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Multidisciplinary Care and Breast Cancer Outcomes: A Systematic Review

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ABSTRACT: Breast cancer care involves many clinical disciplines, but evidence on how discipline-specific and organizational interventions affect outcomes has not been consolidated. We reviewed evidence across six disciplines. Following PRISMA 2020, PubMed, Scopus, and Web of Science were searched for English-language randomized trials and cohort, case-control, cross-sectional, and case-series studies published from January 2009 through December 2024. Risk of bias and certainty were assessed, and heterogeneous findings were synthesized narratively. Fifteen studies (about 76,100 participants) were included: seven randomized trials, six cohort studies, one case-control study, and one cross-sectional study. Regional versus general anesthesia and propofol versus volatile agents showed no difference in recurrence or survival once confounding was addressed. Supervised exercise improved quality of life and upper-limb function (DASH difference 7.81; 95% CI 3.17–12.44), with non-significant survival trends. Nurse-led care improved quality of life (mean difference 5.05; 95% CI 3.30–6.79), whereas adjuvant metformin did not improve invasive disease-free survival (HR 1.01; 95% CI 0.84–1.21). Metabolic syndrome (OR 3.33; 95% CI 1.91–5.81) and diagnostic delays were associated with disease risk and late-stage presentation. Four cohorts linked well-organized multidisciplinary team care to lower mortality or recurrence (HR 0.40–0.84); a disorganized team was associated with worse survival (HR 2.8). Coordinated multidisciplinary organization, nurse-led care, and supervised exercise were associated with better outcomes, whereas anesthetic technique and adjuvant metformin showed no benefit. Metabolic health and timely diagnosis are modifiable targets. Heterogeneity and observational designs limit causal inference.

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1. INTRODUCTION

Breast cancer is the most frequently diagnosed cancer among women worldwide, with an estimated 2.3 million new cases in 2022, and it remains a leading cause of cancer death among women (Bray et al., 2024). Its burden is unevenly distributed. In sub-Saharan Africa, for example, a large share of women still present with stage III or IV disease, which worsens prognosis and strains limited health-system resources. Because screening coverage, access to pathology and surgery, and the availability of systemic and radiation therapy differ widely between and within countries, the same diagnosis can carry very different prognoses depending on where a woman is treated (Jedy-Agba et al., 2016).

Modern breast cancer care is delivered across a chain of specialties, and each discipline touches a different link in that chain. Epidemiology identifies who is at risk and why; health administration determines whether care is coordinated and timely; anesthesia and perioperative medicine shape the surgical experience; nursing supports symptom control, education, and follow-up; internal medicine manages comorbidity and metabolic health; and physical therapy addresses functional recovery. International guidelines consider multidisciplinary decision-making an essential component of the management of early breast cancer (Cardoso et al., 2019).

Whether this organizational model improves outcomes remains debated. A systematic review of multidisciplinary team meetings in oncology examined their effects on patient assessment, management, and outcomes (Pillay et al., 2016), and an evaluation of 8,323 patients treated in certified German breast centers reported improved guideline adherence together with better relapse-free and overall survival (Kreienberg et al., 2018). These reports are encouraging but differ in design and setting, and it is not clear how much of any benefit stems from the meeting itself rather than from the quality of the team behind it (Pillay et al., 2016; Kreienberg et al., 2018).

Beyond team organization, individual disciplines have generated largely separate bodies of evidence. In anesthesia, a retrospective analysis suggested that the technique used during breast cancer surgery might influence recurrence (Exadaktylos et al., 2006), a hypothesis that required randomized testing. Nurse-led models of follow-up and supportive care have likewise been proposed as ways to meet patient needs more efficiently than routine specialist visits. In rehabilitation science, physical activity after a breast cancer diagnosis has been linked to biomarkers and disease outcomes in cancer survivors, which has motivated supervised exercise programs during and after treatment (Ballard-Barbash et al., 2012).

Internal medicine and epidemiology approach the problem from a different angle. Obesity, glucose dysregulation, dyslipidemia, and hypertension cluster in metabolic syndrome, and each has plausible biologic links to breast carcinogenesis through insulin signaling, adipose-derived estrogen, and chronic inflammation. Metabolic syndrome and its components have been linked to the risk, treatment response, and prognosis of breast cancer, and this link has stimulated both regional risk-factor studies and trials of metabolic therapies (Dong et al., 2021).

Because these literatures sit in separate specialty silos, clinicians and health planners have no single appraisal of what each discipline contributes to patient outcomes or where the evidence is strongest. A cross-disciplinary view is useful for three reasons: it shows which disciplines rest on randomized evidence and which rely on observational data, it allows the consistency of effects to be judged across very different types of intervention, and it identifies where research effort is thin. Existing syntheses tend to examine one intervention or the team-meeting model in isolation (Pillay et al., 2016).

We therefore conducted a systematic review, following PRISMA 2020 (Page et al., 2021), to summarize the evidence from epidemiology, health administration, general medicine with anesthesia, nursing, internal medicine, and physical therapy on breast cancer outcomes. Specifically, how are epidemiologic, organizational, perioperative, nursing, medical, and rehabilitative factors associated with recurrence, survival, quality of life, or disease risk, and how consistent and reliable are these findings across study designs?

2. MATERIALS AND METHODS

2.1 Protocol and reporting

This review was reported in accordance with the PRISMA 2020 statement (Page et al., 2021). Protocol registration: Not prospectively registered; the review protocol is available from the corresponding author on request.

2.2 Information sources and search strategy

PubMed/MEDLINE, Scopus, and Web of Science Core Collection were searched. To be eligible, studies had to be published from 1 January 2009 through 31 December 2024, inclusive. The strategy combined controlled vocabulary and free-text terms for three concepts: breast cancer; multidisciplinary or discipline-specific care (epidemiology, health administration, anesthesia, nursing, internal medicine, and physical therapy); and eligible study designs. The reference lists of included studies were also screened. The PubMed strategy with the eligibility date filter is shown below.

("Breast Neoplasms"[Mesh] OR "breast cancer"[tiab] OR "breast carcinoma"[tiab])

AND ("Patient Care Team"[Mesh] OR multidisciplinar*[tiab] OR interdisciplinar*[tiab] OR "tumor board"[tiab] OR "nurse-led"[tiab] OR nursing[tiab] OR anesthesi*[tiab] OR anaesthesi*[tiab] OR "Exercise Therapy"[Mesh] OR "physical therapy"[tiab] OR physiotherap*[tiab] OR metformin[tiab] OR "metabolic syndrome"[tiab] OR epidemiolog*[tiab] OR "health services administration"[tiab])

AND ("randomized controlled trial"[pt] OR cohort[tiab] OR "case-control"[tiab] OR "cross-sectional"[tiab] OR "case series"[tiab])

AND ("2009/01/01"[dp] : "2024/12/31"[dp]) AND English[lang]

2.3 Eligibility criteria and PICO

Population: women or men with, or at risk of, breast cancer, including comparison groups without the disease in case-control designs.

Intervention/exposure: discipline-specific interventions or exposures in six areas: epidemiology (risk or prognostic factors), health administration (team or organizational models), general medicine with anesthesia (anesthetic or perioperative care), nursing (nurse-led care), internal medicine (medical or metabolic interventions and conditions), and physical therapy (exercise and rehabilitation).

Comparator: usual care, an alternative technique, placebo, or no exposure.

Outcomes: recurrence, survival, mortality, quality of life, function, stage at diagnosis, or measures of association (odds ratio, hazard ratio, mean difference).

Study design: randomized controlled trials, cohort, case-control, cross-sectional, and case-series studies.

Limits: English language; published 1 January 2009 to 31 December 2024.

Exclusions: reviews, editorials, conference abstracts, animal or in vitro studies, studies without breast cancer-specific data, and duplicate reports.

2.4 Study selection

Two reviewers independently screened titles and abstracts in Rayyan and then full texts against the eligibility criteria; disagreements were resolved by discussion or by a third reviewer. Reasons for exclusion at the full-text stage were recorded (**Figure 1**).

2.5 Data extraction and effect measures

Two reviewers extracted data in duplicate into a standardized Excel form. Extracted items included the first author, year, country, design, population and sample size, intervention or exposure and comparator, follow-up, outcomes, and the authors' conclusions. The primary outcome of each study and its effect measure (hazard ratio, odds ratio, mean difference, or proportion) were recorded with 95% confidence intervals as reported, and secondary outcomes were extracted when they were patient-centered (quality of life, function, pain, toxicity). Disciplines were assigned according to the primary focus of each study; no data were imputed.

2.6 Risk of bias

Randomized trials were assessed with the Cochrane RoB 2 tool (Sterne et al., 2019), and non-randomized studies, including the case-control and cross-sectional studies, with ROBINS-I (Sterne et al., 2016) (adapted for these designs). Two reviewers independently assessed risk of bias and resolved disagreements by consensus. Final judgments are presented in Table 4.

2.7 Synthesis, reporting bias, and certainty of evidence

No meta-analysis was performed because no outcome had at least two studies with comparable interventions, comparators, and effect measures. Funnel plots were not applicable. Certainty of evidence was assessed with GRADE (Guyatt et al., 2008) by two independent reviewers, with disagreements resolved by consensus. Final GRADE ratings are presented in Supplementary Table S2.

3. RESULTS AND DISCUSSION

3.1 Study selection

The reported database counts were 5,423 records identified, 1,987 duplicates removed, 3,436 records screened by title and abstract, 95 full-text reports sought, and 89 assessed. Fifteen studies were included (**Figure 1**). The dates of all 15 included studies fell within the publication window. The saved search and screening logs were unavailable for verifying whether the reported record counts reflect the 31 December 2024 cutoff.

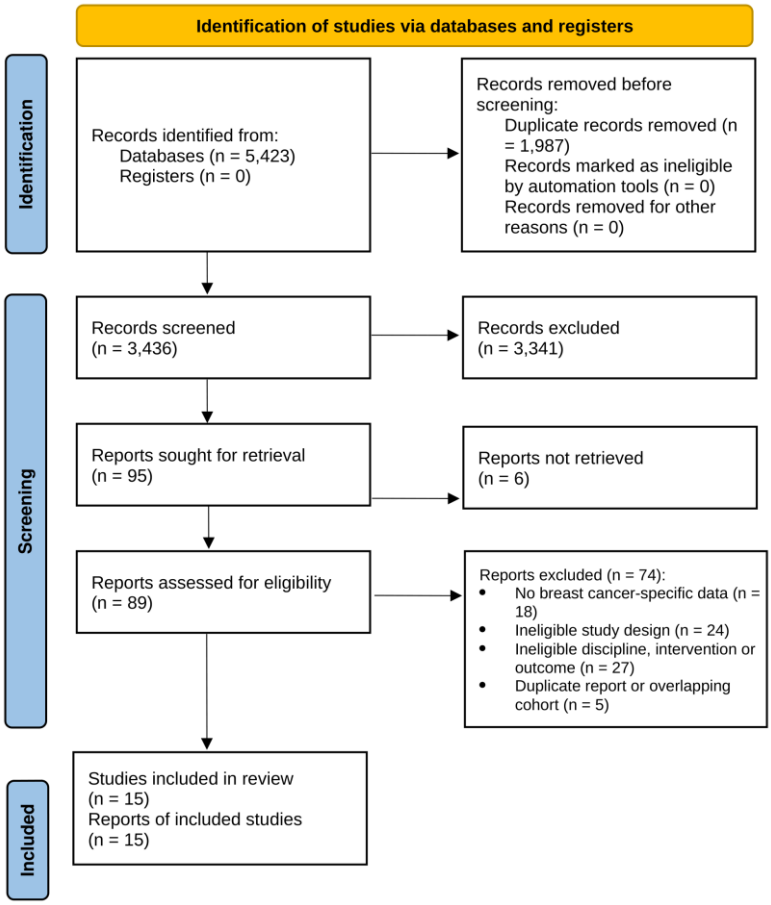

Figure 1. PRISMA 2020 flow diagram. Database records: PubMed/MEDLINE (n = 1,842), Scopus (n = 2,105), and Web of Science (n = 1,476). Adapted from Page et al. (2021), CC BY 4.0.

3.2 Study characteristics

The 15 included studies were published between 2012 and 2024 and enrolled approximately 76,100 participants (sum of study sample sizes before matching, where applicable). Seven were randomized controlled trials: Sessler et al. (2019), Courneya et al. (2014), Dieli-Conwright et al. (2018), Bruce et al. (2021), Saltbæk et al. (2024), Yazicioglu Kucuk and Zorba Bahceli (2024), and Goodwin et al. (2022). Six were cohort studies: Enlund et al. (2022), Karami et al. (2022), Kesson et al. (2012), Lu et al. (2020), Brandão et al. (2021), and Tsai et al. (2020). One was a case-control study, Mohammed et al. (2023), and one was a cross-sectional study, Ismail et al. (2022). No case series met the eligibility criteria. By discipline, three studies addressed anesthesia, three physical therapy/exercise, two nursing, two internal-medicine (Goodwin et al. and Mohammed et al., the latter shared with epidemiology), two epidemiology (Mohammed et al. and Ismail et al., the latter shared with health administration), and five health-administration studies (four MDT cohort studies plus Ismail et al. shared with epidemiology) (Table 1).

Table 1. Characteristics of the included studies

Study	Country; design	Population (N)	Intervention/exposure vs comparator	Main outcome; follow-up	Discipline
Sessler et al. (2019)	Argentina, Austria, China, Germany, Ireland, New Zealand, Singapore, USA (13 sites); RCT	2,108 women undergoing curative primary breast cancer resection (randomized 2007–2018)	Regional anesthesia (paravertebral block + propofol; n = 1,043) vs general anesthesia (sevoflurane + opioid; n = 1,065)	Local or metastatic recurrence; median follow-up 36 months	Anesthesia
Enlund et al. (2022)	Sweden; national registry retrospective cohort (propensity matching)	18,674 women with breast cancer surgery under general anesthesia, 2013–2019 (13,873 propofol; 4,801 volatile)	Propofol vs inhaled volatile anesthetic maintenance	Overall survival; 4,658 matched pairs	Anesthesia
Karami et al. (2022)	Iran (Shiraz); retrospective cohort	994 patients operated 2006–2016 (530 intravenous; 464 volatile/inhalational)	Propofol-remifentanil intravenous anesthesia vs volatile/inhalational anesthesia	Recurrence-free and overall survival to 2 and 5 years	Anesthesia
Courneya et al. (2014)	Canada; RCT (exploratory START follow-up)	242 women with stage I–IIIA disease starting adjuvant chemotherapy	Supervised aerobic (n = 78) or resistance (n = 82) exercise during chemotherapy vs usual care (n = 82)	Disease-free survival; median follow-up 89 months	Physical therapy/exercise

Study	Country; design	Population (N)	Intervention/exposure vs comparator	Main outcome; follow-up	Discipline
Dieli-Conwright et al. (2018)	USA; RCT	100 overweight or obese survivors within 6 months of adjuvant treatment	16 weeks of supervised aerobic + resistance exercise (65–85% HRmax, 3 times/week) vs usual care	Quality of life, fitness, bone health; post-intervention and 3 months (exercise group)	Physical therapy/exercise
Bruce et al. (2021)	UK (17 NHS centers); pragmatic RCT (PROSPER)	392 women at high risk of upper-limb disability after non-reconstructive breast cancer surgery	Physiotherapy-led structured exercise + usual care (n = 196) vs usual care leaflets (n = 196)	DASH at 12 months	Physical therapy/exercise
Saltbæk et al. (2024)	Denmark; RCT (MyHealth, phase III)	503 patients with stage I–II disease after primary treatment	Nurse-led individualized follow-up (n = 251) vs physician-led visits (n = 252)	Quality of life (FACT-B TOI) at 2 years; 3-year follow-up	Nursing
Yazicioglu Kucuk and Zorba Bahceli (2024)	Turkey; parallel-group pilot RCT	42 women with newly diagnosed breast cancer receiving adjuvant chemotherapy	Eight-week nurse-led supportive care (4 weeks face-to-face, 4 weeks by phone) vs routine treatment	EORTC QLQ-C30 at baseline and week 9	Nursing
Goodwin et al. (2022)	Canada, Switzerland, USA, UK; RCT (MA.32)	3,649 patients with high-risk non-metastatic breast cancer without diabetes	Metformin 850 mg twice daily (n = 1,824) vs placebo (n = 1,825) for 5 years	Invasive disease-free survival; median follow-up 96.2 months (ER/PgR+)	Internal medicine
Mohammed et al. (2023)	Egypt; case-control	112 newly diagnosed cases; 112 age-matched controls	Metabolic syndrome (JIS criteria) and its components	Odds of breast cancer	Epidemiology; internal medicine
Ismail et al. (2022)	Egypt; cross-sectional	400 women with pathologically confirmed breast cancer at a tertiary cancer hospital	Patient and provider delay, symptoms, and molecular subtype	Late-stage diagnosis	Epidemiology; health administration

Study	Country; design	Population (N)	Intervention/exposure vs comparator	Main outcome; follow-up	Discipline
Kesson et al. (2012)	UK (west of Scotland); retrospective comparative interventional cohort	13,722 eligible women of 14,358 diagnosed 1990–2000	Multidisciplinary team working introduced in 1995 in Greater Glasgow vs other health board areas	Breast cancer-specific and all-cause mortality	Health administration
Lu et al. (2020)	China (Shanghai); retrospective cohort with propensity matching	16,354 patients (299 MDT; 16,055 non-MDT); surgery 2006–2016	Well-organized MDT or disorganized MDT vs no MDT	Survival at 1, 3, and 5 years	Health administration
Brandão et al. (2021)	Mozambique; prospective cohort	205 patients (98 pre-, 107 post-implementation); diagnosed 2015–2017	Weekly multidisciplinary tumor board vs care before implementation	Overall survival (3 years), disease-free survival, cost-effectiveness	Health administration
Tsai et al. (2020)	Taiwan; retrospective matched cohort	9,266 patients with MDT care vs 9,266 without (diagnosed 2004–2010)	MDT care vs no MDT care	Recurrence and death	Health administration

DASH, Disabilities of the Arm, Shoulder and Hand; DFS, disease-free survival; ER/PgR, estrogen/progesterone receptor; FACT-B TOI, Functional Assessment of Cancer Therapy-Breast Trial Outcome Index; HRmax, maximum heart rate; JIS, Joint Interim Statement; MDT, multidisciplinary team; RCT, randomized controlled trial.

3.3 Key findings by discipline

Anesthesia. Sessler et al. (2019) randomized 2,108 women to regional or general anesthesia; recurrence occurred in 10% of both groups (HR 0.97; 95% CI 0.74–1.28) and persistent incisional pain did not differ. In the Swedish registry cohort of Enlund et al. (2022), propofol was associated with better survival in the crude comparison (HR 0.80; 95% CI 0.70–0.90) but not after propensity matching (HR 0.98; 95% CI 0.85–1.13). Karami et al. (2022) found higher 2-year recurrence-free survival with volatile anesthesia (P = 0.039) but no difference in overall survival (P = 0.520).

Physical therapy and exercise. Bruce et al. (2021) randomized 392 women to a physiotherapy-led exercise program or usual care; upper-limb disability at 12 months was lower with exercise (adjusted mean difference 7.81 DASH points; 95% CI 3.17–12.44; P = 0.001), with lower pain and no increase in complications or lymphedema. Dieli-Conwright et al. (2018) reported a between-group quality-of-life difference of 14.7 points (95% CI 9.7–18.2; P < 0.001). In the START follow-up, Courneya et al. (2014) found hazard ratios below 1 for disease-free survival (0.68), overall survival (0.60), distant disease-free survival (0.62), and recurrence-free interval (0.58), none statistically significant.

Nursing. Saltbæk et al. (2024) found higher quality of life at 2 years with nurse-led follow-up (mean difference 5.05; 95% CI 3.30–6.79; P < .001), with lower fear of recurrence, anxiety, and depression, fewer physician consultations, and unchanged

imaging. In a pilot of 42 women, Yazicioglu Kucuk and Zorba Bahceli (2024) reported that the eight-week nurse-led program was associated with improved global health and functional status and lower symptom burden at week 9.

Internal medicine and epidemiology. Goodwin et al. (2022) found no effect of adjuvant metformin on invasive disease-free survival (HR 1.01; 95% CI 0.84–1.21 in the hormone receptor-positive group), with more grade 3 or higher non-hematologic toxicity (21.5% vs 17.5%). Mohammed et al. (2023) reported metabolic syndrome in 57.1% of cases and 28.6% of controls (OR 3.33; 95% CI 1.91–5.81). In 400 Egyptian women, Ismail et al. (2022) found that patient delay beyond 3 months, provider diagnostic delay beyond 1 month, non-breast symptoms, and aggressive molecular subtypes were associated with late-stage diagnosis.

Health administration. All four cohort studies compared multidisciplinary team care with usual organization. Kesson et al. (2012) reported that breast cancer mortality, 11% higher in the intervention area before team working was introduced, became 18% lower afterward (HR 0.82; 95% CI 0.74–0.91). Tsai et al. (2020) found lower recurrence (HR 0.84; 95% CI 0.70–0.99), and Brandão et al. (2021) lower mortality in early disease (adjusted HR 0.47; 95% CI 0.27–0.81). Lu et al. (2020) found better survival with a well-organized team (HR 0.4) and worse survival with a disorganized team (HR 2.8) than with no team.

Figure 2 is descriptive; no pooled estimate was calculated. Key quantitative findings are summarized in Table 2.

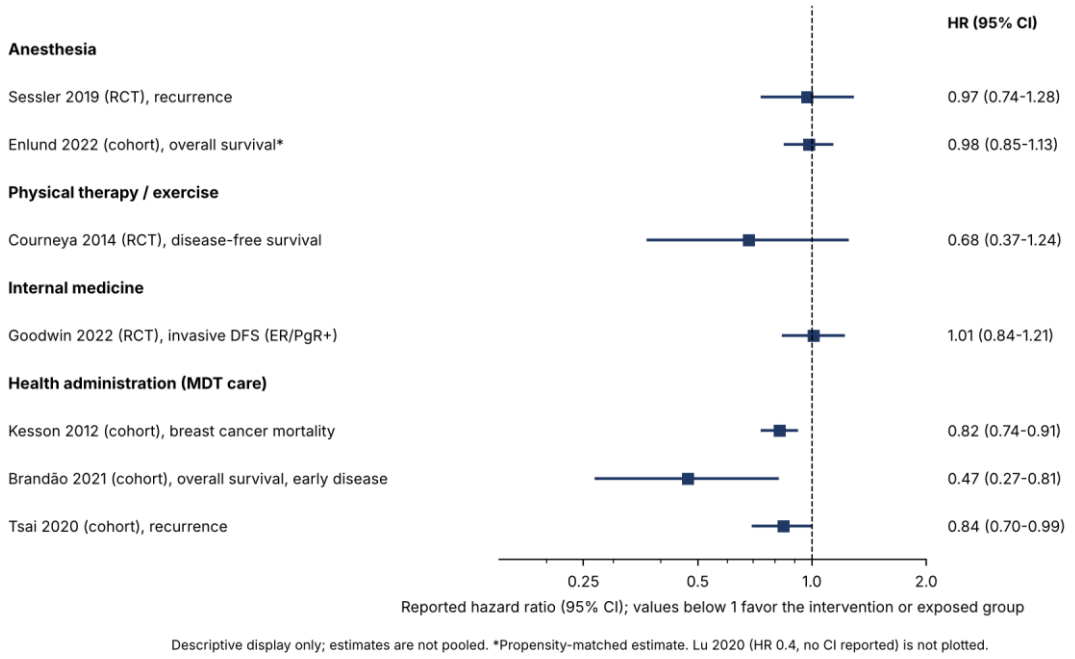

Figure 2. Reported hazard ratios (95% confidence intervals) for time-to-event outcomes, grouped by discipline. No pooled analysis was performed.

Table 2. Key quantitative findings

Study	Outcome	Quantified result	Direction
Sessler et al. (2019)	Recurrence; persistent incisional pain	Recurrence 10% vs 10% (HR 0.97; 95% CI 0.74–1.28; P = .84). Pain at 6 months 52% vs 52% and at 12 months 28% vs 27% (OR 1.00; 95% CI 0.85–1.17).	No difference

Study	Outcome	Quantified result	Direction
Enlund et al. (2022)	Overall survival	Unmatched: 97.2% (propofol) vs 84.1% (volatile), HR 0.80 (0.70–0.90). Matched (4,658 pairs): 92.0% vs 92.1%, HR 0.98 (0.85–1.13; P = 0.756).	No difference after matching
Karami et al. (2022)	Recurrence-free and overall survival	2-year recurrence-free survival higher with volatile/inhalational anesthesia (log-rank P = 0.039); 5-year overall survival not different (P = 0.520).	Short-term recurrence-free difference only
Courneya et al. (2014)	DFS, OS, DDFS, RFI	8-year DFS 82.7% vs 75.6% (HR 0.68; 95% CI 0.37–1.24). OS HR 0.60 (0.27–1.33); DDFS HR 0.62 (0.32–1.19); RFI HR 0.58 (0.30–1.11). Subgroup receiving ≥85% of planned chemotherapy: DFS HR 0.50 (0.25–1.01), RFI HR 0.38 (0.18–0.81).	Favors exercise; not significant overall
Dieli-Conwright et al. (2018)	Quality of life, fitness, bone health	Between-group QoL difference 14.7 (95% CI 9.7–18.2; P < 0.001); fatigue, depression, and estimated VO2max P < 0.001; osteocalcin P = 0.01; bone-specific alkaline phosphatase P = 0.001. Gains persisted at 3 months in the exercise group.	Favors exercise
Bruce et al. (2021)	Upper-limb function (DASH); pain	DASH at 12 months 16.3 (SD 17.6) vs 23.7 (SD 22.9); adjusted mean difference 7.81 (95% CI 3.17–12.44; P = 0.001). Pain intensity difference −0.68 (−1.23 to −0.12; P = 0.02). No increase in complications, lymphedema, or adverse events; cost effective.	Favors exercise
Saltbæk et al. (2024)	Quality of life (FACT-B TOI)	75.69 (SD 12.27) vs 71.26 (SD 14.08); mean difference 5.05 (95% CI 3.30–6.79; P < .001). Differences at 6, 12, and 36 months: 4.37, 4.71, and 4.91. Less fear of recurrence, anxiety, and depression; fewer physician consultations, more nurse contacts, unchanged imaging.	Favors nurse-led follow-up
Yazicioglu Kucuk and Zorba Bahceli (2024)	EORTC QLQ-C30 domains	Global health status and functional status improved more, and symptom status was lower, in the intervention group at week 9.	Favors nurse-led program
Goodwin et al. (2022)	Invasive DFS	ER/PgR+: 2.78 vs 2.74 events per 100 patient-years (HR 1.01; 95% CI 0.84–1.21; P = .93; 465 events). ER/PgR−: 3.58 vs 3.60 (HR 1.01; 0.79–1.30; P = .92). Grade ≥3 non-hematologic toxicity 21.5% vs 17.5% (P = .003).	No benefit; more toxicity

Study	Outcome	Quantified result	Direction
Mohammed et al. (2023)	Odds of breast cancer	Metabolic syndrome 57.1% vs 28.6% (OR 3.33; 95% CI 1.91–5.81). Premenopausal adjusted OR: HDL ≥50 mg/dl 0.187 (0.068–0.513); fasting glucose ≥126 mg/dl 2.97 (1.06–8.36); triglycerides ≥150 mg/dl 2.47 (1.14–5.36). Postmenopausal HDL ≥50 mg/dl 0.172 (0.042–0.706).	Higher odds with metabolic syndrome
Ismail et al. (2022)	Late-stage diagnosis	Adjusted odds of late-stage diagnosis in the published study (Ismail et al., 2022), Table 5: non-luminal subtype, OR 3.82 (95% CI 2.07–7.05); patient delay >3 months, OR 9.22 (5.22–16.30); provider delay >1 month, OR 11.54 (5.59–23.79); non-breast symptoms, OR 5.35 (1.89–15.16).	Delays and aggressive subtypes raise late-stage risk
Kesson et al. (2012)	Breast cancer mortality	Before 1995: 11% higher in intervention area (HR 1.11; 95% CI 1.00–1.20). After: 18% lower (HR 0.82; 0.74–0.91). Interrupted time series showed improvement in 1996 (P = 0.004).	Favors MDT
Lu et al. (2020)	Survival	Well-organized MDT vs no MDT: HR 0.4, with 5-year survival 15.6% higher. Disorganized MDT vs no MDT: HR 2.8, with 5-year survival 19.9% lower.	Favors well-organized MDT; harm if disorganized
Brandão et al. (2021)	OS, DFS, cost	Early disease (n = 163): 3-year OS 48.0% vs 73.0%, adjusted HR 0.47 (0.27–0.81). All patients: OS adjusted HR 0.77 (0.49–1.19). DFS adjusted HR 0.72 (0.46–1.13). Metastatic disease: median OS 19.4 vs 13.6 months. ICER US$802.96 per QALY.	Favors MTB in early disease
Tsai et al. (2020)	Recurrence	HR 0.84 (95% CI 0.70–0.99) after matching; mortality risk with relapse 8.48 times (7.53–9.54) that without relapse.	Favors MDT

CI, confidence interval; DASH, Disabilities of the Arm, Shoulder and Hand (lower is better); DDFS, distant disease-free survival; DFS, disease-free survival; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; MTB, multidisciplinary tumor board; OR, odds ratio; OS, overall survival; QALY, quality-adjusted life year; QoL, quality of life; RFI, recurrence-free interval. Table 3 summarizes the study authors' conclusions and implications.

Table 3. Authors' conclusions and implications

Study	Authors' conclusion (paraphrased)	Implication for breast cancer care
Sessler et al. (2019)	Paravertebral regional anesthesia with propofol did not reduce recurrence compared with sevoflurane and opioid anesthesia, and persistent pain was unaffected.	Either technique can be chosen with respect to recurrence and persistent pain.

Study	Authors' conclusion (paraphrased)	Implication for breast cancer care
Enlund et al. (2022)	No association was observed between propofol or inhaled volatile maintenance and overall survival after breast cancer surgery.	Supports free choice of general anesthetic for survival purposes.
Karami et al. (2022)	Two-year disease-free survival was higher with volatile/inhalational anesthesia, but 5-year overall survival was not associated with technique.	No long-term survival rationale for one agent; short-term signal needs confirmation.
Courneya et al. (2014)	Adding exercise to standard chemotherapy may improve cancer outcomes; this exploratory finding warrants a definitive phase III trial.	Hypothesis-generating; supports adequately powered trials.
Dieli-Conwright et al. (2018)	A 16-week combined exercise program significantly improved quality of life and physical fitness.	Supports supervised clinical exercise programs in survivorship care.
Bruce et al. (2021)	The exercise program was clinically effective and cost effective and reduced upper-limb disability one year after treatment.	Supports offering early structured physiotherapy after surgery to at-risk women.
Saltbæk et al. (2024)	Nurse-led individualized follow-up is a new follow-up strategy that significantly improved quality of life.	Nurse-led models can complement or replace routine physician visits.
Yazicioglu Kucuk and Zorba Bahceli (2024)	The nurse-led supportive care program was an effective, safe, and acceptable way to support women receiving adjuvant chemotherapy.	Feasible low-cost supportive model; needs larger trials.
Goodwin et al. (2022)	Adding metformin to standard treatment did not significantly improve invasive disease-free survival in high-risk operable breast cancer without diabetes.	Adjuvant metformin is not supported for recurrence prevention in this population.
Mohammed et al. (2023)	Metabolic syndrome and its components were associated with breast cancer risk, which rose with the number of components.	Metabolic risk screening and lifestyle prevention are relevant to breast cancer control.
Ismail et al. (2022)	Late-stage diagnosis was associated with aggressive molecular subtypes and with modifiable factors, including patient and provider delays.	Navigation and timely diagnostic pathways could downstage disease.
Kesson et al. (2012)	Introduction of multidisciplinary care was associated with improved survival and reduced variation in survival among hospitals.	Supports organization of care around multidisciplinary teams.
Lu et al. (2020)	A well-organized MDT may improve survival, whereas a disorganized MDT was associated with worse survival.	Team quality, not merely team existence, matters.

Study	Authors' conclusion (paraphrased)	Implication for breast cancer care
Brandão et al. (2021)	Implementing a tumor board was associated with a 53% reduction in mortality in early disease and was cost-effective.	Feasible, low-cost model for low-resource settings.
Tsai et al. (2020)	MDT care was associated with lower risk of recurrence and death; national policy should consider implementing it.	Supports system-level adoption of MDT care.

3.4 Risk of bias

Two trials were at low risk of bias and five raised some concerns, mainly because of unblinded delivery with patient-reported outcomes, small size, or exploratory analysis. Among observational studies, seven were at moderate risk and one at serious risk, chiefly through confounding (Table 4). Several ratings are provisional.

Table 4. Risk-of-bias assessment

Study	Tool	Features considered	Overall judgment
Sessler et al. (2019)	RoB 2	Randomized multicenter trial; intention-to-treat primary analysis; objective primary outcome; stopped at second interim analysis for futility; anesthetic technique cannot be blinded to clinicians.	Low (provisional)
Enlund et al. (2022)	ROBINS-I	National registry retrospective cohort; groups differed in most baseline characteristics before 1:1 propensity matching (4,658 pairs); unmeasured confounding possible.	Moderate (provisional)
Karami et al. (2022)	ROBINS-I	Single-center retrospective registry cohort; non-random allocation of anesthetic technique; multivariable Cox models.	Moderate (provisional)
Courneya et al. (2014)	RoB 2	Randomized with concealed allocation; exploratory follow-up not powered for cancer outcomes; end points abstracted retrospectively from charts; 33% of eligible patients recruited; 30.5% of controls took a 1-month exercise crossover.	Some concerns
Dieli-Conwright et al. (2018)	RoB 2	Randomized; unblinded exercise intervention; patient-reported outcomes; secondary-outcome report; 3-month follow-up in exercise group only.	Some concerns (provisional)
Bruce et al. (2021)	RoB 2	Pragmatic multicenter trial; computer-generated sequence with concealed central allocation; intention-to-treat; unblinded participants with a patient-reported primary outcome.	Some concerns (provisional)

Study	Tool	Features considered	Overall judgment
Saltbæk et al. (2024)	RoB 2	Randomized phase III; intention-to-treat; patient-reported primary outcome in an unblinded trial; stringent alpha (0.005) for multiple comparisons.	Some concerns (provisional)
Yazicioglu Kucuk and Zorba Bahceli (2024)	RoB 2	Single-center pilot with 42 participants; assessor-blinded per registry; patient-completed quality-of-life questionnaire; short follow-up.	Some concerns (provisional)
Goodwin et al. (2022)	RoB 2	Randomized, double-blind, placebo-controlled; stratified; all 3,649 patients analyzed; objective primary outcome.	Low
Mohammed et al. (2023)	ROBINS-I (adapted)	Single-center, hospital-based; controls were visitors matched on age; metabolic measures taken at diagnosis, so temporality is uncertain; adjusted regression.	Moderate
Ismail et al. (2022)	ROBINS-I (adapted)	Single tertiary center; patient-reported delay intervals are open to recall bias; stage and exposures measured together, so direction of association is uncertain.	Moderate (provisional)
Kesson et al. (2012)	ROBINS-I	Retrospective non-randomized comparison with a contemporaneous non-intervention area; adjusted for year, age, and deprivation; interrupted time series; tumor size available only from 1997.	Moderate
Lu et al. (2020)	ROBINS-I	Retrospective single center; groups very unbalanced before matching (stage III tumors 50.8% in MDT vs 12.7% in non-MDT); small MDT group (n = 299); propensity matching.	Serious (provisional)
Brandão et al. (2021)	ROBINS-I	Prospective cohort with before-and-after comparison; adjusted for age, HIV status, stage, and subtype; 11.2% lost to follow-up; cohorts separated by only 15 vs 18 months; residual confounding possible.	Moderate
Tsai et al. (2020)	ROBINS-I	National retrospective database cohort; 1:1 propensity-score matching; residual confounding possible.	Moderate (provisional)

Green, low; orange, some concerns or moderate; red, serious. Judgments marked provisional are based on abstract-level or partial information.

3.5 Synthesis

A pooled analysis was not performed. The studies differ in intervention, outcome (quality-of-life scores, function, recurrence, survival, odds of disease), and effect measure (mean difference, hazard ratio, odds ratio). Within anesthesia, the trial and the matched registry cohort report similar null estimates but for different outcomes (recurrence and overall survival). The four

multidisciplinary-team cohorts address a similar question but report different outcomes (breast cancer mortality, overall survival, recurrence) over different horizons, and one lacks a confidence interval, so pooling would be misleading. **Figure 2** therefore displays the reported hazard ratios descriptively. Formal assessment of reporting bias was not feasible because no outcome had 10 or more studies. Provisional certainty of evidence for each outcome domain is given in Supplementary Table S2.

3.6 Discussion

Breast cancer outcomes depend on far more than the tumor itself: they are shaped by how care is organized, by what happens around surgery and chemotherapy, by supportive and rehabilitative services, and by the metabolic health of the patient. This review brought together studies from six disciplines, and a clear pattern emerged. Interventions that improved coordination or the patient experience tended to show benefit, whereas biologically targeted additions to standard treatment, namely a different anesthetic technique and adjuvant metformin, did not change disease outcomes, and metabolic derangement and diagnostic delay marked a higher likelihood of disease and late presentation.

The large randomized comparison of regional and general anesthesia found no difference in recurrence and no difference in persistent incisional pain, a conclusion that differs from the retrospective signal that prompted the trial (Exadaktylos et al., 2006). The biological rationale was that surgical stress, volatile anesthetics, and opioids impair immune surveillance against residual tumor cells and that regional blockade would blunt these effects. Sessler et al. (2019) did not confirm this. Registry and cohort evidence points the same way: in a national Swedish registry, the apparent survival advantage of propofol-based anesthesia in the crude comparison disappeared after propensity matching (Enlund et al., 2022), and an Iranian single-center cohort found no meaningful difference in long-term overall survival between intravenous and volatile anesthesia, with only a short-term recurrence-free difference favoring volatile agents (Karami et al., 2022). Together these findings suggest that anesthetic choice exerts too small an immune effect to alter recurrence in patients already receiving standard systemic therapy and that earlier associations reflected confounding by indication, since patients receiving different anesthetics differ in age, stage, and setting.

Observational evidence associates physical activity after diagnosis with lower mortality (Ibrahim and Al-Homaidh, 2011), and the exercise trials add randomized support for patient-centered benefit. Exercise after surgery or treatment improved quality of life, fatigue, and fitness, with gains that persisted after supervision ended (Dieli-Conwright et al., 2018), and a large pragmatic physiotherapy-led program improved upper-limb function and pain without increasing complications or lymphedema while remaining cost effective (Bruce et al., 2021). By contrast, the earlier START trial found that neither aerobic nor resistance exercise significantly improved cancer-specific quality of life during chemotherapy while improving fitness and chemotherapy completion (Courneya et al., 2007). The difference may reflect timing, since exercise during chemotherapy competes with treatment toxicity, whereas exercise after surgery targets recovery of function. Survival-related end points in the START follow-up pointed in a favorable direction but were not statistically significant, which is expected for an exploratory analysis not powered for cancer outcomes; Courneya et al. (2014) themselves called for a definitive phase III trial. The most plausible mechanisms are better chemotherapy completion, favorable changes in insulin signaling, inflammation, and immune function, and improved body composition (Ballard-Barbash et al., 2012; Courneya et al., 2014), together with preserved shoulder mobility when exercise starts early after surgery. This pattern parallels dietary trials, in which an intervention accompanied by modest weight loss improved relapse-free survival (Chlebowski et al., 2006) while one without weight change did not (Pierce et al., 2007).

Nurse-led follow-up improved quality of life and reduced fear of recurrence, anxiety, and depression, while physician consultations fell and imaging patterns were unchanged (Saltbæk et al., 2024). A small randomized pilot of an eight-week nurse-led supportive care program in women receiving adjuvant chemotherapy likewise reported better global health and functional status (Yazicioglu Kucuk and Zorba Bahceli, 2024), although its sample was small. Likely mechanisms are structured self-management teaching, systematic symptom reporting, and navigation to services, which address needs that routine physician visits tend to miss. Taken together with the exercise findings, the supportive interventions that worked were active, structured, and individualized rather than passive surveillance.

Adjuvant metformin did not improve invasive disease-free survival irrespective of hormone receptor status and was associated with more severe non-hematologic toxicity (Goodwin et al., 2022), despite encouraging preclinical and observational signals. The rationale was that lowering insulin and related growth signals would slow tumor growth. The metabolic effects of

metformin in this trial program were reported earlier by Goodwin et al. (2015), but the clinical results indicate that such metabolic modulation alone did not translate into better disease control in unselected patients.

The Egyptian case-control study found that metabolic syndrome and its components were more frequent among women with breast cancer, with the proportion of cases rising as the number of components increased (Mohammed et al., 2023). This is consistent with a nested case-cohort study in Italy, in which the highest number of components carried the greatest risk with a significant trend (Agnoli et al., 2015), with a Chinese case-control study that found a higher prevalence of metabolic syndrome among cases (Wu et al., 2018), and with pooled follow-up evidence summarized in a meta-analysis (Guo et al., 2019). Proposed mechanisms include hyperinsulinemia and insulin-like growth factor signaling, adipokines and chronic low-grade inflammation, and increased estrogen production in adipose tissue (Dong et al., 2021). Because metabolic measures were taken after diagnosis, reverse causation cannot be excluded, and some anthropometric associations ran in unexpected directions, so these findings support screening for metabolic risk rather than a causal claim. The Egyptian cross-sectional study adds a health-service dimension: late-stage diagnosis was associated not only with aggressive molecular subtypes but also with modifiable delays by patients and by providers (Ismail et al., 2022), which indicates that stage at diagnosis reflects both tumor biology and system performance, and that both are plausible targets for screening and navigation programs.

Health-administration studies formed the largest group and converged: introducing or optimizing multidisciplinary team care was associated with lower mortality or recurrence in the United Kingdom, China, Taiwan, and Mozambique (Kesson et al., 2012; Lu et al., 2020; Brandão et al., 2021; Tsai et al., 2020). Two features deserve emphasis. First, benefit appeared to depend on how well the team functioned, because a well-organized team was associated with improved survival whereas a disorganized one was associated with worse survival than no team (Lu et al., 2020). Second, gains were concentrated in potentially curable disease, which suggests that coordination matters most where timely, sequenced, high-quality treatment can change the outcome (Brandão et al., 2021). Plausible mechanisms include standardized staging and treatment planning, better sequencing between surgery, systemic therapy, and follow-up, higher guideline adherence, more complete surgery and chemotherapy delivery, and active follow-up that improves adherence (Pillay et al., 2016; Kreienberg et al., 2018; Brandão et al., 2021). These findings agree with the certified-center evaluation of Kreienberg et al. (2018) but conflict with a German registry analysis that found no survival benefit for treatment in certified centers (Schrodi et al., 2015); differences in era, follow-up, and team models may explain the divergence. Critics have also questioned the added value and resource demands of routine team meetings (Munro, 2015; De Ieso et al., 2013), although cost-effectiveness was favorable in the Mozambican cohort and has been examined for multidisciplinary teams in secondary care more broadly (Ke et al., 2013).

3.6.1 Strengths and limitations

Strengths of this review include a structured PRISMA 2020 framework, a cross-disciplinary scope that places organizational and clinical interventions side by side, inclusion of randomized and observational designs, and structured appraisal of risk of bias and certainty. Several limitations temper the conclusions. The included studies are heterogeneous in design, population, intervention, and outcome, which precluded pooling, so the plotted effect estimates are descriptive only. Most evidence on organizational interventions is observational and vulnerable to confounding and time trends, and the exploratory exercise analysis was not powered for cancer outcomes. Only English-language publications were considered, and some disciplines are represented by few studies, so conclusions about those disciplines are preliminary. The completeness of study selection could not be verified from search logs, and several risk-of-bias judgments relied on partial reports.

3.6.2 Implications for practice and research

The evidence is strongest where organizational coordination and supportive care are concerned and weakest where single perioperative or pharmacologic additions have been tested. For practice, the findings support investment in functioning multidisciplinary teams, structured nurse-led follow-up, supervised exercise, attention to metabolic risk, and reduction of diagnostic delays, while discouraging the use of a particular anesthetic technique or adjuvant metformin solely to prevent recurrence outside trials. Future research should adopt standardized outcomes across disciplines, prospective multicenter designs in low- and middle-income settings, adequately powered trials of exercise on survival, and head-to-head evaluation of what makes a multidisciplinary team effective.

4. CONCLUSION

Across six disciplines, the strongest and most consistent signals favored well-organized multidisciplinary team care, nurse-led follow-up, and supervised exercise, whereas anesthetic technique and adjuvant metformin did not improve disease outcomes, and metabolic syndrome and diagnostic delay marked higher disease risk and late presentation. Because most evidence is observational and heterogeneous, causal conclusions should be drawn cautiously, and adequately powered trials and standardized outcome reporting are needed.

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AUTHOR CONTRIBUTIONS

All authors contributed to conception, screening, data extraction, risk-of-bias assessment, and manuscript writing and approved the final version.

CONFLICT OF INTEREST

The authors declare no competing interests.

Ethics Statement

Not applicable; this review used published data.

Data Availability Statement

Extracted study data are presented in the article and supplementary tables.

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Supplementary Table S2. Provisional certainty of evidence (GRADE) by outcome domain

Ratings are based on design, risk of bias, consistency, and precision.

Outcome domain	Studies (design)	Consistency and size of effect	Certainty (provisional)	Main reasons
Anesthetic technique and recurrence or survival	3 (1 RCT, 2 cohorts) (Sessler et al., 2019; Enlund et al., 2022; Karami et al., 2022)	Consistent null after confounding addressed	Moderate	Large RCT with interval compatible with small effects; cohorts at risk of confounding
Exercise and function or quality of life	3 RCTs (Courneya et al., 2014; Dieli-Conwright et al., 2018; Bruce et al., 2021)	Consistent benefit in two of three trials; timing may matter	Moderate	Unblinded, patient-reported outcomes
Exercise and survival outcomes	1 RCT (Courneya et al., 2014)	Favorable but non-significant	Low	Exploratory, underpowered, wide intervals
Nurse-led care and quality of life	2 RCTs (Saltbæk et al., 2024; Yazicioglu Kucuk and Zorba Bahceli, 2024)	Consistent benefit; one pilot	Moderate	Unblinded, patient-reported; small pilot
Metformin and invasive DFS	1 RCT (Goodwin et al., 2022)	Precise null	High	Large double-blind placebo-controlled trial
Multidisciplinary team care and survival or recurrence	4 cohorts (Kesson et al., 2012; Lu et al., 2020; Brandão et al., 2021; Tsai et al., 2020)	Consistent benefit; one study shows harm if disorganized	Low	Observational; confounding and time trends; large effects partly offset downgrading
Metabolic syndrome and breast cancer risk	1 case-control study (Mohammed et al., 2023)	Higher odds	Very low	Single study; temporality uncertain
Delays, subtype, and late-stage diagnosis	1 cross-sectional study (Ismail et al., 2022)	Delays and aggressive subtypes associated with late stage	Very low	Single study; recall bias; temporality uncertain

Supplementary Table S3. PRISMA 2020 checklist

Item	Checklist topic	Location in manuscript
1	Title: identify as a systematic review	Title page
2	Abstract	Abstract
3	Rationale	Introduction, paragraphs 1–6

Item	Checklist topic	Location in manuscript
4	Objectives	Introduction, paragraph 7
5	Eligibility criteria	Materials and methods 2.3
6	Information sources	Materials and methods 2.2
7	Search strategy	Materials and methods 2.2 (PubMed strategy)
8	Selection process	Materials and methods 2.4
9	Data collection process	Materials and methods 2.5
10	Data items	Materials and methods 2.5
11	Risk of bias assessment	Materials and methods 2.6
12	Effect measures	Materials and methods 2.5
13	Synthesis methods	Materials and methods 2.7
14	Reporting bias assessment	Materials and methods 2.7
15	Certainty assessment	Materials and methods 2.7; Supplementary Table S2
16	Study selection	Results and discussion 3.1; Figure 1
17	Study characteristics	Results and discussion 3.2; Table 1
18	Risk of bias in studies	Results and discussion 3.4; Table 4
19	Results of individual studies	Results and discussion 3.3; Tables 2–3; Figure 2
20	Results of syntheses	Materials and methods 2.7; Results and discussion 3.5
21	Reporting biases	Materials and methods 2.7
22	Certainty of evidence	Supplementary Table S2
23	Results and discussion 3.6	Results and discussion 3.6
24	Registration and protocol	Materials and methods 2.1
25	Support	Funding
26	Competing interests	Conflict of Interest
27	Availability of data, code, and materials	Data Availability Statement