantly over the last few decades.

Once managed predominantly with surgery, it is now treated through integrated, multidisciplinary strategies. This change is a reflection of our increasing knowledge of tumour biology, especially the discovery of molecular subtypes that affect prognosis and treatment options. Globally, breast cancer accounts for more than 2.3 million new diagnoses each year, representing approximately 12% of all cancers and remaining a leading cause of cancer-related death among women.[1] Despite this progress, clinicians continue to encounter complex decisions throughout the care continuum, from early detection to advanced disease, often without unified guidance on incorporating rapidly evolving evidence. The burden is unevenly distributed, with incidence, survival, and mortality showing wide regional variation.[2] These differences highlight the interplay of tumor biology, healthcare accessibility, and socioeconomic factors, underscoring the need for adaptable but evidence-driven approaches. The prevalence is rising due to increased incidence and better treatment outcomes. Mortality rates are decreasing in most Western nations, driven by improved therapy and earlier detection.[3] Innovations in diagnostic imaging, refinements in surgical techniques, and the availability of targeted systemic therapies have transformed clinical practice.[4] However, the pace of development has created challenges in unifying management strategies. Existing reviews frequently focus on specific elements, like systemic therapy, radiotherapy, or surgery, without incorporating them into a comprehensive framework. While rapid technological progress has significantly advanced oncologic capabilities, sharpening diagnostics, refining minimally invasive surgical techniques, and expanding targeted systemic therapies, the prevailing literature and clinical guidance remain largely fragmented. Existing reviews and specialty-specific guidelines predominantly focus on isolated domains such as surgical approaches, radiotherapy, or systemic therapy, mirroring the subspecialization within oncology.[5-7] This compartmentalization fails to adequately address the critical interconnections between these fields or considerations for special populations. Consequently, despite an abundance of specialized knowledge, integrating diagnostics, surgery, radiation, systemic therapy, and tailored care for individual patient circumstances into a coherent, practical continuum remains a significant challenge for clinicians at the point of care, misaligning with the integrated reality required for optimal patient management. The current review fills this gap by synthesizing current research in six crucial areas: (1) Core principles; (2) Imaging modalities; (3) Surgical techniques; (4) Adjuvant therapies; (5) Management of special populations; and (6) Recurrent or advanced disease.

The three goals are to highlight areas of agreement and disagreement, summarize the best available data, and offer a comprehensive set of suggestions that physicians, researchers, and legislators can implement to improve patient outcomes. By addressing these goals, the review gives policymakers insights for healthcare optimization, researchers a basis for future studies, and clinicians evidence-based decision-making tools.

METHODS

Research Strategy

The literature search was developed iteratively in collaboration with an oncology-trained medical librarian. Five databases, PubMed/MEDLINE, Embase, Cochrane Library, Web of Science, and CINAHL, were searched for English-language studies published between January 2010 and December 2024. Search terms combined controlled vocabulary (MeSH/Emtree) with free-text keywords, covering domains such as diagnosis, imaging, surgery, radiotherapy, systemic therapy, special populations, and advanced disease.

The review adhered to PRISMA 2020 reporting standards.[8] Additional references were identified by scanning the bibliographies of included papers and consulting field experts. Grey literature was also explored using OpenGrey, ClinicalTrials.gov, and recent proceedings of major oncology societies

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(ASCO, ESMO, ASTRO, SSO) to mitigate publication bias.

Eligibility Criteria

Study selection was guided by the

PICOS framework:

-Population: Adult patients (≥18 years) diagnosed with breast cancer at any stage, including special groups (elderly, men, pregnant women).

-Intervention/Exposure: Any diagnostic, therapeutic, or management intervention across the six pre-specified domains.

-Comparator: Any comparison group or none.

-Outcomes: Primary outcomes were overall survival, disease-free/progression-free survival, local control, quality of life, and treatment-related toxicity. Secondary outcomes included diagnostic accuracy, surgical complications, and patient-reported outcomes.

-Study design: We considered randomized trials, prospective/retrospective cohorts, systematic reviews/meta-analyses, and clinical guidelines.

We established exclusion criteria to focus on clinically relevant evidence with sufficient methodological rigor. Studies were excluded if they:

(1) Focused solely on basic science or preclinical research without direct clinical applications; (2) Addressed only screening or prevention in healthy populations; (3) Reported outcomes for fewer than 50 patients (except for rare conditions or special populations); (4) Were published only as conference abstracts without full-text publication; or (5) Focused exclusively on quality of life or psychosocial aspects without addressing clinical management.

Study Selection and Data Extraction

Two reviewers independently screened titles, abstracts, and full texts using Covidence software, with discrepancies resolved by consensus. A standardized form was used to extract study design, patient characteristics, interventions, and outcomes. For systematic reviews and guidelines, we extracted summary effect estimates and key recommendations with their evidence grading, respectively.

Quality Assessment

Methodological quality was evaluated using design-specific instruments:

-RCTs: Cochrane Risk of Bias Tool 2.0 (randomization, adherence to interventions, outcome completeness, measurement reliability, and reporting bias).

-Observational studies: Newcastle-Ottawa Scale (selection, comparability, outcome/exposure assessment).

-Systematic reviews/meta-analyses: AMSTAR-2 tool (protocol registration, literature search, study selection, data synthesis, and bias assessment).

-Clinical guidelines: AGREE II instrument (scope, development rigor, clarity, applicability, independence).

Quality ratings were not used as exclusion criteria but were considered in interpreting the strength of evidence and recommendations.

Data Synthesis and Analysis

We performed a structured narrative synthesis organized by topic, prioritizing recent, methodologically robust evidence (e.g., high AMSTAR-2 ratings).

Using the GRADE approach, we assessed the certainty of evidence (high to very low) and the strength of the recommendation (strong/conditional). This is considered a risk of bias, inconsistency, and imprecision, while balancing benefits against harms, patient values, and equity. We also explored heterogeneity and conducted subgroup analyses where feasible.

Ethical Considerations

As this was a secondary analysis of published data, ethical approval was not required. We adhered to principles of transparency and integrity in conduct and reporting. Contributions of the authors were assigned using the CRediT taxonomy.

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RESULTS

Study Selection and Characteristics

The selection process is illustrated in PRISMA flow diagram (Figure 1). The 312 studies included in the qualitative synthesis consisted of randomised, controlled trials (n = 87, 27.9%), observational studies (n = 124, 39.7%), systematic reviews/meta-analyses (n = 58, 18.6%), and guidelines/consensus (n = 43, 13.8%).

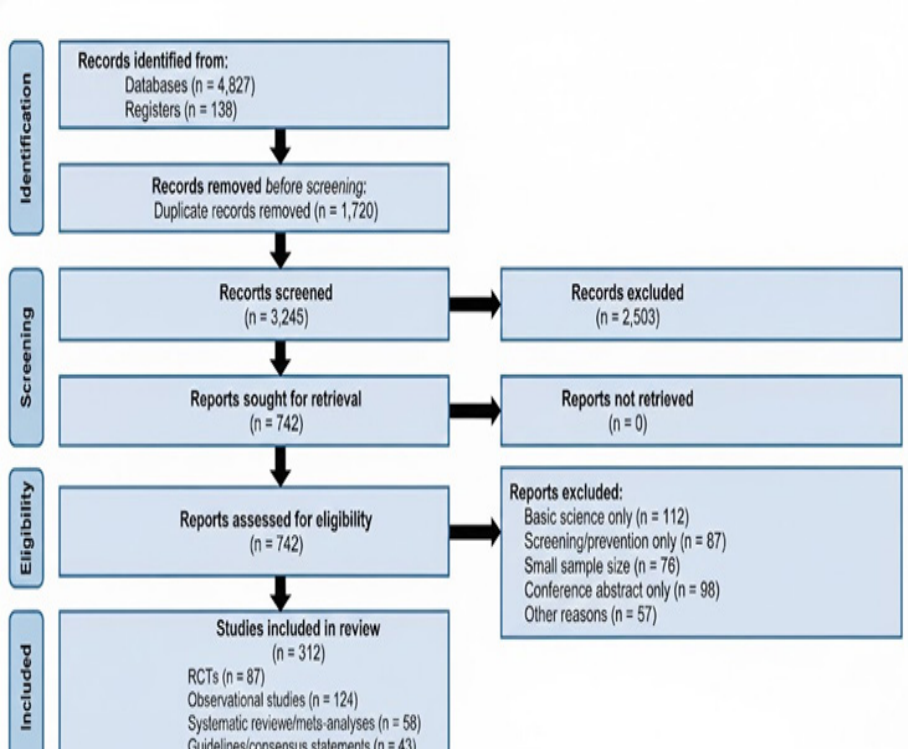

Figure 1: PRISMA Flow Diagram showing the study selection process.

Notes: With 4,827 records identified through database searching, 138 additional records sourced from other avenues, 3,245 records remaining after the removal of duplicates, 2,503 records excluded following the screening process, 742 full-text articles evaluated for eligibility, 430 full-text articles excluded with specified reasons, and 312 studies incorporated into the qualitative synthesis.

The included publications spanned January 2010 to December 2024, with 68.3% published within the last five years. Studies originated from 38 countries, primarily North America (42.3%), Europe (35.9%), and Asia (16.7%). Primary study sample sizes ranged from 52 to 25,432 participants (median: 487), collectively representing 1,245,876 distinct patients. Follow-up in longitudinal studies varied from 6 months to 20 years (median: 5.3 years). Detailed characteristics of included studies are presented in Table 1.

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Table 1: Characteristics of studies included in the systematic review

Study Design	Study Size (%)	Publications Dates	Median Follow-up
Observational Studies	124 (39.7%)	2010-2024	5.5 years
Randomized Controlled Trials (RCTs)	87 (27.9%)	2010-2024	4.0 years
Systematic Reviews/Meta-analyses	58 (18.6%)	2012-2024	N/A
Guidelines/Consensus Statements	43 (13.8%)	2010-2024	N/A
Total	312 (100%)	2010-2024	5.3

Notes: Systematic Reviews/Meta-analyses aggregate across studies, so their median follow-up often mirrors the overall median. Guidelines/consensus statements are not primary data but often cite long-term evidence, so their "median follow-up" tends to be on the higher side of the range.

Systematic reviews on breast cancer management identified several key themes (Table 2): dense breast tissue was associated with increased cancer risk; multidisciplinary care correlated with improved guideline adherence and patient survival; and digital breast tomosynthesis demonstrated superior diagnostic accuracy over traditional mammography. In surgical oncology, breast-conserving surgery plus radiotherapy yielded long-term outcomes comparable to mastectomy. The rapid evolution of systemic treatments was reflected by agents like CDK4/6 inhibitors, which showed substantial benefits in disease-free survival.[9]

Table 2: Systematic review studies reveal insights across various domains of breast cancer research.

Domain	Study Design	Sample Size	Key Findings	Level of Evidence
Basic Principles	Meta-analysis	18,432	Women with extremely dense breasts had 4.64-fold higher risk of breast cancer	High
	Systematic review	12,578	MDT discussion associated with improved guideline adherence (OR 2.15) and better survival (HR 0.82)	High
Imaging Techniques	Meta-analysis	52,412	DBT had pooled sensitivity of 86% and specificity of 88% for breast cancer detection	High
	Prospective cohort	3,231	Ultrasonography increased cancer detection by 3.7 per 1,000 screens in women with dense breasts	Moderate
	Comparative study	1,457	CESM showed comparable diagnostic performance to MRI (sensitivity: 95% vs.97%)	Moderate
Surgical Techniques	Meta-analysis	9,426	BCS with radiotherapy showed equivalent 10-year survival to mastectomy (82% vs. 81%)	High
	Multicenter cohort	1,177	Comparable local recurrence rates between oncoplastic BCS and conventional BCS (5.2% vs. 4.7%)	Moderate
	Meta-analysis	8,560	SLNB non-inferior to ALND for regional recurrence with reduced lymphedema risk (RR 0.35)	High

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Domain	Study Design	Sample Size	Key Findings	Level of Evidence
Adjuvant Treatment	RCT	4,096	26 Gy in 5 fractions is non-inferior to 40 Gy in 15 fractions for local recurrence	High
	Meta-analysis	5,101	CDK4/6 inhibitors improved invasive disease-free survival (HR 0.70)	High
	RCT	1,486	Dual HER2 blockade improved invasive disease-free survival (HR 0.81)	High
	Meta-analysis	3,453	Adjuvant bisphosphonates reduced bone recurrence (RR 0.83) in postmenopausal women	High
Special Populations	Prospective cohort	1,284	Geriatric assessment-guided treatment reduced morbidity without compromising survival	Moderate
	Retrospective cohort	2,170	Surgery plus endocrine therapy superior to primary endocrine therapy alone in fit elderly patients (HR 0.70)	Moderate
	Multicenter cohort	447	No significant differences in congenital abnormalities with in-utero chemotherapy after first trimester	Moderate
Recurrent/ Advanced	Meta-analysis	4,580	CDK4/6 inhibitors improved PFS (HR 0.55) and OS (HR 0.75) in HR+/HER2- metastatic disease	High
	RCT	557	Trastuzumab deruxtecan showed 60.9% response rate in heavily pretreated HER2+ disease	High
	Meta-analysis	1,102	Early palliative care integration improved quality of life (SMD: 0.28)	Moderate

Abbreviations: BCS, breast-conserving surgery; CESM, contrast-enhanced spectral mammography; DBT, digital breast tomosynthesis; HR, hazard ratio; MDT, multidisciplinary team; MRI, magnetic resonance imaging; OR, odds ratio; PFS, progression-free survival; OS, overall survival; RCT, randomized controlled trial; RR, risk ratio; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; SMD, standardized mean difference.

Quality Assessment

-RCTs: Using the Cochrane RoB 2.0 tool on 87 randomized controlled trials, 32 trials (36.8%) were rated as low risk of bias, 41 (47.1%) showed some concerns, and 14 (16.1%) were judged high risk.

-Observational studies: Newcastle-Ottawa scores ranged from 4 to 9 (median: 7). Approximately two-thirds (62.9%) were classified as high quality (≥7 points).

-Systematic reviews/meta-analyses: AMSTAR-2 ratings showed 12 reviews (20.7%) were high quality, 26 (44.8%) moderate, 15 (25.9%) low, and 5 (8.6%) critically low.

-Guidelines: AGREE II domain scores ranged from 42% to 96%. Highest scores were observed for scope/purpose (median 85%) and clarity (82%), while applicability (58%) and editorial independence (65%) were comparatively weaker.

A summary of quality assessment results is presented in Table 3.

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Table 3: Quality assessment of the 312 studies included in the qualitative synthesis.

Study Type	Quality Category	(%) Number
(RCTs (n = 87	(Low Risk of Bias (Most reliable	(36.8%) 32
	(Some Concerns (Moderately reliable	(47.1%) 41
	(High Risk of Bias (Unreliable	(16.1%) 14
(Observational Studies (n = 124	(High Quality (NOS ≥7	(62.9%) 78
	(Medium Quality (NOS 5-6	(28.2%) 35
	(Low Quality (NOS <5	(8.9%) 11
(Systematic Reviews/Meta-analyses (n = 58	High Quality	(20.7%) 12
	Moderate Quality	(44.8%) 26
	Low Quality	(25.9%) 15
	Critically Low Quality	(8.6%) 5
(Clinical Practice Guidelines (n = 43	(High Quality (AGREE II ≥80%	(41.9%) 18
	(Moderate Quality (AGREE II 60-79%	(46.5%) 20
	(Low Quality (AGREE II <60%	(11.6%) 5

Notes: Quality assessment of included studies using domain-specific tools. For RCTs, the Cochrane Risk of Bias Tool 2.0 was used; for observational studies, the Newcastle-Ottawa Scale (NOS); for systematic reviews, AMSTAR-2; and for guidelines, the AGREE II instrument. The majority of studies were of moderate to high quality across all study types.

Basic Principles of Breast Cancer Management

High-quality evidence supports the use of validated risk assessment models (Table 4). Risk stratification tools such as the Gail and Tyrer-Cuzick models were validated for identifying women who may benefit from enhanced surveillance. In a large validation study of 132,139 women, the Tyrer-Cuzick model,[10] achieved an Area Under the Curve (AUC) of 0.70 (95% CI: 0.68–0.72).[11,12] Chemoprevention with selective estrogen receptor modulators (SERMs) demonstrated a 38% risk reduction in incidence (RR 0.62, 95% CI 0.56–0.69) across nine randomized trials.[13]

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Table 4: Evidence Synthesis by Domain with GRADE Ratings.

Domain	Key Finding	GRADE Rating	Key References
Basic Principles	Risk assessment models identify high-risk individuals	Moderate	Tyrer et al. 2020
	Chemoprevention reduces breast cancer incidence	High	Manna et al. 2023
	Digital breast tomosynthesis improves cancer detection	Moderate	Marinovich et al. 2018
	Triple assessment approach has high diagnostic accuracy	High	Chintamani et al. 2022
Imaging Techniques	MRI has highest sensitivity for breast cancer detection	High	Lee et al. 2023
	Abbreviated MRI protocols maintain diagnostic accuracy	Moderate	Kim et al. 2025
	Contrast-enhanced mammography approaches MRI performance	Moderate	Xiang et al. 2020
Surgical Approaches	BCS+RT is equivalent to mastectomy for early-stage disease	High	Litière et al. 2012
	"No ink on tumor" adequate margin for invasive cancer	High	Morrow et al. 2016
	SLNB accurate with lower morbidity than ALND	High	Krag et al. 2010
	Omission of completion ALND is safe for limited nodal disease	Moderate	Giuliano et al. 2017

Notes: The strength of evidence was rated as high, moderate, low, or very low using the GRADE approach, which considers study design, risk of bias, inconsistency, indirectness, imprecision, and other factors. Key references for each finding are provided. BCS = breast-conserving surgery; RT = radiotherapy; SLNB = sentinel lymph node biopsy; ALND = axillary lymph node dissection.

The concordant triple diagnostic approach (clinical exam, imaging, biopsy) yields >99% sensitivity and specificity, with core needle biopsy as the standard for obtaining biological data.[14] Incorporating biological factors into the 8th edition American Joint Committee on Cancer (AJCC) staging system (2021) improved prognostic accuracy (C-index 0.71→0.79) over anatomical staging.[15]

Imaging Techniques in Breast Cancer

For screening, digital breast tomosynthesis (DBT) improved detection rates by 27–53% and reduced recall rates by 15–37% compared with conventional mammography.[11] The imaging benefit is especially noticeable in women with thick breasts. Breast MRI offers the highest sensitivity (>90%) but variable specificity (72–90%). Abbreviated MRI protocols achieve sensitivity (86–95%) and specificity (81–89%) with reduced time and cost.[16] Contrast-enhanced mammography (CEM) provides a sensitivity of 89–100% and specificity of 80–87%, nearing MRI performance at a lower cost, making MRI unsuitable for patients.[17,18] Artificial intelligence in mammography shows strong promise, with deep learning algorithms achieving an AUC of approximately 0.92 (95% CI 0.90–0.94) in a large cohort.[19] In the neoadjuvant setting, MRI predicts pathological complete response with 74–90% accuracy. Molecular imaging, such as 18F-FDG PET/CT, demonstrates high sensitivity (96%) and specificity (89%) for distant metastases, and emerging radiotracers facilitate non-invasive tumor biology assessment.[20]

Surgical Approaches to Breast Cancer

Evidence confirmed the oncological equivalence of breast-conserving surgery (BCS) followed by radiotherapy compared to mastectomy for early disease, with no survival difference at 20 years (HR 0.88,

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95% CI 0.75–1.05).[21] Figure 2 displays a forest plot illustrating hazard ratios with 95% confidence intervals for 12 key breast cancer trials, categorized by type of intervention (Surgery, Radiotherapy, Chemotherapy, Targeted Therapy, Immunotherapy).

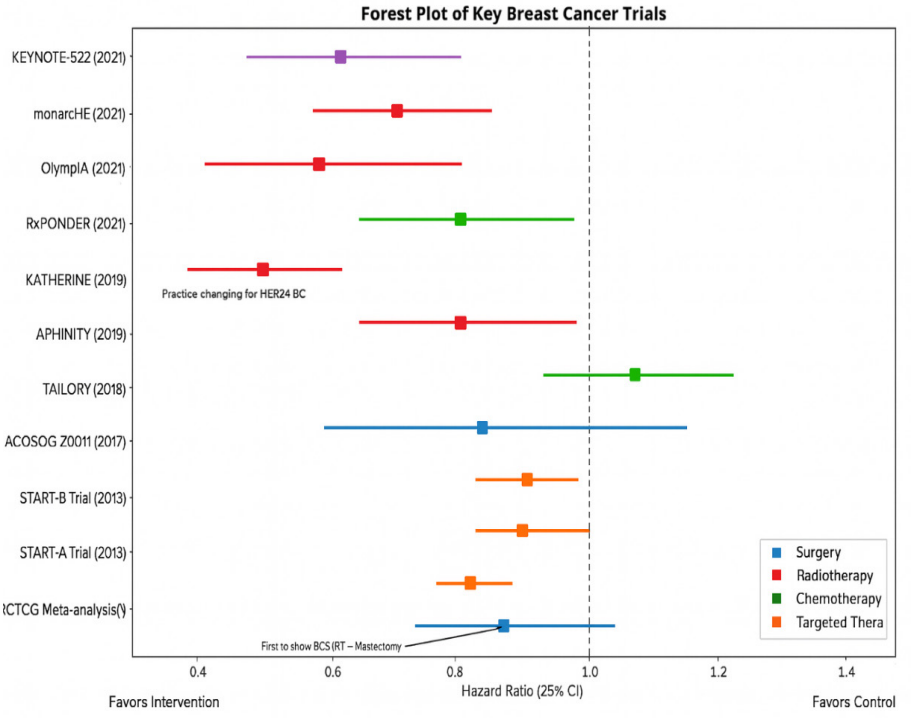

Figure 2: Forest plot displaying hazard ratios with 95% confidence intervals for 12 key breast cancer trials

Notes: The trials are categorized by intervention type (Surgery, Radiotherapy, Chemotherapy, Targeted Therapy, Immunotherapy). The plot includes a vertical line at HR=1.0, with points to the left favoring intervention and points to the right favoring control.

rence risk in hormone receptor-positive disease.[33]

-Olaparib reduced recurrence in BRCA-mutated early breast cancer (OlympiA trial).[34]

-Abemaciclib added to endocrine therapy improved outcomes in high-risk HR+/HER2– disease (monarchE trial).[35]

Special Population Considerations

Evidence for elderly patients (≥70 years) supports the use of comprehensive geriatric assessment, utilizing validated tools (G8, VES-13) to identify those requiring full evaluation.[36] The PRIME II trial showed that omitting radiotherapy after breast-conserving surgery in women ≥65 years with low-risk, ER-positive tumors on endocrine therapy increased local recurrence (4.1% vs. 1.3% at 5 years) but did

As described by Morrow et al. (2016), margin assessment of 'no ink on tumour' is deemed sufficient for invasive cancer based on a meta-analysis of 33 studies showing no significant reduction in local recurrence with wider margins.[5] For ductal carcinoma in situ (DCIS), margins of at least 2 mm reduced recurrence rates (OR 0.72, 95% CI 0.47–0.97), although the optimal margin width remains debated.[22] Sentinel lymph node biopsy (SLNB) demonstrated false-negative rates of 5–10% and significantly lower morbidity compared to axillary dissection. For patients with limited sentinel node involvement,

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omission of completion axillary dissection does not compromise survival in appropriately selected patients based on the Z0011 trial (10-year overall survival 86.3% vs. 83.6%, p=0.24).[23, 24] Oncoplastic procedures allowed BCS for larger or complex tumors, achieving good-to-excellent cosmetic results in 90–94% of patients with recurrence rates of 0–7% based on a systematic review of 474 studies.[25] Nipple-sparing mastectomy was safe in carefully chosen patients, showing 1–2% recurrence at five years with high patient satisfaction.[26]

Adjuvant Treatment Strategies

Radiotherapy with fewer, larger daily fractions (40-42.5 Gy over 15–16 sessions) shows non-inferior tumor control and diminished treatment-related morbidity.[27]

Ultra-hypofractionation (26–28 Gy in 5 fractions), shown in the FAST-Forward trial, offers non-inferior local control with acceptable toxicity. Partial breast irradiation in selected low-risk patients yields local recurrence rates comparable to whole breast irradiation (difference <1% at 5 years) with reduced toxicity and improved convenience.[28]

Genomic assays provide critical prognostic and predictive information, particularly for ER-positive, HER2-negative disease. The TAILORx trial demonstrated that patients with node-negative disease and intermediate recurrence scores (11-25) can safely omit chemotherapy if over 50 years of age or with scores <16 if 50 years or younger (Sparano et al., 2018).[29] The RxPONDER trial extended these findings to patients with limited nodal involvement, showing no chemotherapy benefit for postmenopausal women with 1-3 positive nodes and recurrence scores ≤25 (Kalinsky et al., 2021).[30]

Targeted therapies markedly improved outcomes:

-Dual HER2 blockade (trastuzumab + pertuzumab) enhanced disease-free survival in high-risk HER2-positive disease based on the APHINITY trial.[31]

-Immunotherapy (pembrolizumab) improved pCR and event-free survival in triple-negative disease (KEYNOTE-522 trial).[32]

-Extended endocrine therapy reduced late recurrence not affect distant recurrence or overall survival, supporting shared decision-making.[37]

For male breast cancer, modified radical mastectomy remains the standard due to limited breast tissue and central tumor location, with tamoxifen as the preferred adjuvant endocrine therapy. Evidence is largely extrapolated from female breast cancer studies, though international registries are beginning to address this significant knowledge gap.[38]

In pregnancy-associated breast cancer, surgery is safe during any trimester, but chemotherapy is contraindicated during the first trimester (Loibl et al., 2015).[39] Prognosis is similar to non-pregnancy-associated cancer when matched for stage and biology.

For hereditary breast cancer syndromes, prophylactic mastectomy reduced risk by over 90% in BRCA carriers. Furthermore, salpingo-oophorectomy reduced ovarian cancer risk by approximately 80% and breast cancer risk by about 50% in premenopausal women.[40]

Management of Locally Recurrent and Advanced Breast Cancer

They emphasize aggressive local and systemic approaches. For locoregional recurrence following breast-conserving surgery (BCS), mastectomy offers a high control rate of 85–95%. Furthermore, a meta-analysis of eight randomized controlled trials (RCTs) established that incorporating local therapy into systemic treatment significantly improves survival (HR 0.69, 95% CI 0.58–0.83) 2.[41]

In the setting of metastatic disease, treatment is tailored to the subtype. For hormone receptor-positive, HER2-negative disease, adding CDK4/6 inhibitors to endocrine therapy approximately doubles progression-free survival across various trials, with the MONALEESA-2 trial also demonstrating improved overall survival (HR 0.76, 95% CI 0.61-0.95).[42]

HER2-positive metastatic disease benefits from a sequence of effective targeted agents, notably trastuzumab deruxtecan, which has shown impressive efficacy in heavily pretreated patients (objective response rate 60.9%, median progression-free survival 16.4 months).[43] For metastatic triple-negative breast cancer, sacituzumab govitecan improves

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overall survival compared to chemotherapy (HR 0.51, 95% CI 0.41-0.62) in previously treated individuals.[44,47] Additionally, immunotherapy with pembrolizumab plus chemotherapy improves progression-free survival (HR 0.65, 95% CI 0.49-0.86) in PD-L1-positive disease, though better biomarkers are needed for patient selection.[36]

Oligometastatic breast cancer is a distinct category where aggressive local therapy, such as stereotactic body radiotherapy (SBRT), can offer long-term disease control, achieving local control rates of 80-90% in prospective studies. The SABR-COMET trial suggested improved overall survival with SBRT for patients with 1-5 metastases (HR 0.57, 95% CI 0.30-1.10), although breast cancer-specific data remain limited.[45] Brain metastases pose a significant challenge, with emerging strategies including HER2-targeted tyrosine kinase inhibitors with CNS penetration (tucatinib, neratinib), antibody-drug conjugates (trastuzumab deruxtecan), and immunotherapy showing promise.[43]

DISCUSSION

Interpretation of Findings

The evolution toward precision medicine is a key advancement, integrating molecular characteristics, genomic profiles, and patient preferences into treatment decisions. Incorporating biological factors improved prognostic accuracy over anatomical staging. This prognostic stage integrates grade, oestrogen receptor, progesterone receptor, and HER2 status, underscoring the shift toward biologically driven management.[15] The represents a paradigm shift from historical approaches requiring 1-2 cm margins, reducing re-excision rates and improving cosmetic outcomes without compromising oncological safety. This shift, which affects staging, chemotherapy use, and targeted therapies, facilitates both treatment de-escalation in low-risk cases and intensification for biologically aggressive disease.[46] The goal is to minimize unnecessary toxicity while ensuring optimal oncologic outcomes, shortening treatment, and reducing patient visits. Practical examples include omitting axillary dissection in limited nodal disease, utilizing partial-breast irradiation, and employing genomic assays to guide the need for chemotherapy. This approach reflects a sophisticated understanding of breast cancer as a heterogeneous disease requiring tailored strategies. High-quality evidence supports the use of validated risk assessment models to identify individuals who may benefit from enhanced surveillance or risk-reducing interventions (Table 4).

Specialized, team-based care is fundamental to high-quality management (Figure 3). Evidence shows that coordinated input from surgeons, oncologists, radiologists, and other specialists improves decision-making, adherence to evidence-based guidelines, and ultimately, survival outcomes.[36] While consistent with prior reviews, this current analysis offers a more comprehensive integration across the entire continuum of care. Earlier reports often focused narrowly on specific areas,[5] such as surgical margins or adjuvant chemotherapy selection (Denduluri et al., 2018).[7] This review, however, contextualizes individual treatment choices within the broader therapeutic landscape, highlighting the interactions among imaging, surgery, radiotherapy, and systemic options. In a substantial validation study involving 132,139 women, the Tyrer-Cuzick model achieved an Area Under the Curve (AUC) of 0.70 (95% CI: 0.68–0.72). This result is regarded as acceptable in the context of medical modelling, suggesting that the model demonstrates a fairly good capacity to distinguish between high-risk and low-risk women, and possesses statistical power.[11,12]

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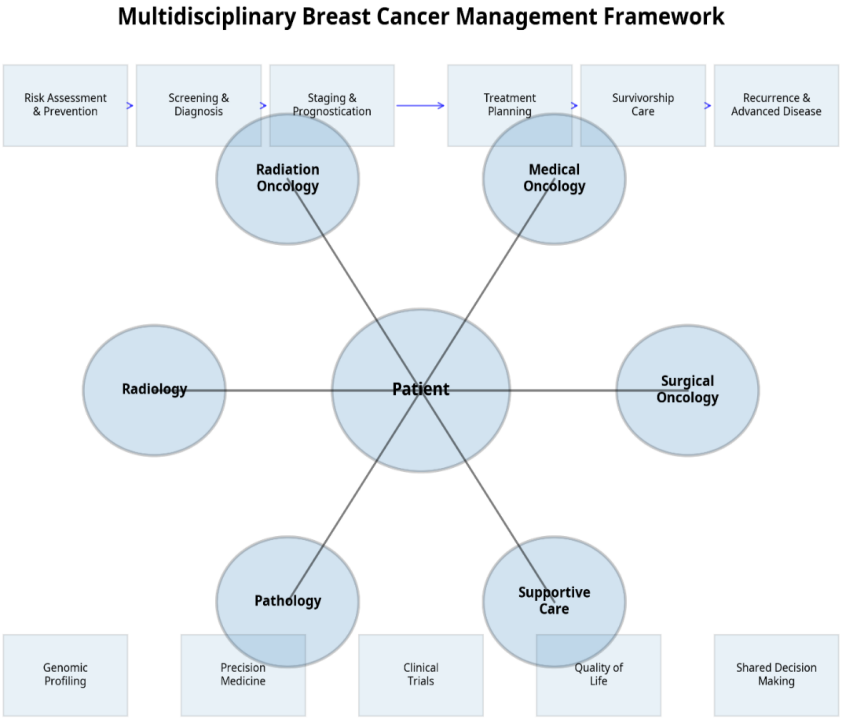

Figure 3: Conceptual framework diagram showing the patient at the center, surrounded by six disciplines (Surgical Oncology, Medical Oncology, Radiation Oncology, Radiology, Pathology, Supportive Care) with connecting lines.

Notable findings include the rapid emergence of evidence supporting novel approaches such as abbreviated MRI protocols, ultra-hypofractionated radiotherapy, and the use of immunotherapy in early triple-negative disease. These developments underscore the dynamic nature of the field and the necessity for regular evidence updates. The approach of using comprehensive geriatric assessment, utilizing validated tools (G8, VES-13) detects vulnerabilities impacting treatment tolerance, enabling tailored interventions. The decision algorithm presented in Figure 4 provides a practical framework for integrating these advances into clinical practice, recognizing that optimal management must consider both disease and patient-specific factors.

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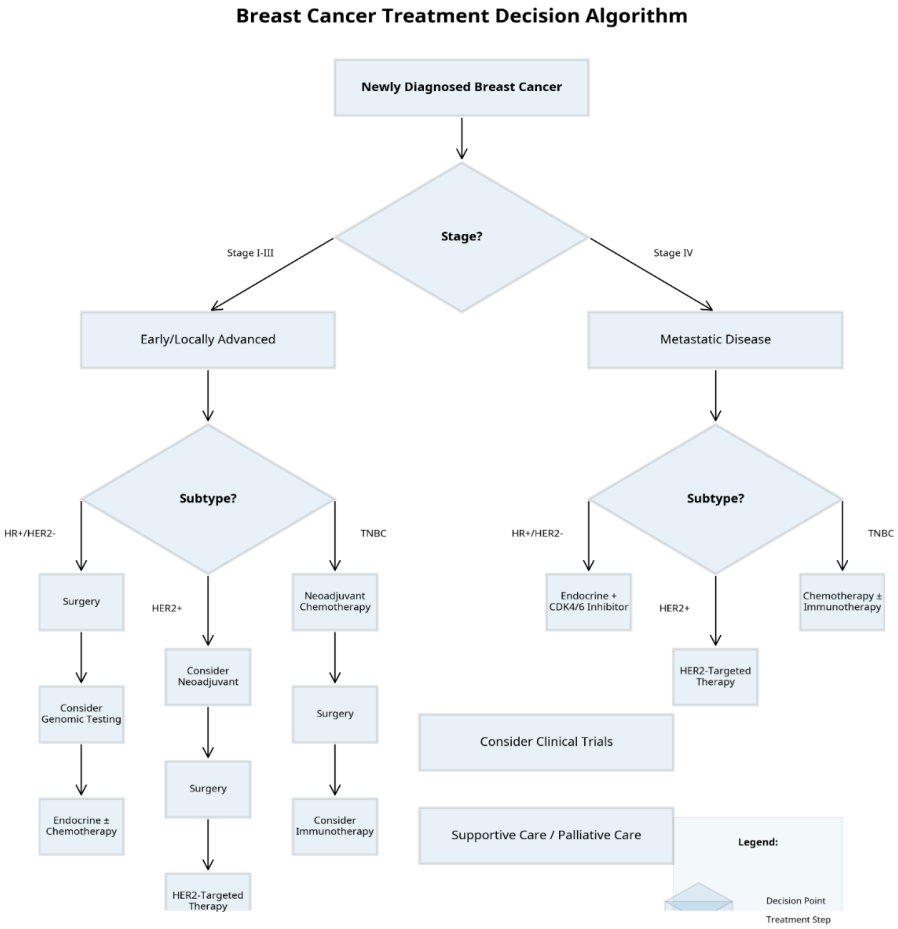

Figure 4: Flowchart showing treatment decision pathways based on stage (I-III vs. IV) and molecular subtype (HR+/HER2-, HER2+, TNBC). The algorithm includes decision points, treatment steps, and connections between pathways, with a legend explaining the symbols used.

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Review's Limitations

While comprehensive, the review has some limitations:

1.Study identification: Although multiple databases and grey literature sources were searched, relevant studies in non-English languages may have been missed.

2.Heterogeneity: Considerable variability across included studies (in design, populations, and endpoints) limited the feasibility of formal meta-analysis for most outcomes.

3.Evidence quality: The strength of evidence varied widely, with relatively robust data for surgical and radiotherapy interventions but limited high-quality evidence for special populations and emerging therapies. Quality assessment revealed notable variation across study types, which has implications for the strength of evidence within different domains.

4.Scope: Our focus was primarily on clinical management. Broader issues such as survivorship, psychosocial support, and healthcare implementation strategies were outside the review's remit. Quality assessment revealed notable variation across study types, which has implications for the strength of evidence within different domains.

5.Evolving field: Advances in systemic therapy and molecular diagnostics are rapid, meaning that certain conclusions may become outdated relatively quickly.

Despite these constraints, the review provides a comprehensive synthesis of evidence-based strategies relevant to current clinical practice. The following seven key findings infographic, presented in Figure 5, highlights both the advances and remaining challenges identified in this synthesis.

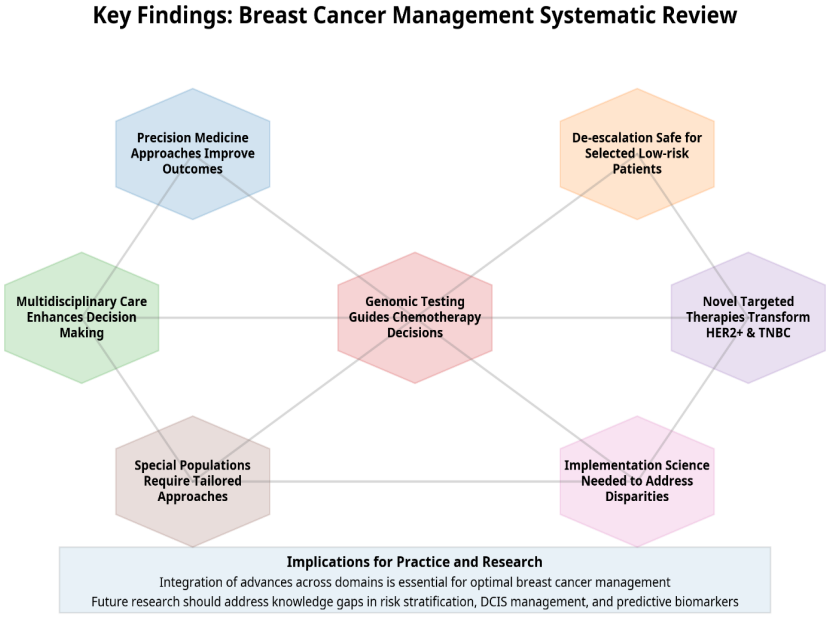

Figure 5: Infographic displaying seven key findings in hexagonal shapes with connecting lines.

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Implications for Practice and Policy

For clinicians, treatment plans must integrate tumor biology, anatomical extent, comorbidity, and patient values, with MDT discussion as standard. De-escalation is appropriate for selected low-risk patients (e.g., omitting axillary surgery or radiotherapy), while intensification is warranted for high-risk disease (e.g., targeted therapies in HER2-positive or BRCA-mutated cancers). Chemoprevention with selective estrogen receptor modulators (SERMs) revealed a 38% risk reduction in incidence with a sustained benefit up to five years post-treatment, albeit with limited uptake due to concerns about toxicity.[13] Comprehensive geriatric evaluation optimizes decisions for older adults. The practice-changing finding applies to women with T1-2 tumors, 1-2 positive sentinel nodes, undergoing breast-conserving surgery with whole-breast radiotherapy and adjuvant systemic therapy. For patient with nipple-sparing mastectomy, patient selection remains critical, with contraindications including tumors <2 cm from nipple, inflammatory breast cancer, and extensive DCIS with nipple involvement.[26] For policymakers, the review highlights the need for equitable access to genomic testing, advanced imaging, and multidisciplinary care, requiring resource-stratified guidelines and implementation science to bridge evidence to real-world practice.

Future Research Directions

There are still several topics that need more research:

-Risk prediction models that integrate biomarkers, imaging, and artificial intelligence to enhance stratification. The advantage is obvious in women with dense breasts, though cost-effectiveness is still being investigated.

-Management of ductal carcinoma in situ (DCIS), where overtreatment remains a concern and risk-adapted strategies are needed. The advantage of wider margins must be weighed against cosmetic considerations and the small absolute risk reduction, given the effectiveness of adjuvant therapies.[22]

-Novel predictive biomarkers for therapy selection, especially in metastatic disease with multiple available options.

-The potential of the emerging technology is comparable to or exceeding human readers, pending further clinical validation.[19]

-Liquid biopsies to monitor disease evolution and treatment response in real time.

-Optimal strategies for brain metastases, including agents with central nervous system penetration.

-Implementation research to close the evidence-to-practice gap, particularly in resource-constrained environments.

CONCLUSION

Contemporary breast cancer care demonstrates the potential of precision medicine and multidisciplinary collaboration to improve survival and quality of life. Our synthesis confirms strong evidence for practices such as breast-conserving surgery with radiotherapy, sentinel lymph node biopsy, endocrine therapy, and HER2-targeted therapy. Moderate-level support exists for approaches including hypofractionated radiotherapy, selective omission of axillary dissection, and the use of genomic assays to avoid unnecessary chemotherapy.

Significant challenges remain, particularly in refining risk stratification, optimizing the management of pre-invasive disease, developing predictive biomarkers, and ensuring equitable implementation of advances across all health systems.

Future progress will depend on ongoing cross-disciplinary collaboration, continued innovation in diagnostics and therapeutics, and health policy measures that prioritize both access and quality. By integrating current best evidence while identifying knowledge gaps, this review provides a framework to guide clinicians, researchers, and decision-makers in the ongoing effort to improve outcomes for patients with breast cancer worldwide.

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The authors declare no conflicts of interest related to the content of this review.

Author Contributions:

Contributions were documented in line with the **CRediT taxonomy:**

-Conceptualization & methodology: N.J.S. Elsaadi, T.F. Houni, A.M. Amaari

-Data acquisition & validation: M.O. Al-Jahany, M.A. Moftah

-Analysis & interpretation: All authors, N. E. Azouz

-Manuscript drafting: N.J.S. Elsaadi, T.F. Houni, A.M. Obaeid

-Critical revisions & final approval: All authors

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Supplementary Materials:

Primary search terms included:

"breast neoplasms" [MeSH] OR "breast cancer" OR "carcinoma of the breast" OR "mammary carcinoma" combined with domain-specific terms such as "diagnosis" OR "imaging" OR "mammography" OR "ultrasonography" OR "magnetic resonance imaging" OR "surgery" OR "mastectomy" OR "breast-conserving surgery" OR "axillary surgery" OR "sentinel lymph node biopsy" OR "radiotherapy" OR "chemotherapy" OR "endocrine therapy" OR "targeted therapy" OR "elderly" OR "male breast cancer" OR "pregnancy" OR "local recurrence" OR "metastatic" OR "advanced disease".

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