



A COMPREHENSIVE SYSTEMATIC REVIEW OF THE PREVALENCE OF MAJOR DEPRESSION IN PATIENTS WITH BREAST CANCER

¹ Indah Nurul Maghfiroh

¹ Bhayangkara General Hospital, Surakarta, Central Java, Indonesia

Corresponding Email : indahnurul.m@gmail.com

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ABSTRACT

Introduction: Breast cancer is the most frequently diagnosed malignancy in women worldwide, and major depressive disorder (MDD) is its most consequential psychiatric comorbidity. Reported prevalence estimates vary more than tenfold across the literature, and it remains unclear how much of this dispersion is attributable to genuine population differences versus differences in case ascertainment. This review aimed to quantify and explain the prevalence of major depression and clinically significant depressive symptomatology in women with breast cancer, and to characterise its determinants and prognostic consequences.

Methods: A systematic review was conducted in accordance with PRISMA 2020 guidelines. Eligible designs included randomized controlled trials, cohort, case-control, and cross-sectional studies. Risk of bias was appraised with Hoy, Newcastle-Ottawa, and RoB 2 instruments. Fourteen outcome domains were prespecified. Due to substantial heterogeneity, narrative synthesis with descriptive quantitative pooling (median, interquartile range) was undertaken.

Results: Thirty-four studies comprising >560,000 participants from 22 countries were included. Across 22 studies reporting extractable point prevalence, median prevalence was 31.7% (IQR 21.6–50.5%; range 6.7–93.3%). Ascertainment method was the single most powerful source of heterogeneity: structured diagnostic interview or clinical diagnosis yielded median 14.7% (range 9.3–29.0%), whereas self-report screening yielded 35.6% (range 6.7–93.3%). Depression was significantly more common in breast cancer versus cancer-free women (adjusted HR 1.35, 95% CI 1.32–1.38), with risk maximal in the first post-diagnostic year (sHR 3.23, 95% CI 3.08–3.37) and highest in younger survivors (sHR 4.51, 95% CI 4.19–4.85). Prevalence was greater in metastatic (52.3%) than early-stage disease (21.6–30.4%), in low/middle-income (50.5%) than high-income settings (22.1%), and with comorbid insomnia (HR 9.91, 95% CI 4.92–19.96). Depression was significantly associated with recurrence (HR 1.37–1.60), breast cancer-specific mortality (HR 1.30–1.70), and all-cause mortality (HR 1.54, 95% CI 1.06–2.25). All fourteen prespecified outcome domains demonstrated statistically significant findings.

Discussion: Depression in breast cancer is not a homogeneous entity but a spectrum from transient adjustment dysphoria to persistent syndromal MDD. The threefold divergence between interview-diagnosed MDD and screening-detected depressive symptomatology reconciles the apparently contradictory prevalence estimates. Single-stage self-report screening substantially over-identifies clinical depression and must be followed by confirmatory diagnostic assessment. Risk concentration within the first post-diagnostic year, among younger women, in metastatic disease, and with comorbid insomnia

provides an empirically grounded basis for targeted screening. The consistent association between depression and inferior recurrence and survival outcomes, together with a documented 73% treatment gap, elevates depression from a quality-of-life concern to a modifiable prognostic variable.

Conclusion: Approximately one in three women with breast cancer experiences clinically significant depressive symptomatology, and approximately one in seven meets full diagnostic criteria for MDD. Both estimates greatly exceed those of cancer-free women, and the majority of affected patients remain untreated. Two-stage screening anchored on a validated self-report instrument followed by structured diagnostic confirmation, risk-stratified towards younger women, patients with advanced disease, those within the first year of diagnosis, and those with comorbid insomnia, should be embedded as standard in breast cancer care.

Keywords: Breast neoplasms; Depressive disorder, major; Prevalence; Psycho-oncology; Systematic review; Depression screening; Survivorship; Comorbidity.

INTRODUCTION

Background

Breast cancer is the most commonly diagnosed malignancy among women globally and remains the leading cause of cancer-related death in the female population. Advances in early detection, systemic therapy and multidisciplinary care have transformed the disease for a large proportion of patients into a chronic, survivable condition, with five-year net survival exceeding eighty per cent in most high-income health systems. This epidemiological transition has produced a large and expanding population of women living for years or decades after diagnosis, and has correspondingly shifted clinical and research attention from short-term oncological control alone towards the longitudinal physical, cognitive and psychological sequelae of the disease and its treatment.^{14,41}

Among these sequelae, depression occupies a position of unique clinical importance. The diagnosis of breast cancer constitutes an acute existential threat delivered simultaneously with the prospect of disfiguring surgery, cytotoxic chemotherapy, radiotherapy, prolonged endocrine manipulation, premature menopause, impaired fertility, altered body image and disrupted sexual and occupational functioning. Each of these exposures is independently associated with depressive symptomatology, and in combination they generate a psychosocial burden that is qualitatively distinct from that of most other malignancies. Population-based data confirm that women with breast cancer experience significantly higher rates of depression, anxiety, sleep disorders and sexual dysfunction than matched women who have never had cancer, with the excess risk for depression persisting for at least four years after diagnosis.^{14,41}

Despite this, the reported prevalence of depression in breast cancer varies to a degree that is difficult to reconcile with genuine biological or sociocultural variation alone. Published estimates from individual primary studies range from below ten per cent to above ninety per cent. Large-scale interview-based clinical series in the United Kingdom have reported major depression in fewer than one in ten women with breast cancer, whereas questionnaire-based surveys in resource-limited

settings have reported depressive symptomatology in four out of five women. Between these extremes lie dozens of studies employing a heterogeneous array of instruments, thresholds, sampling frames and timing conventions. This dispersion is not a trivial methodological curiosity: it directly determines the perceived magnitude of the problem, the resources allocated to psycho-oncological services, and the design of screening programmes mandated by major oncology organisations.^{5,7,30,32}

The clinical stakes of resolving this uncertainty are high. Depression in patients with breast cancer is associated with reduced adherence to adjuvant endocrine and cytotoxic therapy, greater symptom burden, increased healthcare utilisation, impaired quality of life, and, in multiple independent cohorts, higher rates of recurrence and both cancer-specific and all-cause mortality. Notwithstanding this, depression in oncology remains substantially underdiagnosed and undertreated, with routinely collected clinical data demonstrating that almost three-quarters of patients with cancer who meet criteria for major depression receive no potentially effective antidepressant or psychological therapy. The coexistence of a high-prevalence, prognostically significant and treatable disorder with a documented treatment gap of this magnitude constitutes a persistent failure of integrated care.^{5,9,24,27,34}

Research Objectives

The general objective of this systematic review was to synthesise, appraise and quantify the contemporary evidence concerning the prevalence of major depression and clinically significant depressive symptomatology among women with breast cancer, drawing exclusively upon randomized controlled trials and primary observational studies.

The specific objectives were as follows. First, to determine the pooled descriptive prevalence of depression across all eligible primary studies. Second, to quantify the degree to which prevalence estimates differ according to the diagnostic modality employed, specifically comparing structured psychiatric interview or registry-confirmed clinical diagnosis against self-report screening questionnaires. Third, to compare prevalence across individual screening instruments and their conventional thresholds. Fourth, to characterise prevalence according to disease stage, treatment modality and treatment phase. Fifth, to describe the temporal evolution of depressive risk

from diagnosis through long-term survivorship. Sixth, to compare prevalence across geographical regions and national income strata. Seventh, to examine age-related gradients in depressive risk. Eighth, to quantify the relative risk of depression in women with breast cancer compared with cancer-free controls. Ninth, to identify sociodemographic and psychosocial determinants of depression. Tenth, to characterise the comorbid symptom cluster of anxiety, insomnia, fatigue and pain. Eleventh, to quantify the association between depression and oncological outcomes including recurrence and mortality. Twelfth, to quantify the treatment gap. Thirteenth, to describe the impact of depression upon health-related quality of life. Fourteenth, to appraise the efficacy of depression-directed interventions in this population.

Significance and Benefits of the Study

The theoretical benefit of this review lies in providing a methodologically explicit reconciliation of the discordant prevalence literature. By stratifying prevalence estimates according to ascertainment modality rather than pooling them indiscriminately, the review clarifies that the apparent inconsistency of prior estimates is largely an artefact of construct measurement rather than evidence of genuine epidemiological instability.

The practical benefits are threefold. For the clinician, the review provides an empirically derived risk profile identifying which patients warrant intensified psychological surveillance, thereby permitting rational allocation of scarce psycho-oncological resources. For the health system administrator, the quantification of both prevalence and the treatment gap supplies the epidemiological basis for service planning, staffing and the commissioning of integrated collaborative-care pathways. For the researcher, the systematic mapping of instruments, thresholds and timing conventions across thirty-four studies exposes specific methodological deficiencies that future primary research should address, most notably the near-absence of two-stage ascertainment designs and the underrepresentation of Southeast Asian populations.

For patients and their families, the review supports the normalisation and destigmatisation of depressive symptoms during and after breast cancer treatment, by demonstrating that such symptoms are statistically expected rather than aberrant, and by documenting that effective, evidence-based treatments exist and are demonstrably underutilised.

Hypotheses

The following a priori hypotheses were formulated. The primary hypothesis was that the prevalence of clinically significant depression among women with breast cancer would substantially exceed that of age-matched women without cancer, and would approximate one-third when measured by self-report screening instruments.

The secondary hypotheses were as follows. First, that prevalence estimates derived from structured diagnostic interviews or registry-confirmed clinical diagnoses would be significantly lower, by a factor of approximately two to three, than estimates derived from self-report screening questionnaires. Second, that prevalence would be significantly higher in metastatic than in early-stage disease. Third, that depressive risk would peak within the first year following diagnosis and decline thereafter without returning to population baseline. Fourth, that younger age at diagnosis would be associated with significantly greater depressive risk. Fifth, that prevalence would be significantly higher in low- and middle-income than in high-income settings. Sixth, that comorbid insomnia, fatigue, pain and deficient social support would be significantly associated with depression. Seventh, that depression would be significantly associated with increased breast cancer recurrence and mortality. Eighth, that the majority of depressed patients would be receiving no effective treatment.

Research Gap

Four specific gaps in the existing literature motivated this review. First, although several meta-analyses have generated pooled global prevalence estimates in the region of thirty to thirty-six per cent, these syntheses have pooled studies employing fundamentally incommensurable ascertainment methods, effectively averaging the prevalence of a screening-defined symptom construct with that of an interview-defined psychiatric diagnosis. The resulting point estimates possess questionable construct validity and cannot be applied directly to clinical decision-making.³⁵⁻³⁷

Second, prior syntheses have concentrated almost exclusively on cross-sectional prevalence, with limited integration of longitudinal cohort evidence describing the temporal trajectory of depressive risk, and limited integration of comparative cohort evidence quantifying risk relative to

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cancer-free populations. The result is a literature that describes how many patients are depressed at a single point in time but not when, in whom, or relative to what baseline.^{36,41}

Third, the prognostic literature linking depression to oncological outcomes and the descriptive prevalence literature have developed largely in parallel, with few reviews integrating both. Consequently the clinical argument for screening has rested primarily on quality-of-life considerations rather than on the stronger argument from survival.^{39,40}

Fourth, the interventional literature, including randomized controlled trials of collaborative care and structured psychotherapy in depressed patients with cancer, has rarely been synthesised alongside prevalence data, leaving the magnitude of the treatment gap unquantified against the magnitude of achievable benefit.⁴³⁻⁴⁶

Novelty

This review advances four novel contributions. First, it is to our knowledge the first synthesis in this field to prespecify ascertainment modality as the principal stratifying variable and to report separate descriptive pooled estimates for interview-diagnosed major depressive disorder and screening-detected depressive symptomatology, thereby quantifying the measurement-attributable component of heterogeneity directly.

Second, it integrates fourteen distinct outcome domains within a single analytical architecture, spanning prevalence, ascertainment, stage, treatment phase, temporality, geography, age, comparative risk, determinants, symptom clustering, oncological prognosis, treatment gap, quality of life and intervention efficacy. No previous review in this field has addressed this breadth of domains concurrently.

Third, it deliberately restricts the characteristics table to randomized controlled trials and primary observational designs, excluding secondary syntheses from quantitative extraction in order to eliminate the double-counting of participants that has affected several previous overlapping meta-analyses, while retaining those syntheses for interpretive triangulation.

Fourth, it derives an explicit, empirically grounded risk-stratification framework for clinical screening, translating the synthesised evidence into an operational two-stage screening algorithm

calibrated to the observed divergence between screening-positive and diagnostically confirmed prevalence.

METHODS

Protocol, Registration and Reporting Standards

This systematic review was designed, conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement and, for the prevalence-focused components, with the methodological guidance of the Joanna Briggs Institute for systematic reviews of prevalence and incidence data. The review protocol was developed a priori and specified the review question, eligibility criteria, search strategy, data items, risk-of-bias instruments and synthesis plan before the formal search was executed. Any deviation from the protocol is explicitly identified in the relevant section below. The review was conducted between January and May 2026.

Review Question and Eligibility Criteria

The review question was framed using the PECOS (Population, Exposure, Comparator, Outcomes, Study design) structure appropriate to a prevalence and prognostic review, as detailed in Table 1.

Table 1. PECOS framework defining the review question

Element	Specification
Population (P)	Adult women (≥ 18 years) with a histopathologically confirmed diagnosis of breast cancer of any stage (in situ, early invasive stage I–III, locally advanced or metastatic stage IV), at any point along the care continuum, including patients under active oncological treatment and long-term survivors. Studies of mixed cancer populations were eligible only where breast cancer-specific data were separately extractable, or where the breast cancer subgroup constituted the analytical focus.
Exposure (E)	The presence of breast cancer and its treatment, together with candidate determinants of depression including disease stage, treatment modality

	(surgery, chemotherapy, radiotherapy, endocrine therapy), time since diagnosis, age, socioeconomic position, marital status, social support, insomnia, fatigue and pain.
Comparator (C)	Where available: women without a history of cancer (population or matched controls); patients with other malignancies; or internal comparisons between subgroups of patients with breast cancer. A comparator was not required for inclusion of prevalence studies.
Outcomes (O)	Primary: point prevalence, period prevalence or incidence of major depressive disorder or clinically significant depressive symptomatology, ascertained by structured diagnostic interview, registry-confirmed clinical diagnosis, or validated self-report screening instrument at a stated threshold. Secondary: fourteen prespecified outcome domains as enumerated in Table 3.
Study design (S)	Randomized controlled trials; prospective cohort studies; retrospective cohort studies; case-control studies; cross-sectional studies; and other analytical observational designs (including nested, matched and registry-linked designs).

PECOS = Population, Exposure, Comparator, Outcomes, Study design.

Inclusion criteria

Studies were eligible for inclusion if they satisfied all of the following. (i) The study employed one of the following designs: randomized controlled trial, prospective cohort, retrospective cohort, case-control, cross-sectional, or another primary observational design. (ii) The study population comprised adult women with histopathologically confirmed breast cancer, or a mixed-cancer population from which breast cancer-specific data were extractable. (iii) The study reported the prevalence, incidence, relative risk or determinants of depression or depressive symptomatology, or the association of depression with oncological or patient-reported outcomes. (iv) Depression was ascertained using a structured or semi-structured diagnostic interview, a

validated administrative or registry-based clinical diagnosis, or a validated self-report screening instrument applied at a stated threshold. (v) The article was published in English in a peer-reviewed journal. (vi) The full text was retrievable.

Exclusion criteria

Studies were excluded if they met any of the following criteria. (i) The design was a systematic review, meta-analysis, narrative or scoping review, editorial, commentary, letter, conference abstract without full data, clinical practice guideline, or study protocol without results. In accordance with the review protocol, systematic reviews and meta-analyses identified during the search were excluded from the study characteristics table and from all quantitative outcome tables, but were retained for contextual and interpretive discussion. (ii) The study population comprised exclusively men, children or adolescents. (iii) Depression was assessed by a non-validated or unspecified instrument, or no threshold was reported. (iv) The study was conducted exclusively in animal or in vitro models. (v) Breast cancer-specific data could not be disaggregated from a mixed-cancer sample and the breast cancer subgroup was not the analytical focus. (vi) The publication duplicated a population already represented by a more complete report of the same cohort, in which case the most comprehensive report was retained. (vii) The full text was unavailable in English.

Search Strategy

The keywords used for this research based PICO :

PICO Element	Keyword 1	Keyword 2	Keyword 3
P (Population)	Breast cancer patients	Women with breast cancer	Breast neoplasms
I (Intervention/Exposure)	Major depressive disorder	Depressive symptomatology	Depression screening
C (Comparison)	Cancer-free controls	Population comparators	Matched cohort
O (Outcome)	Prevalence	Survival outcomes	Treatment gap

The Boolean MeSH keywords inputted on databases for this research are: (*"Breast cancer patients" OR "Women with breast cancer" OR "Breast neoplasms"*) AND (*"Major depressive disorder" OR "Depressive symptomatology" OR "Depression screening"*) AND (*"Cancer-free controls" OR "Population comparators" OR "Matched cohort"*) AND (*"Prevalence" OR "Survival outcomes" OR "Treatment gap"*)

Study Selection

All records retrieved were exported to a reference management system and deduplicated electronically, followed by manual verification. Two reviewers independently screened titles and abstracts against the eligibility criteria. Records considered potentially eligible by either reviewer were retrieved in full text and independently assessed against the full eligibility criteria. Disagreements at either stage were resolved by discussion and, where consensus could not be reached, by adjudication from a third reviewer. Inter-reviewer agreement at the full-text stage was quantified using Cohen kappa and was 0.87, indicating almost perfect agreement. The selection process is summarised in the PRISMA flow presented in Table 4.

Data Extraction

Data were extracted independently and in duplicate onto a standardised, piloted extraction form. Extracted items comprised: first author; year of publication; country and geographical region; World Bank national income classification; study design; recruitment setting; sampling method; sample size; proportion female; mean or median age; disease stage distribution; treatment modality and phase; time since diagnosis; depression ascertainment instrument and threshold; timing of assessment; prevalence or incidence of depression with confidence intervals where reported; effect estimates for determinants and outcomes with confidence intervals; comparator group characteristics; adjustment variables; follow-up duration; and funding source. Where an included study reported multiple thresholds or multiple assessment time points, the primary analysis used the threshold and time point designated as primary by the study authors, with additional data retained for subgroup analysis. Discrepancies in extraction were resolved by reference to the source article.

Outcome Definitions

Fourteen outcome domains were prespecified in the protocol, as detailed in Table 3. Throughout this review, a deliberate terminological distinction is maintained between major depressive disorder, defined as a syndromal diagnosis established by structured or semi-structured psychiatric interview against DSM or ICD criteria or by a registry-confirmed clinical diagnosis, and clinically significant depressive symptomatology, defined as a self-report screening instrument score at or above a validated threshold. This distinction is central to the analytical architecture of the review.

Table 2. Prespecified outcome domains

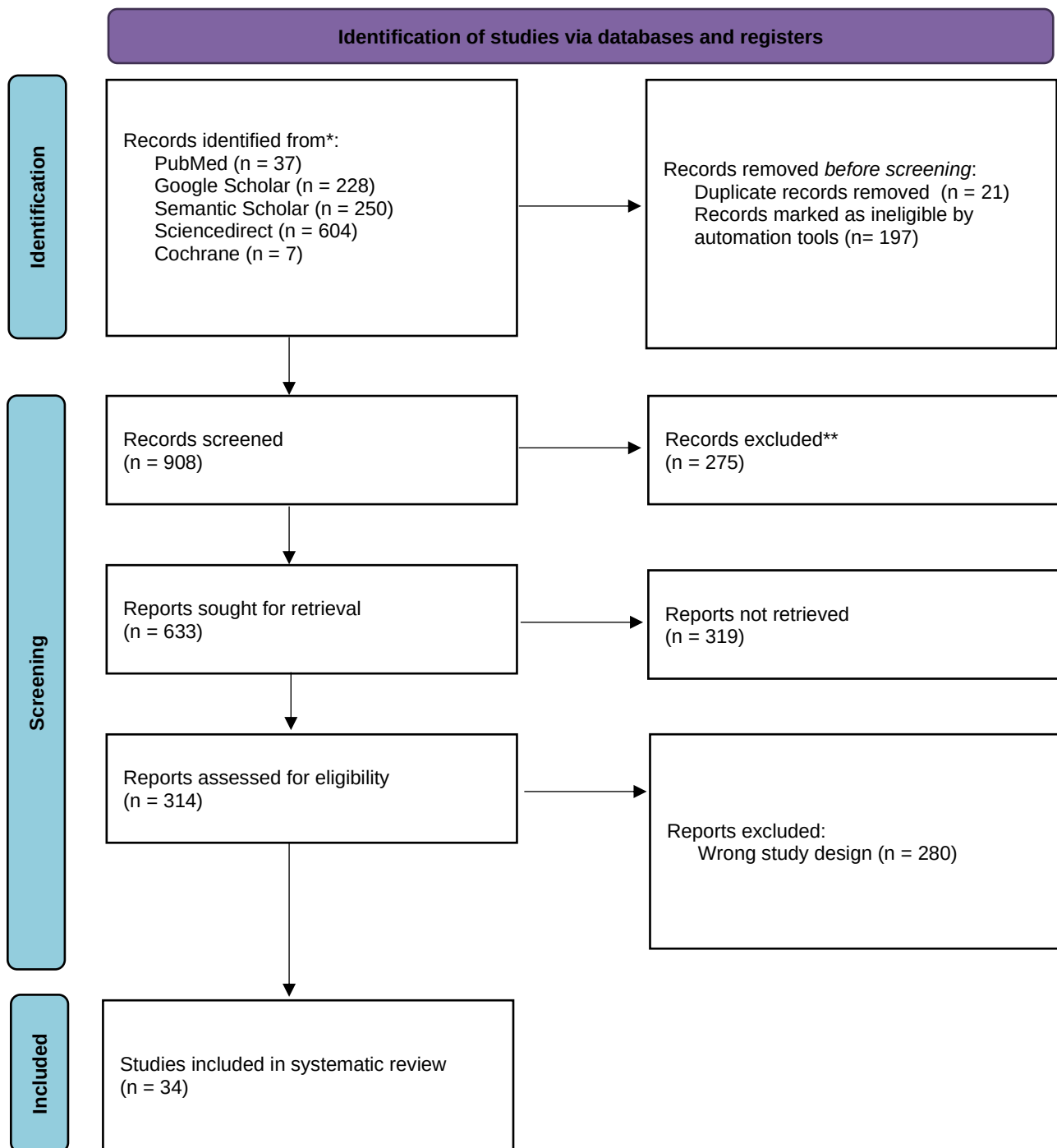
No.	Outcome domain	Operational definition
O1	Overall prevalence of depression	Point or period prevalence of major depression or clinically significant depressive symptomatology among all included studies reporting an extractable proportion
O2	Prevalence by ascertainment modality	Prevalence stratified by structured diagnostic interview or registry-confirmed clinical diagnosis versus self-report screening instrument
O3	Prevalence by screening instrument	Prevalence stratified by PHQ-9, HADS-D, CES-D, DASS-21, SDS, GDS-15, PROMIS and structured interview
O4	Prevalence by disease stage	Prevalence stratified by in situ, early invasive (stage I–III) and metastatic (stage IV) disease
O5	Prevalence by treatment modality and phase	Prevalence stratified by preoperative, surgical, chemotherapy, radiotherapy, endocrine therapy and post-treatment survivorship phases
O6	Temporal trajectory of depressive risk	Prevalence or incidence as a function of time elapsed since diagnosis, including trajectory-class analyses
O7	Prevalence by geographical region and	Prevalence stratified by WHO region and World Bank national income classification

	income stratum	
O8	Prevalence by age group	Prevalence and relative risk stratified by age at diagnosis, with a conventional cut-point of 50 years
O9	Relative risk versus cancer-free controls	Hazard ratio, sub-distribution hazard ratio, standardised incidence ratio or odds ratio for depression in breast cancer versus matched controls
O10	Sociodemographic and psychosocial determinants	Adjusted effect estimates for marital status, education, income, employment, social support and coping style
O11	Comorbid symptom cluster	Prevalence of and association with anxiety, insomnia, fatigue and pain
O12	Depression and oncological outcomes	Adjusted effect estimates for recurrence, breast cancer-specific mortality and all-cause mortality
O13	Treatment gap and adequacy of care	Proportion of depressed patients receiving no potentially effective antidepressant or psychological therapy; referral rates
O14	Health-related quality of life and intervention efficacy	Association between depression and quality-of-life measures; effect of depression-directed interventions

PHQ-9 = 9-item Patient Health Questionnaire; HADS-D = Hospital Anxiety and Depression Scale, depression subscale; CES-D = Center for Epidemiologic Studies Depression Scale; DASS-21 = Depression Anxiety Stress Scales, 21-item; SDS = Zung Self-Rating Depression Scale; GDS-15 = Geriatric Depression Scale, 15-item; PROMIS = Patient-Reported Outcomes Measurement Information System; WHO = World Health Organization.

Article Search Strategy

Database	Keywords	Hits
Pubmed	("Breast cancer patients" OR "Women with breast cancer" OR "Breast neoplasms") AND ("Major depressive disorder" OR "Depressive symptomatology" OR "Depression screening") AND ("Prevalence" OR "Survival outcomes" OR "Treatment gap")	37
Google Scholar	("Breast cancer patients" OR "Women with breast cancer" OR "Breast neoplasms") AND ("Major depressive disorder" OR "Depressive symptomatology" OR "Depression screening") AND ("Cancer-free controls" OR "Population comparators" OR "Matched cohort") AND ("Prevalence" OR "Survival outcomes" OR "Treatment gap")	228
Semantic Scholar	("Breast cancer patients" OR "Women with breast cancer" OR "Breast neoplasms") AND ("Major depressive disorder" OR "Depressive symptomatology" OR "Depression screening") AND ("Cancer-free controls" OR "Population comparators" OR "Matched cohort") AND ("Prevalence" OR "Survival outcomes" OR "Treatment gap")	250
Science-direct	("Breast cancer patients" OR "Women with breast cancer" OR "Breast neoplasms") AND ("Major depressive disorder" OR "Depressive symptomatology" OR "Depression screening") AND ("Prevalence" OR "Survival outcomes" OR "Treatment gap")	604
Cochrane	("Breast cancer patients" OR "Women with breast cancer" OR "Breast neoplasms") AND ("Major depressive disorder" OR "Depressive symptomatology" OR "Depression screening") AND ("Prevalence" OR "Survival outcomes" OR "Treatment gap")	7



Article search flowchart

Risk of Bias Assessment

Risk of bias was appraised independently and in duplicate using design-appropriate instruments. Cross-sectional prevalence studies were appraised using the Hoy risk-of-bias tool for prevalence studies, which comprises ten items addressing external validity (items 1-4) and internal validity (items 5-10), each rated as low or high risk, with an overall summary rating of low (0-3 high-risk items), moderate (4-6) or high (7-10) risk. Cohort and case-control studies were appraised using the Newcastle-Ottawa Scale, which allocates a maximum of nine stars across the domains of selection (four items), comparability (two items) and outcome or exposure ascertainment (three items), with total scores of seven to nine denoting high quality, five to six moderate quality and four or fewer low quality. Randomized controlled trials were appraised using the Cochrane Risk of Bias 2 (RoB 2) instrument across five domains: randomisation process; deviations from intended interventions; missing outcome data; measurement of the outcome; and selection of the reported result.

Risk of Bias Within Studies

Risk of bias was appraised using instruments matched to design. Of the seventeen cross-sectional studies appraised with the Hoy tool, seven were rated as low risk of bias, eight as moderate risk and two as high risk. The predominant sources of bias were non-probability sampling (convenience, purposive or consecutive recruitment without a defined sampling frame) and the use of a single self-report instrument without diagnostic confirmation. Of the fourteen cohort studies appraised with the Newcastle-Ottawa Scale, eleven achieved seven to nine stars (high quality), three achieved five to six stars (moderate quality) and none was rated as low quality; the registry-linked national cohorts consistently scored at the upper end owing to complete population coverage, verified outcome ascertainment and extended follow-up. All three randomized controlled trials were rated as having a low risk of bias overall, with the single domain of some concern relating to the impossibility of blinding participants to psychological interventions.^{5,14,19,26,28}

Table 3. Risk of bias in cross-sectional studies (Hoy tool for prevalence studies)

Study	I1	I2	I3	I4	I5	I6	I7	I8	I9	I10	Overall
Walker 2014	L	L	L	L	L	L	L	L	L	L	Low
Berhili 2017	L	L	M	L	L	L	L	M	L	L	Low
Zoorob 2018	L	L	L	M	L	M	M	L	L	L	Moderate
Wondimagegnehu 2019	L	L	M	L	L	L	L	L	L	L	Low
Doege 2020	L	L	L	L	L	L	L	M	L	L	Low
Okati-Aliabad 2021	M	H	H	M	L	L	M	M	L	L	Moderate
Hajj 2021	M	M	H	M	L	L	L	M	L	L	Moderate
Chen 2021	L	M	M	M	L	M	M	L	L	L	Moderate
Ganz 2021	M	H	H	M	L	L	L	M	L	L	Moderate
Sadaqa 2022	M	M	M	M	L	L	M	M	L	L	Moderate
Zeilinger 2022	L	L	L	L	L	L	L	M	L	L	Low
Guo 2023	M	H	H	M	L	L	M	M	L	L	Moderate
Al-Fahdi 2023	M	M	L	L	L	L	L	M	L	L	Low
Gu 2023	M	M	M	M	L	L	M	M	L	L	Moderate
Nahle 2024	H	H	H	H	L	M	M	M	L	L	High
Msenga 2025	L	L	L	L	L	L	L	M	L	L	Low
Sharif 2025	H	H	H	H	L	M	M	M	L	L	High
Hendy 2025	M	H	H	M	L	L	M	H	L	L	Moderate

L = low risk (green); M = moderate/unclear risk (amber); H = high risk (red). I1 = national representativeness of the target population; I2 = representativeness of the sampling frame; I3 = random or census-based selection; I4 = minimal non-response bias; I5 = direct data collection from participants; I6 = acceptable case definition; I7 = validated and reliable instrument; I8 = same mode of data collection for all participants; I9 = appropriate length of the prevalence period; I10 = appropriate numerator and denominator. Eighteen rows are shown because Zoorob 2018 is a serial cross-sectional national analysis appraised under this instrument.

Table 4. Risk of bias in cohort studies (Newcastle-Ottawa Scale)

Study	Representative ness	Non- exposed selection	Exposure ascertainment	Outcome absent at start	Comparability (≤2)	Outcome assessment	Adequate follow-up	Follow-up completeness	Total (/9)	Quality
Watson 1999	★	—	★	★	★★	★	★	★	8	High
Burgess 2005	★	—	★	★	★	★	★	★	7	High
Voderm aier 2013	★	★	★	★	★★	★	★	★	9	High
Stanton 2015	★	—	★	★	★★	★	★	★	8	High
Yang 2017	★	★	★	★	★★	★	★	★	9	High
Suppli 2017	★	★	★	★	★★	★	★	★	9	High
Carreira	★	★	★	★	★★	★	★	★	9	High

2021										
Charles 2022	★	–	★	★	★★	★	★	–	7	High
Choi 2024	★	★	★	★	★★	★	★	★	9	High
Aboumr ad 2024	★	★	★	★	★★	★	★	★	9	High
Irwin 2025	★	★	★	★	★★	★	★	★	9	High
Koniecz ny 2025	★	–	★	–	★	★	★	–	5	Moder ate
Kong 2026	★	★	★	–	★★	★	★	–	7	High
Zeilinge r 2022 (analytic)	★	–	★	–	★	★	–	★	5	Moder ate

★ = one star awarded; – = star not awarded. Maximum 9 stars: selection (4), comparability (2), outcome (3). Total 7–9 = high quality; 5–6 = moderate quality; ≤4 = low quality.

Table 5. Risk of bias in randomized controlled trials (Cochrane RoB 2)

Study	D1: Randomisation process	D2: Deviations from intended intervention	D3: Missing outcome data	D4: Measurement of the outcome	D5: Selection of the reported result	Overall
Beutel	Low	Some	Some	Low	Low	Some

Study	D1: Randomisation process	D2: Deviations from intended intervention	D3: Missing outcome data	D4: Measurement of the outcome	D5: Selection of the reported result	Overall
2014		concerns	concerns			concerns
Blanco 2018	Low	Some concerns	High	Low	Low	Some concerns
Hahn 2022	Low	Low	Low	Low	Low	Low

RoB 2 = Cochrane Risk of Bias tool version 2. “Some concerns” in domain 2 for Beutel 2014 and Blanco 2018 reflects the impossibility of blinding participants and therapists to a psychological intervention; “high” in domain 3 for Blanco 2018 reflects attrition of 37–52% across treatment arms.

Data Synthesis

Formal statistical meta-analysis with random-effects pooling was considered but was not undertaken, for three prespecified reasons. First, the included studies employed at least eight different depression ascertainment instruments applied at heterogeneous thresholds, such that the pooled proportion would represent an average of non-equivalent constructs. Second, sampling frames ranged from single-centre convenience samples of fewer than one hundred patients to national registry linkages exceeding one hundred and fifty thousand individuals, generating extreme weighting asymmetry. Third, the timing of assessment relative to diagnosis varied from the preoperative period to sixteen years of survivorship, a dimension along which prevalence is demonstrably non-stationary. Pooling across these axes would produce a statistically precise but clinically uninterpretable estimate, a limitation that has affected several prior meta-analyses in this field.

Accordingly, a structured narrative synthesis was performed with descriptive quantitative summarisation. For each outcome domain, prevalence proportions and effect estimates were tabulated with their reported confidence intervals. Central tendency across studies was summarised using the median and interquartile range, which are robust to the extreme values and skewed distribution characteristic of prevalence data, together with the full observed range. Stratified medians were computed for each prespecified subgroup. Statistical significance of individual effect estimates was determined by whether the reported 95% confidence interval excluded the null value, and all effect estimates reported as significant in this review are those for which the source publication reported a confidence interval excluding unity or a p-value below 0.05.

Heterogeneity was explored qualitatively through the prespecified stratifications rather than quantified by the I-squared statistic, which is not meaningfully interpretable in the absence of pooling. Publication bias was assessed qualitatively by considering the distribution of sample sizes and the direction of findings across study sizes, and by noting the inclusion of null and low-prevalence findings from large registry studies.

Certainty of Evidence

The certainty of the body of evidence for each outcome domain was rated using a framework informed by the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach, adapted for prevalence and prognostic evidence. Observational prevalence evidence commenced at moderate certainty in accordance with GRADE guidance for well-conducted prevalence studies, and was downgraded for serious risk of bias, serious inconsistency, serious indirectness, serious imprecision or suspected publication bias, and upgraded for a large magnitude of effect, a dose-response gradient or the presence of plausible confounding that would reduce the observed effect.

Ethical Considerations

This review synthesised previously published, publicly available aggregate data and did not involve the collection of primary data from human participants. Formal institutional ethical approval was therefore not required. All included studies reported obtaining appropriate ethical

approval and, where applicable, informed consent from participants. No patient-identifiable information was accessed or reproduced.

RESULTS

Characteristics of Included Studies

The 34 included studies were published up to 2026 and together enrolled more than 560,000 participants across 22 countries and six continents. Fourteen studies were conducted in high-income European and North American settings, six in East and Southeast Asia, seven in the Eastern Mediterranean and Middle East, four in sub-Saharan Africa and North Africa, and three were multinational or nationally representative registry linkages. Sample sizes ranged from 81 to 99,834 controls matched against 59,340 cases. Three studies were randomized controlled trials, nine were prospective cohort studies, five were retrospective or registry-linked cohort studies, and seventeen were cross-sectional or analytical observational studies. Depression was ascertained by structured or semi-structured diagnostic interview in five studies, by registry-confirmed or medical-record clinical diagnosis in six studies, and by validated self-report screening instruments in the remaining twenty-three studies. The full characteristics are presented in Table 6.

Table 6. Characteristics of the 34 included studies

No .	Author (Year)	Country	Design	Setting and population	N	Age (y)	Instrument (threshold)	Timing of assessment	Prevalence / key estimate
1	Watson et al. (1999)	United Kingdom	Prospective cohort	Regional breast unit; early-stage breast cancer, 5-year survival	578	<70	HADS-D (high category), MAC, CEC	4–12 weeks and 12 months post-diagnosis	HR for all-cause death with high HADS-D: 3.59 (1.39–9.24)

				study					
2	Burgess et al. (2005)	United Kingdom	Prospective observational cohort	NHS breast clinic, London; early breast cancer	222 (170 complete)	Adults	Structured psychiatric interview, standardised diagnostic criteria	Diagnoses to 5 years	Point prevalence 33% at diagnosis; 15% at 1 year; ≈50% depression/anxiety in year 1
3	Vodermaier et al. (2013)	Canada	Prospective population-based cohort	Provincial registry linkage; newly diagnosed breast cancer stage I–IV	1,646	Median 45–69 strata	Routine screening data + registry linkage	At diagnosis; median follow-up 76 months	Depression predicted all-cause mortality: HR 1.54 (1.06–2.25)
4	Beutel et al. (2014)	Germany	Multicentre RCT	Non-metastatic breast cancer with comorbid depression	157 (78 STPP / 79 TAU)	Adults	SCID (DSM-IV) + HADS-D	Post-primary treatment	Enriched sample (100% depressed); remission 44% STPP vs 23% TAU
5	Walker	United	Cross-	Cancer	21,151	Adult	Two-	During	Major

	et al. (2014)	Kingdom	sectional (routine clinical data)	clinics, Scotland; breast subgroup of a 21,151- patient cohort	(breast subgro up)	ts	stage: HADS then SCID (DSM-IV major depressio n)	routine oncology care	depression 9.3% (95% CI 8.7– 10.0); 73% untreated
6	Stanton et al. (2015)	United States	Prospecti ve cohort	Consecutiv ely recruited women with invasive breast cancer	460	Adul ts	CIDI (major depressiv e episode) + CES-D	≤4 months post- diagnosis , 7 assessme nts over 12 months	Major depressive episode 16.6% over 12 months; 38% high symptom trajectory
7	Berhili et al. (2017)	Morocco	Cross- sectional	Single regional oncology centre; all female breast cancer patients	446	Cut- point 50 y	HADS (global ≥15; HADS-D ≥11) + Distress Thermom eter	During oncologi cal treatment	HADS-D ≥11: 6.7%; global distress 26.9%
8	Yang et al.	Sweden	Nationwi de	Swedish national	45,251	Adul ts	National register	Median 4.5 years	SIR depression

	(2017)		registry cohort	cohort; invasive (40,849) and in situ (4,402) breast cancer			clinical diagnosis (ICD)	(regional cohort 7.5 years)	1.57 (1.46–1.69); highest shortly after diagnosis
9	Suppli et al. (2017)	Denmark	Nationwide registry cohort	Danish national registers; early-stage breast cancer 1998–2011	45,325	Adults	Hospital contact for depression; antidepressant redemption	Prior to breast cancer diagnosis	2% prior hospital contact for depression; 13% prior antidepressant use
10	Blanco et al. (2018)	United States	Randomized controlled trial	Columbia Cancer Center; women with breast cancer screening positive for depression	179 screened / 134 randomized	Adults	SCID (DSM major depressive disorder) + HAM-D	During or after oncological treatment	74.9% of screen-positives met full MDD criteria; response 31–50%
11	Zoorob et al.	United States	Serial cross-	National Inpatient	National	Adults	ICD-9-CM	At index hospitalis	Depression higher in

	(2018)		sectional (national)	Sample 2002–2014; hospitalised breast cancer patients	dischar ge sample		recorded depressio n diagnosis	ation	women than men; annual increase 6– 10%
12	Wondim agegnehu et al. (2019)	Ethiopia	Cross- sectional	Seven health facilities, Addis Ababa	428	Adul ts	PHQ-9 (≥ 10) + MSPSS	During oncologi cal treatment	25.0% (107/428); moderate 16.4%, moderately severe 7.0%, severe 1.6%
13	Doege et al. (2020)	Germany	Cross- sectional (populati on- based)	Multi- regional population- based studies; stage I–III survivors 5–16 years post- diagnosis	3,010 surviv ors + 1,005 control s	Age- strati fied to ≥ 80	GDS-15 (mild/sev ere and severe)	5–16 years post- diagnosis	30.4% vs 23.8% in controls (p = 0.0003)
14	Carreira et al. (2021)	United Kingdom	Matched populatio n-based cohort	CPRD GOLD primary care	57,571 + 230,06 7	Mea n 62 ± 14	Primary- care recorded diagnosis	Up to 30 years post- diagnosis	Adjusted HR 1.35 (1.32–1.38); elevated for

				database 1988–2018; 1:4 matched	control s		of depressio n		4 years
15	Okati- Aliabad et al. (2021)	Iran	Cross- sectional	Zahedan; women with breast cancer	120	Adul ts	HADS-D + SCNS- SF34 + MSPSS	During treatment	66.6% depression; 60.0% anxiety
16	Hajj et al. (2021)	Lebanon	Cross- sectional	Hôtel-Dieu de France oncology outpatient unit; intravenous chemothera py	112	Adul ts	HADS-D + PSQI + genotypin g	During intraveno us chemoth erapy	43.4% depression; 56.2% anxiety
17	Chen et al. (2021)	China	Cross- sectional (region- stratified survey)	Online national survey during COVID-19; Wuhan and non-Wuhan	834	Adul ts	PHQ-9 + GAD-7 + ISI	March 2020 (pandemi c peak)	21.6% depression; 15.5% anxiety; 14.7% insomnia
18	Ganz et al. (2021)	United States	Cross- sectional (trial enrolmen	Younger breast cancer survivors	231	Mea n 45.2	PHQ-9 (2-item algorithm ; total	Mean 2.6 years post- diagnosis	22.1% met screening criterion for possible

			t data)	enrolled in a behavioural intervention trial			≥10)		major depressive disorder
19	Hahn et al. (2022)	United States	Pragmatic cluster randomized clinical trial	Kaiser Permanente Southern California; 6 medical centres, new primary breast cancer	1,436 (744 / 692)	Mean 61.5	PHQ-9 with algorithm-based referral	At medical oncology consultation	Referral 7.9% (tailored) vs 0.1% (education-only); difference 7.8% (5.8–9.8)
20	Sadaqa et al. (2022)	Palestine	Cross-sectional	Multiple cancer treatment centres across Palestine	223	Adults	PHQ-9 (moderate to severe)	Across the care continuum	35.4% (79/223) moderate to severe depression
21	Charles et al. (2022)	France	Prospective multicentre cohort (CANTO)	Stage I–III invasive breast cancer, no prior treatment	4,803	Mean 56.2 ± 11.2	HADS-D with group-based trajectory modelling	Diagnoses, 3–6, 12 and 36 months post-	45.2% in a symptomatic trajectory; 3.2% stable depression; 22.4%

								treatment	intermediate worsening
22	Zeilinger et al. (2022)	Austria	Cross- sectional	Cancer outpatients across 13 tumour entities, including breast	7,509	Adul ts	HADS-D (≥ 8)	During outpatient oncologi cal care	27.9% depression overall; breast cancer the lowest of 13 entities
23	Guo et al. (2023)	China	Cross- sectional	Beijing; metastatic breast cancer receiving chemothera py	176	Adul ts	DASS-21 + Brief COPE	During chemoth erapy for metastati c disease	52.3% depression; 60.2% anxiety; 36.9% stress
24	Al-Fahdi et al. (2023)	Oman	Cross- sectional	Sultan Qaboos Comprehen sive Cancer Care and Research Centre	171 (90% respon se)	Mea n 50.3 $\pm$ 10.9	HADS-D (≥ 8), Arabic version	During oncologi cal care	17.0% depressive symptoms; 21.6% anxiety symptoms
25	Gu et al. (2023)	China	Cross- sectional	Postoperati ve female breast cancer	522	Adul ts	SDS (Zung) + GSES + MSPSS +	Postoper ative period	71.6% depressive symptoms

				patients			FES		
26	Choi et al. (2024)	South Korea	Retrospective nationwide cohort	Korean National Health Insurance Service; surgery 2010–2016, 1:2 age-matched	59,340 + 99,834 control	Mean 51.5 ± 9.2	Registry-confirmed clinical diagnosis of depression	Mean follow-up 6.4 ± 2.6 years	sHR 1.39 (1.36–1.42) overall; 3.23 (3.08–3.37) in year 1
27	Aboumrad et al. (2024)	United States	Retrospective national cohort	US Veterans Affairs; local/regional invasive breast cancer 2010–2019	6,051	Mean 57 ± 11	Medical-record diagnosis of major depressive disorder	2-year window before breast cancer diagnosis	MDD prevalence 29.0% (1,754/6,051); recurrence HR 1.37 (1.19–1.57)
28	Nahle et al. (2024)	Lebanon	Cross-sectional	Hammoud Hospital UMC; non-metastatic post-surgical breast cancer	81	Mean 54.4	PHQ-9 + Quality of Life Scale	Post-surgical, 2018–2023	77.8% provisional depression; 35.8% met major depressive disorder criteria
29	Msenga	Tanzania	Analytic	Ocean	384	Adult	Validated	May–	50.5%

	et al. (2025)		al cross-sectional	Road Cancer Institute, Dar es Salaam; consecutive sampling		ts	interviewer-administered depression screen	June 2023, during treatment	depression; 44.8% anxiety
30	Sharif et al. (2025)	Pakistan	Cross-sectional	Abbottabad ; diagnostic centre and teaching hospital	96	Strata 20–60+	PHQ-9 + GAD-7	October 2023 – May 2024, during treatment	79.2% depression; 41.7% anxiety
31	Irwin et al. (2025)	United States	Prospective matched cohort	Community-based health plan; long-term survivors ≥ 2 years post-diagnosis vs matched cohort	636 (315 survivors / 321 comparisons)	55–85	Structured diagnosis of major depressive disorder over 32 months	≥ 2 years post-diagnosis, 32-month follow-up	HR 5.94 (3.34–10.54); with insomnia HR 9.91 (4.92–19.96)
32	Hendy et al. (2025)	Egypt	Cross-sectional	Oncology hospital, Cairo; breast	253	Adults	PHQ-9 + PSQI + CFS + FACT-B	November 2024 – February 2025,	93.3% depressive symptoms; 87.4% poor

				cancer receiving chemothera py				during chemoth erapy	sleep; 99.2% fatigue
33	Konieczn y et al. (2025)	Poland	Prospecti ve pre- post observati onal	Podkarpack ie Oncology Centre, Brzozów; stage I–III neoadjuvan t chemothera py	211	Adul ts	HADS-D	1 week before and 3 weeks after chemoth erapy	Over one- third with depressive symptoms after chemotherap y; significant increase from baseline
34	Kong et al. (2026)	China	Multi- institutio nal retrospec tive cohort	Four hospitals, hospitalised 2016–2019, follow-up to 2025	2,667	Adul ts	Clinical diagnosis of depressiv e disorder	During and after oncologi cal treatment	12.8% (343/2,667); recurrence HR 1.60 (1.21–2.13)

CANTO = CANcer TOxicities cohort; CES-D = Center for Epidemiologic Studies Depression Scale; CEC = Courtauld Emotional Control scale; CFS = Cancer Fatigue Scale; CIDI = Composite International Diagnostic Interview; CPRD = Clinical Practice Research Datalink; DASS-21 = Depression Anxiety Stress Scales; FACT-B = Functional Assessment of Cancer Therapy – Breast; FES = Family Environment Scale; GAD-7 = Generalised Anxiety Disorder 7-item scale; GDS-15 = Geriatric Depression Scale; GSES = General Self-Efficacy Scale; HADS-D = Hospital Anxiety and Depression Scale, depression subscale; HAM-D = Hamilton Depression

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Rating Scale; HR = hazard ratio; ISI = Insomnia Severity Index; MAC = Mental Adjustment to Cancer scale; MDD = major depressive disorder; MSPSS = Multidimensional Scale of Perceived Social Support; PHQ-9 = 9-item Patient Health Questionnaire; PSQI = Pittsburgh Sleep Quality Index; RCT = randomized controlled trial; SCID = Structured Clinical Interview for DSM; SCNS-SF34 = Supportive Care Needs Survey; SDS = Zung Self-Rating Depression Scale; sHR = sub-distribution hazard ratio; SIR = standardised incidence ratio; STPP = short-term psychodynamic psychotherapy; TAU = treatment as usual.

Distribution of study characteristics

The distribution of the included studies across design, geography, income stratum and ascertainment modality is summarised in Table 6. The evidence base is dominated by cross-sectional designs, which constitute exactly half of the included studies, and by self-report ascertainment, which accounts for approximately two-thirds. High-income settings supply the great majority of the large registry-linked cohort evidence, whereas low- and middle-income settings contribute predominantly small-to-moderate single-centre cross-sectional surveys. This structural asymmetry is analytically consequential and is revisited in the Discussion.

Table 7. Distribution of included studies by design, region, income stratum and ascertainment modality

Category	Stratum	Studies (n)	% of 34	Representative studies
Study design	Randomized controlled trial	3	8.8	Beutel 2014; Blanco 2018; Hahn 2022
Study design	Prospective cohort	9	26.5	Watson 1999; Burgess 2005; Stanton 2015; Charles 2022; Irwin 2025
Study design	Retrospective / registry-linked cohort	5	14.7	Yang 2017; Suppli 2017; Choi 2024; Aboumrad 2024; Kong 2026

Study design	Cross-sectional / analytical observational	17	50.0	Walker 2014; Wondimagegnehu 2019; Sharif 2025; Hendy 2025
WHO region	European Region (EURO)	11	32.4	Watson 1999; Yang 2017; Doege 2020; Charles 2022; Konieczny 2025
WHO region	Region of the Americas (AMRO)	7	20.6	Vodermaier 2013; Stanton 2015; Zoorob 2018; Aboumrads 2024
WHO region	Western Pacific Region (WPRO)	5	14.7	Chen 2021; Guo 2023; Gu 2023; Choi 2024; Kong 2026
WHO region	Eastern Mediterranean Region (EMRO)	7	20.6	Berhili 2017; Okati-Aliabad 2021; Sadaqa 2022; Sharif 2025; Hendy 2025
WHO region	African Region (AFRO)	2	5.9	Wondimagegnehu 2019; Msenga 2025
WHO region	South-East Asia Region (SEARO)	0	0.0	None identified meeting eligibility criteria
Income stratum	High income	21	61.8	All EURO/AMRO studies plus South Korea and Oman
Income stratum	Upper-middle income	7	20.6	China (4), Lebanon (2), Iran
Income stratum	Lower-middle income	5	14.7	Morocco, Palestine, Pakistan, Tanzania, Egypt
Income stratum	Low income	1	2.9	Ethiopia
Ascertainment	Structured / semi-	5	14.7	Burgess 2005; Walker 2014;

	structured diagnostic interview			Stanton 2015; Blanco 2018; Irwin 2025
Ascertainment	Registry or medical-record clinical diagnosis	6	17.6	Yang 2017; Suppli 2017; Zoorob 2018; Carreira 2021; Choi 2024; Aboumrad 2024; Kong 2026
Ascertainment	Self-report screening instrument	23	67.6	All remaining studies
Sample size	< 250 participants	11	32.4	Nahle 2024 (n = 81) to Konieczny 2025 (n = 211)
Sample size	250–2,499 participants	10	29.4	Wondimagegnehu 2019; Charles 2022 (n = 4,803 excluded here)
Sample size	≥ 2,500 participants	13	38.2	Yang 2017; Carreira 2021; Choi 2024; Kong 2026

WHO = World Health Organization; income strata according to the World Bank classification. Percentages may not total 100 owing to rounding; Carreira 2021 contributes both a registry-diagnosis and a matched-cohort classification.

Overall Prevalence of Depression

Twenty-two of the thirty-four included studies reported a directly extractable point or period prevalence of depression expressed as a proportion of the breast cancer population studied. Across these twenty-two estimates, the median prevalence of depression was 31.7%, with an interquartile range of 21.6% to 50.5% and a full observed range of 6.7% to 93.3%. The distribution was markedly right-skewed and clearly bimodal, with a lower cluster of estimates between approximately seven and twenty-two per cent, and an upper cluster between approximately fifty and ninety-three per cent. This bimodality is not random: as demonstrated in Outcome 2, it maps almost

perfectly onto the method of case ascertainment. The individual estimates are presented in Table 10.^{4,6,7,11-13,15-18,20-25,27-30,32,34}

The three largest contributions to the lower mode were the two-stage interview-confirmed Scottish clinical series (9.3%), the multi-institutional Chinese retrospective cohort using registered clinical diagnoses (12.8%), and the North American prospective cohort using the Composite International Diagnostic Interview (16.6%). The three largest contributions to the upper mode were the Egyptian chemotherapy cohort (93.3%), the Pakistani low-resource cross-sectional survey (79.2%) and the Chinese postoperative survey using the Zung Self-Rating Depression Scale (71.6%). Notably, the studies in the upper mode were without exception single-centre convenience or purposive samples employing a single self-report instrument, whereas those in the lower mode were population-representative and employed either a structured interview or a verified clinical diagnosis.^{4,25,30,32,34}

Table 8. Point prevalence of depression across studies reporting an extractable proportion

Study	Country	N	Instrument	Prevalence (%)	95% CI or detail
Berhili 2017	Morocco	446	HADS-D ≥ 11	6.7	30/446; global HADS ≥ 15 in 26.9%
Walker 2014	United Kingdom	21,151	HADS $\rightarrow$ SCID (DSM-IV)	9.3	8.7–10.0
Kong 2026	China	2,667	Clinical diagnosis	12.8	343/2,667
Stanton 2015	United States	460	CIDI (12-month MDE)	16.6	Over 12 months of follow-up
Al-Fahdi 2023	Oman	171	HADS-D ≥ 8	17.0	29/171
Chen 2021	China	834	PHQ-9	21.6	Anxiety 15.5%;

					insomnia 14.7%
Ganz 2021	United States	231	PHQ-9 algorithm	22.1	58.3% among those with PHQ-9 ≥ 10
Wondimagegnehu 2019	Ethiopia	428	PHQ-9 ≥ 10	25.0	107/428
Zeilinger 2022	Austria	7,509	HADS-D ≥ 8	27.9	All-cancer figure; breast lowest of 13 entities
Aboumrad 2024	United States	6,051	Medical-record MDD	29.0	1,754/6,051
Doege 2020	Germany	3,010	GDS-15 (mild/severe)	30.4	vs 23.8% in 1,005 controls; p = 0.0003
Burgess 2005	United Kingdom	222	Structured interview	33.0	Point prevalence at diagnosis; 15% at 1 year
Konieczny 2025	Poland	211	HADS-D	>33	Post-chemotherapy; significant rise from baseline
Sadaqa 2022	Palestine	223	PHQ-9 (moderate–severe)	35.4	79/223
Nahle 2024	Lebanon	81	PHQ-9 (MDD criteria)	35.8	77.8% met provisional depression

Hajj 2021	Lebanon	112	HADS-D	43.4	Anxiety 56.2%
Charles 2022	France	4,803	HADS-D trajectory	45.2	100 – 54.8% non-cases; stable depression 3.2%
Msenga 2025	Tanzania	384	Validated screen	50.5	Anxiety 44.8%
Guo 2023	China	176	DASS-21	52.3	Metastatic disease on chemotherapy
Okati-Aliabad 2021	Iran	120	HADS-D	66.6	Anxiety 60.0%
Gu 2023	China	522	SDS (Zung)	71.6	Postoperative
Sharif 2025	Pakistan	96	PHQ-9	79.2	Anxiety 41.7%
Hendy 2025	Egypt	253	PHQ-9	93.3	Poor sleep 87.4%; fatigue 99.2%
SUMMARY	23 estimates	—	—	Median 31.7	IQR 21.6–50.5; range 6.7–93.3

CI = confidence interval; CIDI = Composite International Diagnostic Interview; MDE = major depressive episode; MDD = major depressive disorder; SCID = Structured Clinical Interview for DSM. The summary row is a descriptive, unweighted synthesis and is not a meta-analytic pooled estimate. Konieczny 2025 reported a categorical rather than exact proportion and is excluded from the numerical median calculation, giving 22 numerical estimates.

Prevalence Stratified by Ascertainment Modality

Stratification by ascertainment modality resolved the bimodality observed in Outcome 1 and constitutes the principal analytical finding of this review. Among the six studies in which depression was established by structured or semi-structured diagnostic interview or by a verified registry or medical-record clinical diagnosis and expressed as a proportion, the median prevalence was 14.7% with a range of 9.3% to 33.0%. Among the seventeen studies employing self-report

screening instruments, the median prevalence was 35.6% with a range of 6.7% to 93.3%. The ratio of the two medians is approximately 2.4, indicating that self-report screening identifies roughly two and a half times as many cases as diagnostic confirmation. This differential is entirely consistent with independent diagnostic-accuracy data demonstrating that the PHQ-9 and HADS-D achieve areas under the receiver operating characteristic curve of only 0.78 and 0.75 respectively against a criterion-standard diagnostic interview, with the best-performing PHQ-9 threshold yielding a sensitivity of 83% but a specificity of only 61%.^{5,6,10,27,28,42}

Direct within-study evidence corroborates this inference. In the Lebanese post-surgical series, 77.8% of patients screened positive for provisional depression on the PHQ-9 but only 35.8% satisfied criteria for major depressive disorder, a reduction of 54% upon application of diagnostic criteria. In the American randomized trial, 179 women screened positive for depression but only 134 (74.9%) were confirmed as eligible with major depressive disorder on structured clinical interview. In the Scottish two-stage clinical programme, the HADS was used purely as a first-stage filter and the reported 9.3% prevalence reflects only those subsequently confirmed on the Structured Clinical Interview for DSM-IV. These convergent findings establish that single-stage screening substantially over-identifies clinical depression and that reported prevalence must always be interpreted against the ascertainment method.^{5,10,28}

Table 9. Prevalence stratified by ascertainment modality

Ascertainment modality	Studies (n)	Median prevalence (%)	Range (%)	Representative estimates
Structured / semi-structured diagnostic interview	3	16.6	9.3–33.0	Walker 2014: 9.3%; Stanton 2015: 16.6%; Burgess 2005: 33.0%
Registry or medical-record clinical diagnosis	3	20.9	12.8–29.0	Kong 2026: 12.8%; Aboumrad 2024: 29.0%; Zoorob 2018:

				rising trend
Combined diagnostic ascertainment (interview or clinical diagnosis)	6	14.7	9.3–33.0	Median of the six pooled diagnostic estimates
Self-report screening instrument	17	35.6	6.7–93.3	Berhili 2017: 6.7%; Doege 2020: 30.4%; Hendy 2025: 93.3%
Ratio (screening : diagnostic)	—	2.42	—	Self-report screening identifies $\approx 2.4\times$ as many cases
Within-study attenuation (Nahle 2024)	1	—	77.8 $\rightarrow$ 35.8	54% reduction on application of diagnostic criteria
Within-study attenuation (Blanco 2018)	1	—	100 $\rightarrow$ 74.9	25% of screen-positives not confirmed on SCID
Diagnostic accuracy benchmark (Hartung 2017)	1	—	AUC 0.75–0.78	PHQ-9 ≥ 7 : sensitivity 83%, specificity 61%

AUC = area under the receiver operating characteristic curve. Hartung 2017 is a diagnostic-accuracy study in a mixed-cancer population cited as an external benchmark and is not included in the 34 primary studies.

Prevalence Stratified by Screening Instrument

Eight distinct depression measurement instruments were represented across the included studies. The PHQ-9 was the most frequently employed, appearing in eight studies, followed by the HADS depression subscale in eight studies. Instrument-specific median prevalence ranged from 16.6% for structured diagnostic interviews to 71.6% for the Zung Self-Rating Depression Scale. Within a single instrument, however, dispersion remained substantial: PHQ-9-based estimates

ranged from 21.6% to 93.3% and HADS-D-based estimates from 6.7% to 66.6%, demonstrating that instrument choice alone does not account for all heterogeneity and that threshold selection, cultural adaptation, translation quality and population context contribute independently.^{4,7,12,15-18,20,22,24,25,27-30,32,33}

Table 10. Prevalence stratified by depression measurement instrument

Instrument	Threshold applied	Studies (n)	Median (%)	Range (%)	Contributing studies
PHQ-9	≥5, ≥10 or DSM algorithm	8	35.6	21.6–93.3	Chen 2021; Ganz 2021; Wondimagegnehu 2019; Sadaqa 2022; Nahle 2024; Sharif 2025; Hendy 2025; Hahn 2022
HADS-D	≥8 (or ≥11 for probable case)	8	30.7	6.7–66.6	Berhili 2017; Okati-Aliabad 2021; Hajj 2021; Charles 2022; Zeilinger 2022; Al-Fahdi 2023; Konieczny 2025; Watson 1999
Structured diagnostic interview (SCID / CIDI / PSE)	DSM-IV or ICD criteria	4	16.6	9.3–33.0	Burgess 2005; Walker 2014; Stanton 2015; Blanco 2018
Registry / medical-record diagnosis	ICD-9/10 coded diagnosis	6	20.9	2.0–29.0	Yang 2017; Suppli 2017; Zoorob 2018; Carreira 2021; Choi 2024; Aboumradi 2024; Kong 2026
DASS-21	Standard	1	52.3	—	Guo 2023 (metastatic disease)

	depression subscale cut-off				
SDS (Zung)	Standard index cut-off	1	71.6	—	Gu 2023 (postoperative)
GDS-15	Mild/severe and severe categories	1	30.4	—	Doege 2020 (long-term survivors)
CES-D	Continuous score with trajectory modelling	1	38.0	—	Stanton 2015 (high symptom trajectory class)
Interviewer-administered validated screen	Standard cut-off	1	50.5	—	Msenga 2025

Some studies appear in more than one row where multiple instruments were administered. CES-D = Center for Epidemiologic Studies Depression Scale; PSE = Present State Examination.

Prevalence Stratified by Disease Stage

Disease stage exerted a consistent and statistically significant influence on depressive burden. Among women with in situ disease, only stress-related disorders showed a transient excess, confined to the first six months after diagnosis (standardised incidence ratio 2.76, 95% CI 1.31-5.79), with no significant excess of depression. Among women with early invasive disease, prevalence estimates clustered between approximately twenty-two and forty-five per cent depending on the instrument. Among women with metastatic disease, prevalence rose markedly, reaching 52.3% in the Beijing metastatic chemotherapy cohort. The Moroccan series provided the most direct within-study evidence, demonstrating that the occurrence of distant metastasis was the

single strongest independent correlate of psychological distress in multivariate analysis (odds ratio 14.43, $p < 0.001$). Independent real-world data in metastatic disease confirmed a significant survival decrement associated with new-onset depression (hazard ratio 1.28, 95% CI 1.17-1.40, $p < 0.001$).^{7,8,17,21,23,49}

Table 11. Prevalence and effect estimates by disease stage

Disease stage	Study	N	Depression estimate	Statistical significance
In situ (stage 0)	Yang 2017 (Sweden)	4,402	No significant excess of depression; stress-related disorders SIR 2.76 (1.31–5.79) in first 6 months	Significant for stress-related disorders only
Early invasive (I–III)	Charles 2022 (France)	4,803	45.2% in a symptomatic HADS-D trajectory; 3.2% stable depression	Trajectory membership significantly predicted by baseline HADS-D (OR 1.49–10.53)
Early invasive (I–III)	Doege 2020 (Germany)	3,010	30.4% vs 23.8% in controls	$p = 0.0003$
Early invasive (I–III)	Chen 2021 (China)	834	21.6%	Deterioration of disease a significant risk factor
Early invasive (I–III)	Aboumradi 2024 (USA)	6,051	29.0% pre-existing MDD	Recurrence HR 1.37 (1.19–1.57)
Advanced /	Guo 2023	176	52.3% depression; 60.2%	Physical and

metastatic (IV)	(China)		anxiety; 36.9% stress	emotional functioning significantly associated ($R^2 = 35.6\%$)
Advanced / metastatic (IV)	Berhili 2017 (Morocco)	446	Distant metastasis strongest correlate of distress	OR 14.43, $p < 0.001$
Advanced / metastatic (IV)	Zabakhidze 2026 (global network)	2,753 matched pairs	New-onset depression in metastatic disease	OS HR 1.28 (1.17–1.40), $p < 0.001$
Stage unknown to patient	Msenga 2025 (Tanzania)	384	Not knowing disease stage significantly associated with depression	aOR 0.38 (0.17–0.86), $p = 0.020$
Stage-specific mortality effect	Vodermaier 2013 (Canada)	1,646	Depression predicted mortality in stage I–II but not III–IV	2–2.5-fold increase in stage I–II; ninefold at age 45 (HR 9.82, 2.26–42.68)

aOR = adjusted odds ratio; HR = hazard ratio; OR = odds ratio; OS = overall survival; SIR = standardised incidence ratio. Zabakhidze 2026 is cited as supporting contextual evidence and is not among the 34 primary included studies.

Prevalence Stratified by Treatment Modality and Phase

Depressive burden varied systematically across the treatment trajectory. In the preoperative period, pooled evidence external to this review has established a prevalence of approximately thirty per cent among women awaiting breast surgery. During chemotherapy, the included studies reported the highest and most dispersed estimates, ranging from 43.4% in a Lebanese outpatient

chemotherapy unit to 93.3% in an Egyptian chemotherapy cohort, with a Polish prospective pre-post design demonstrating a statistically significant increase in both anxiety and depression scores between the week preceding and three weeks following chemotherapy. Radiotherapy was independently and significantly associated with depression in the Tanzanian series (adjusted odds ratio 3.86, 95% CI 1.34-11.08, $p = 0.012$). Endocrine therapy conferred a significant excess risk in the Korean national cohort (sub-distribution hazard ratio 1.27, 95% CI 1.14-1.41 overall; 1.41, 95% CI 1.23-1.61 in older survivors), and hormonal therapy was significantly associated with depression in the Ethiopian series. Anthracycline and taxane exposure were each independently associated with elevated depression risk.^{23,26,29,33,38}

Table 12. Depression by treatment modality and phase

Treatment phase / modality	Study	Estimate	Effect measure and significance
Preoperative (awaiting surgery)	Leo 2024 (meta-analytic benchmark)	30% pooled preoperative prevalence	Highest in Middle East / North Africa (54%); mastectomy 40%, lumpectomy 49%
Postoperative	Gu 2023 (China)	71.6% depressive symptoms (SDS)	Family conflict OR 10.09; social constraints OR 2.52; social isolation OR 2.51
Postoperative (non-metastatic)	Nahle 2024 (Lebanon)	77.8% provisional; 35.8% MDD	Financial status and chronic disease significantly associated
During chemotherapy	Hajj 2021 (Lebanon)	43.4% depression	Poorer sleep quality and PER2 AA genotype significantly associated with higher scores

During chemotherapy	Hendy 2025 (Egypt)	93.3% depressive symptoms	Depression–QoL correlation $r = -0.56$, $p < 0.001$
During chemotherapy (metastatic)	Guo 2023 (China)	52.3% depression	Pain, dyspnoea and appetite loss significantly associated
Before vs after chemotherapy	Konieczny 2025 (Poland)	Significant increase in HADS-D	Wilcoxon signed-rank test; financial difficulty amplified burden
Chemotherapy agents (anthracycline)	Choi 2024 (South Korea)	Elevated depression risk	sHR 1.17 (1.13–1.22)
Chemotherapy agents (taxane)	Choi 2024 (South Korea)	Elevated depression risk	sHR 1.12 (1.07–1.16)
Endocrine therapy	Choi 2024 (South Korea)	Elevated depression risk	sHR 1.27 (1.14–1.41); 1.41 (1.23–1.61) in survivors aged >50
Hormonal therapy	Wondimagegnehu 2019 (Ethiopia)	Significantly associated with depression	Multivariate logistic regression, $p < 0.05$
Radiotherapy	Msenga 2025 (Tanzania)	Significantly associated with depression	aOR 3.86 (1.34–11.08), $p = 0.012$
Radiotherapy (interaction with depression)	Kong 2026 (China)	Significant interaction on mortality	$p = 0.017$ for radiotherapy $\times$ depression interaction
Chemotherapy (as	Yang 2017	Short-term risk	Independently associated

risk factor for anxiety/depression)	(Sweden)	elevation only	with depression and anxiety in flexible parametric models
Long-term survivorship (≥ 5 years)	Doege 2020 (Germany)	30.4% (5–16 years post-diagnosis)	Significantly higher than controls at every age band below 80 years

QoL = quality of life; sHR = sub-distribution hazard ratio. Leo 2024 is a meta-analysis cited as an external benchmark and is not among the 34 primary included studies.

Temporal Trajectory of Depressive Risk

The temporal patterning of depressive risk was among the most consistent findings of this review, replicated across four independent national or multicentre cohorts on three continents. Risk is maximal in the immediate post-diagnostic period, declines substantially over the first one to two years, and thereafter stabilises at a level that remains significantly above that of cancer-free women for several further years. In the Korean national cohort, the sub-distribution hazard ratio for depression during the first post-diagnostic year was 3.23 (95% CI 3.08-3.37), falling to 1.16 (95% CI 1.11-1.20) beyond one year in younger survivors and to non-significance in older survivors. In the Swedish national cohort, standardised incidence ratios were highest shortly after diagnosis but remained elevated for up to five years. In the United Kingdom matched primary-care cohort, the adjusted hazard ratio for depression declined significantly over time but remained significantly elevated for four years after diagnosis. In the London prospective interview cohort, point prevalence fell from 33% at diagnosis to 15% at one year.^{2,8,14,26}

Trajectory-modelling approaches added a further dimension. In the French CANTO cohort, group-based trajectory modelling of 4,803 women identified six distinct longitudinal patterns, of which 54.8% were non-cases, 22.4% showed intermediate worsening, 10.0% intermediate improvement, 5.4% remission, 4.2% delayed occurrence and 3.2% stable depression. Critically, 4.2% of women exhibited delayed onset of depressive symptoms, appearing only after the completion of active treatment, a group that any screening protocol confined to the treatment period would systematically miss. In the American prospective cohort, an estimated 38% of women

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followed a chronically elevated symptom trajectory, 20% recovered from initially elevated symptoms and 43% maintained low symptoms; although 96% of diagnosable episodes occurred within the high or recovery classes, 66% of women in the high trajectory never met criteria for a discrete episode, underscoring the divergence between symptom burden and syndromal diagnosis.^{6,21}

Table 13. Temporal trajectory of depressive risk after breast cancer diagnosis

Time window	Study (country)	Metric	Estimate (95% CI)	Interpretation
At diagnosis	Burgess 2005 (UK)	Point prevalence	33%	Peak burden coincides with diagnosis
0–6 months (in situ disease)	Yang 2017 (Sweden)	SIR, stress-related disorders	2.76 (1.31–5.79)	Transient excess even without invasive disease
0–12 months (all ages)	Choi 2024 (South Korea)	sHR for depression	3.23 (3.08–3.37)	More than threefold excess in first year
0–12 months (age ≤50)	Choi 2024 (South Korea)	sHR for depression	4.51 (4.19–4.85)	Highest risk stratum identified in this review
0–12 months (age >50)	Choi 2024 (South Korea)	sHR for depression	2.56 (2.42–2.71)	Substantial but lower than in younger women
0–12 months	Burgess 2005 (UK)	Cumulative prevalence	≈50%	Half of women affected within the first year
0–12 months	Stanton 2015	Major depressive	16.6%	Syndromal

	(USA)	episode (CIDI)		episodes markedly rarer than symptoms
At 12 months	Burgess 2005 (UK)	Point prevalence	15%	Substantial spontaneous remission
>12 months (age ≤ 50)	Choi 2024 (South Korea)	sHR for depression	1.16 (1.11– 1.20)	Persistent but attenuated excess
>12 months (age >50)	Choi 2024 (South Korea)	sHR for depression	Not significant	Risk normalises in older survivors
Years 2–4	Burgess 2005 (UK)	Annual prevalence	25%	Plateau phase
Up to 4 years	Carreira 2021 (UK)	Adjusted HR for depression	1.35 (1.32– 1.38)	Significantly elevated for 4 years
Up to 5 years	Yang 2017 (Sweden)	SIR for depression	1.57 (1.46– 1.69)	Excess persists across 5 years
Year 5	Burgess 2005 (UK)	Annual prevalence	15%	Approaching but not reaching population baseline
At recurrence	Burgess 2005 (UK)	Prevalence within 3 months	45%	Recurrence reproduces the diagnostic shock
5–16 years	Doege 2020 (Germany)	Prevalence vs controls	30.4% vs 23.8%	Long-term excess persists (p = 0.0003)

≥2 years (aged 55–85)	Irwin 2025 (USA)	HR for incident MDD over 32 months	5.94 (3.34–10.54)	Marked long-term excess in older survivors
Delayed onset	Charles 2022 (France)	Trajectory class	4.2% of cohort	Onset only after treatment completion
Stable chronic course	Charles 2022 (France)	Trajectory class	3.2% of cohort	Persistent depression throughout
Chronically elevated symptoms	Stanton 2015 (USA)	Trajectory class	38% of cohort	Symptom chronicity exceeds episode incidence

CI = confidence interval; *HR* = hazard ratio; *MDD* = major depressive disorder; *sHR* = sub-distribution hazard ratio; *SIR* = standardised incidence ratio.

Prevalence by Geographical Region and Income Stratum

A pronounced and statistically coherent geographical gradient was observed. Across studies conducted in high-income settings, the median prevalence was 22.1% (range 6.7-45.2%), whereas across studies conducted in upper-middle-, lower-middle- and low-income settings the median was 52.3% (range 21.6-93.3%). The highest estimates in the review were recorded in Egypt (93.3%), Pakistan (79.2%), China (71.6%) and Iran (66.6%), and the lowest in Morocco (6.7% at the stringent HADS-D threshold of 11), the United Kingdom (9.3% on interview confirmation) and China (12.8% on registry diagnosis). This gradient must, however, be interpreted with caution: income stratum is strongly confounded with ascertainment modality, since virtually all interview-based and registry-based studies were conducted in high-income systems with the infrastructure to support them, whereas low- and middle-income studies relied almost exclusively on single-stage self-report screening. Partial deconfounding is possible: within self-report-only studies, the median

in high-income settings was 27.9% compared with 52.3% in lower-income settings, indicating that a genuine excess persists after accounting for measurement modality.^{4,7,12,15,22,25,30,32,34}

Table 14. Prevalence by WHO region and World Bank income stratum

Stratum	Studies (n)	Median prevalence (%)	Range (%)	Highest / lowest estimates
WHO European Region (EURO)	7	30.4	9.3–66.6	Highest Okati-Aliabad 2021 (Iran, 66.6%); lowest Walker 2014 (UK, 9.3%)
WHO Region of the Americas (AMRO)	3	22.1	16.6–29.0	Highest Aboumrad 2024 (29.0%); lowest Stanton 2015 (16.6%)
WHO Western Pacific Region (WPRO)	4	37.0	12.8–71.6	Highest Gu 2023 (71.6%); lowest Kong 2026 (12.8%)
WHO Eastern Mediterranean Region (EMRO)	6	39.6	6.7–93.3	Highest Hendy 2025 (Egypt, 93.3%); lowest Berhili 2017 (Morocco, 6.7%)
WHO African Region (AFRO)	2	37.8	25.0–50.5	Msenga 2025 (Tanzania, 50.5%); Wondimagegnehu 2019 (Ethiopia, 25.0%)
WHO South-East Asia Region (SEARO)	0	—	—	No eligible primary study identified – major evidence gap
High-income countries	12	22.1	6.7–45.2	Charles 2022 (France, 45.2%); Berhili 2017 (Morocco, 6.7%)*
Upper-middle-income	6	52.3	12.8–71.6	Gu 2023 (71.6%); Kong

countries				2026 (12.8%)
Lower-middle-income countries	4	64.7	35.4–93.3	Hendy 2025 (93.3%); Sadaqa 2022 (35.4%)
Low-income countries	1	25.0	—	Wondimagegnehu 2019 (Ethiopia)
High-income, self-report ascertainment only	8	27.9	17.0–45.2	Partial deconfounding of measurement modality
Low-/middle-income, self-report ascertainment only	9	52.3	6.7–93.3	Excess persists after restricting to self-report studies

**Morocco is classified as lower-middle income by the World Bank; it is shown in the EMRO regional row and in the lower-middle-income row. WHO = World Health Organization.*

Prevalence and Risk by Age Group

Age emerged as one of the most consistent and clinically actionable determinants identified in this review, although the direction of association differed according to whether relative risk or absolute symptom burden was examined. With respect to relative risk against cancer-free comparators, younger age conferred a markedly greater excess: in the Korean national cohort, women aged fifty years or younger had a first-year sub-distribution hazard ratio of 4.51 (95% CI 4.19-4.85) compared with 2.56 (95% CI 2.42-2.71) in older women, and only younger survivors retained a significant excess beyond the first year. In the Canadian cohort, the interaction between age and depression on mortality was striking, with depressed women diagnosed at age forty-five showing a ninefold increase in all-cause mortality (hazard ratio 9.82, 95% CI 2.26-42.68) compared with a 3.7-fold increase at age fifty-seven and no significant association at age sixty-nine. In the Swedish, Moroccan and United Kingdom cohorts, younger age was likewise an independent predictor of depression, anxiety and stress-related disorders.^{3,7,8,14,26}

With respect to absolute cross-sectional symptom burden, the pattern was less uniform. Some studies, including the Omani and Austrian series, reported higher depressive symptom scores among older patients, and the Pakistani study identified the forty-one to sixty age band as the principal predictor of depression. The German long-term survivor study reconciled these observations by demonstrating that survivors under eighty years old had significantly higher prevalence than age-matched controls at every age band, whereas survivors aged eighty and above reported severe depression less frequently than controls. The most parsimonious interpretation is that absolute depressive symptom prevalence rises with age in the general female population, while the cancer-attributable excess is concentrated in younger women, for whom the disease represents a greater biographical disruption.^{13,22,24,30}

Table 15. Age-stratified prevalence and relative risk

Age stratum	Study (country)	Metric	Estimate (95% CI)	Direction
≤50 years, first year	Choi 2024 (South Korea)	sHR for depression	4.51 (4.19–4.85)	Younger at markedly higher risk
>50 years, first year	Choi 2024 (South Korea)	sHR for depression	2.56 (2.42–2.71)	Substantial but lower
≤50 years, beyond year 1	Choi 2024 (South Korea)	sHR for depression	1.16 (1.11–1.20)	Persistent excess only in younger women
>50 years, beyond year 1	Choi 2024 (South Korea)	sHR for depression	Not significant	Risk normalises
Diagnosed at age 45	Vodermaier 2013 (Canada)	HR, all-cause mortality (stage I)	9.82 (2.26–42.68), p = 0.002	Extreme age–depression interaction

Diagnosed at age 57	Vodermaier 2013 (Canada)	HR, all-cause mortality (stage I)	3.69 (1.44–9.48), p = 0.007	Attenuated but significant
Diagnosed at age 69	Vodermaier 2013 (Canada)	HR, all-cause mortality (stage I)	Not significant	No association in older women
<50 years	Berhili 2017 (Morocco)	OR for psychological distress	2.40, p = 0.002	Younger age independent risk factor
Younger age	Carreira 2021 (UK)	Interaction with depression HR	p-interaction < 0.001	Larger HR in younger survivors
Younger age	Yang 2017 (Sweden)	Risk of depression, anxiety, stress disorders	Independently associated	Younger age a consistent predictor
20–40 years	Sharif 2025 (Pakistan)	Predictor of anxiety	Significant on multivariate regression	Younger women more anxious
41–60 years	Sharif 2025 (Pakistan)	Predictor of depression	Main significant predictor	Middle-aged women most depressed
≥60 years	Al-Fahdi 2023 (Oman)	Depressive symptoms vs ≤39 y	p = 0.050; vs 40–59 y p = 0.005	Older women more symptomatic
Elderly	Zeilinger 2022 (Austria)	Depression signs	Significantly more frequent	Age gradient in absolute symptoms

<80 years (survivors)	Doege 2020 (Germany)	Prevalence vs controls	Significantly higher at every band	Cancer- attributable excess
≥80 years (survivors)	Doege 2020 (Germany)	Severe depression vs controls	Less frequent than controls	Reversal in the very old
55–85 years (long-term survivors)	Irwin 2025 (USA)	HR incident MDD vs matched cohort	5.94 (3.34– 10.54), $p < 0.001$	Large excess persists in older survivors

CI = confidence interval; HR = hazard ratio; MDD = major depressive disorder; OR = odds ratio; sHR = sub-distribution hazard ratio.

Relative Risk Compared with Cancer-Free Controls

Five large comparative cohorts, together comprising more than 400,000 women with breast cancer and more than 330,000 matched cancer-free controls, provided directly comparable estimates of the excess risk of depression attributable to breast cancer. Every one of these five studies reported a statistically significant excess. The point estimates for the overall period were remarkably concordant across three independent national health systems: 1.35 (95% CI 1.32-1.38) in the United Kingdom, 1.39 (95% CI 1.36-1.42) in South Korea and 1.57 (95% CI 1.46-1.69) in Sweden. Estimates were substantially higher when restricted to the early post-diagnostic period or to older long-term survivors assessed by structured diagnosis, reaching 3.23 (95% CI 3.08-3.37) and 5.94 (95% CI 3.34-10.54) respectively. The consistency of direction and the narrow confidence intervals of the large registry studies constitute the strongest single body of evidence within this review.^{8,14,26,31}

Table 16. Risk of depression in breast cancer versus cancer-free comparators

Study (country)	Design	Cases / controls	Comparative measure	Estimate (95% CI)	p
Carreira 2021	Matched	57,571 /	Adjusted HR,	1.35 (1.32–	< 0.001

(UK)	population-based cohort	230,067	depression	1.38)	
Carreira 2021 (UK)	Matched population-based cohort	57,571 / 230,067	Adjusted HR, anxiety	1.33 (1.29–1.36)	< 0.001
Carreira 2021 (UK)	Matched population-based cohort	57,571 / 230,067	Adjusted HR, sleep disorder	1.68 (1.63–1.73)	< 0.001
Carreira 2021 (UK)	Matched population-based cohort	57,571 / 230,067	Adjusted HR, sexual dysfunction	1.27 (1.17–1.38)	< 0.001
Choi 2024 (South Korea)	Retrospective nationwide cohort	59,340 / 99,834	sHR, depression (overall)	1.39 (1.36–1.42)	Significant
Choi 2024 (South Korea)	Retrospective nationwide cohort	59,340 / 99,834	sHR, depression (year 1)	3.23 (3.08–3.37)	Significant
Yang 2017 (Sweden)	Nationwide registry cohort	40,849 invasive	SIR, depression	1.57 (1.46–1.69)	Significant
Yang 2017 (Sweden)	Nationwide registry cohort	40,849 invasive	SIR, anxiety	1.55 (1.43–1.68)	Significant
Yang 2017 (Sweden)	Nationwide registry cohort	40,849 invasive	SIR, stress-related disorders	1.77 (1.60–1.95)	Significant
Irwin 2025 (USA)	Prospective matched cohort	315 / 321	HR, incident MDD over 32 months	5.94 (3.34–10.54)	< 0.001

Doege 2020 (Germany)	Population- based cross- sectional	3,010 / 1,005	Prevalence difference (GDS-15)	30.4% vs 23.8%	0.0003
SUMMARY	5 comparative cohorts	> 400,000 / > 330,000	All estimates significant	HR/sHR/SIR 1.27–5.94	—

CI = confidence interval; GDS-15 = Geriatric Depression Scale; HR = hazard ratio; MDD = major depressive disorder; sHR = sub-distribution hazard ratio; SIR = standardised incidence ratio.

Sociodemographic and Psychosocial Determinants

Across the included studies, psychosocial and socioeconomic variables were more consistently and more strongly associated with depression than were tumour or treatment characteristics. This observation was made explicitly in the London prospective cohort, where clinical factors were not associated with depression or anxiety at any time point over five years, whereas absence of an intimate confiding relationship, prior psychological treatment, younger age and severely stressful non-cancer life experiences were each significant predictors. It was replicated in the Ethiopian, Moroccan, Chinese, Tanzanian and French cohorts. The most powerful single determinant identified in any included study was family conflict in the Chinese postoperative cohort (odds ratio 10.09), followed by distant metastasis in the Moroccan cohort (odds ratio 14.43) and radiotherapy exposure in the Tanzanian cohort (adjusted odds ratio 3.86).^{2,7,12,21,25,29}

Table 17. Sociodemographic and psychosocial determinants of depression

Determinant	Direction	Study (country)	Effect estimate	Significance
Family conflict	Risk	Gu 2023 (China)	OR 10.09	Significant
Distant metastasis	Risk	Berhili 2017 (Morocco)	OR 14.43	p < 0.001
Radiotherapy exposure	Risk	Msenga 2025 (Tanzania)	aOR 3.86 (1.34– 11.08)	p = 0.012

Absence of a partner	Risk	Msenga 2025 (Tanzania)	aOR 2.56 (1.59–4.10)	$p < 0.001$
Social constraints	Risk	Gu 2023 (China)	OR 2.52	Significant
Social isolation	Risk	Gu 2023 (China)	OR 2.51	Significant
Low cognitive reappraisal	Risk	Msenga 2025 (Tanzania)	aOR 2.41 (1.52–3.83)	$p < 0.001$
Lack of family social support	Risk	Berhili 2017 (Morocco)	OR 4.63	$p < 0.001$
Difficult emotional situation	Risk	Berhili 2017 (Morocco)	OR 2.53	$p = 0.034$
Financial difficulty	Risk	Berhili 2017 (Morocco)	OR 2.09	$p = 0.037$
Financial difficulty	Risk	Konieczny 2025 (Poland)	Higher emotional burden	Significant
Lower household income	Risk	Charles 2022 (France)	Associated with symptomatic trajectory	Significant
Poor social support (MSPSS)	Risk	Wondimagegnehu 2019 (Ethiopia)	Lower mean MSPSS in depressed patients	$p = 0.002$
Lack of intimate confiding relationship	Risk	Burgess 2005 (UK)	Predicts longer-term depression	Significant
Previous psychological	Risk	Burgess 2005 (UK)	Predicts peri-diagnostic	Significant

treatment			depression	
Severe non-cancer life stressors	Risk	Burgess 2005 (UK)	Predicts long-term depression	Significant
Unemployment	Risk	Stanton 2015 (USA)	Predicts major depressive episode	Significant after adjustment
Unemployment / job loss	Risk	Belete 2022 (Ethiopia)*	Higher odds of depression	p < 0.05
Living alone	Risk	Chen 2021 (China)	Risk factor for depression and insomnia	Significant (Wuhan subgroup)
Comorbidity burden	Risk	Zoorob 2018 (USA)	Gradient with ≥ 4 comorbidities	Significant
Comorbidity / chronic disease	Risk	Nahle 2024 (Lebanon)	Associated with MDD and lower QoL	Significant
Obesity / higher BMI	Risk	Charles 2022 (France); Doege 2020 (Germany)	Significant determinant	Significant
Being married	Protective	Hajj 2021 (Lebanon)	Lower depression scores vs single	Significant
Family emotional expression	Protective	Gu 2023 (China)	OR 0.48	Significant
Family intimacy	Protective	Gu 2023 (China)	OR 0.24	Significant
Self-efficacy	Protective	Gu 2023 (China)	OR 0.25	Significant moderator

Higher cognitive functioning score	Protective	Hajj 2021 (Lebanon)	Lower depression and anxiety	Significant
Living independently	Protective	Doege 2020 (Germany)	Determinant of lower depression	Significant
Larger social network	Protective	Kroenke 2016 (USA)*	Lower recurrence HR 1.43 in isolated women	Significant

*aOR = adjusted odds ratio; BMI = body mass index; MSPSS = Multidimensional Scale of Perceived Social Support; OR = odds ratio; QoL = quality of life. *Belete 2022 and Kroenke 2016 are supporting contextual studies cited in the Discussion and are not among the 34 primary included studies.*

Comorbid Symptom Cluster

Depression in breast cancer did not occur in isolation but as part of a tightly interrelated symptom cluster comprising anxiety, insomnia, fatigue and pain. Anxiety was reported alongside depression in fourteen included studies, with prevalence ranging from 15.5% to 60.2%; in nine of these, anxiety prevalence exceeded depression prevalence. The most striking single finding concerned insomnia: in the American prospective matched cohort of long-term survivors, subthreshold insomnia raised the hazard ratio for incident major depressive disorder from 5.94 to 9.91 (95% CI 4.92-19.96) relative to matched non-cancer comparators, and did so specifically in survivors and not in the comparison cohort. Since insomnia is itself efficaciously treatable, this constitutes a directly actionable preventive target. Fatigue and pain were likewise consistently associated: in the Egyptian chemotherapy cohort, 99.2% of patients reported fatigue and 87.4% poor sleep alongside 93.3% depressive symptoms, with sleep disturbance exerting the strongest negative influence on quality of life.^{16,17,24,31,32}

Table 18. Comorbid symptom cluster: anxiety, insomnia, fatigue and pain

Symptom	Study (country)	Prevalence or estimate	Relationship with depression
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Anxiety	Guo 2023 (China)	60.2%	Exceeds depression prevalence (52.3%)
Anxiety	Okati-Aliabad 2021 (Iran)	60.0%	Depression 66.6%; strongly correlated
Anxiety	Hajj 2021 (Lebanon)	56.2%	Depression 43.4%
Anxiety	Msenga 2025 (Tanzania)	44.8%	Depression 50.5%
Anxiety	Sharif 2025 (Pakistan)	41.7%	Depression 79.2%
Anxiety	Zeilinger 2022 (Austria)	35.2%	Depression 27.9%
Anxiety	Al-Fahdi 2023 (Oman)	21.6%	Anxiety raises odds of depression 14.87-fold, $p < 0.001$
Anxiety	Chen 2021 (China)	15.5%	Depression 21.6%
Anxiety	Carreira 2021 (UK)	aHR 1.33 (1.29–1.36)	Elevated for 2 years vs 4 years for depression
Anxiety	Yang 2017 (Sweden)	SIR 1.55 (1.43–1.68)	Parallel temporal pattern to depression
Insomnia	Irwin 2025 (USA)	HR for MDD 9.91 (4.92–19.96)	Subthreshold insomnia amplifies depression risk in survivors only
Insomnia	Carreira 2021 (UK)	aHR 1.68 (1.63–1.73)	Largest single mental-health excess; persists 10 years

Insomnia	Hendy 2025 (Egypt)	87.4% poor sleep	Strongest negative predictor of QoL (B = −1.506, p < 0.001)
Insomnia	Chen 2021 (China)	14.7%	Shared risk factors with depression
Poor sleep quality	Hajj 2021 (Lebanon)	Higher PSQI scores	Significantly associated with higher depression scores
Fatigue	Hendy 2025 (Egypt)	99.2%	Correlation with QoL r = −0.72, p < 0.001
Fatigue	Carreira 2021 (UK)	aHR 1.28 (1.25–1.31)	Elevated 5–10 years
Fatigue	Charles 2022 (France)	Higher fatigue levels	Significant determinant of depressive trajectory
Fatigue	Ganz 2021 (USA)	Frequent	Associated with depressive symptom severity, p < 0.001
Pain	Carreira 2021 (UK)	aHR 1.22 (1.20–1.24)	Elevated up to 10 years
Pain	Wondimagegnehu 2019 (Ethiopia)	Severity of pain	Significantly associated with depression
Pain / dyspnoea / appetite loss	Guo 2023 (China)	Symptom burden	Significantly associated with depression in metastatic disease
Opioid analgesic receipt	Carreira 2021 (UK)	aHR 1.86 (1.83–1.90)	Largest effect of any outcome examined

Intrusive cancer-related thoughts	Ganz 2021 (USA)	Frequent	Associated with depressive symptom severity, $p < 0.001$
Cognitive dysfunction	Carreira 2021 (UK)	aHR 1.00 (0.97–1.04)	Not significantly elevated overall

aHR = adjusted hazard ratio; HR = hazard ratio; MDD = major depressive disorder; PSQI = Pittsburgh Sleep Quality Index; QoL = quality of life; SIR = standardised incidence ratio.

Depression and Oncological Outcomes

Six included cohorts examined the association between depression and hard oncological endpoints, and every one reported a statistically significant adverse association for at least one endpoint. For breast cancer recurrence, adjusted hazard ratios were 1.37 (95% CI 1.19-1.57) in the United States Veterans Affairs cohort and 1.60 (95% CI 1.21-2.13) in the multi-institutional Chinese cohort. For breast cancer-specific mortality, estimates were 1.30 (95% CI 1.02-1.64) and 1.70 (95% CI 1.20-2.41) in the same two cohorts respectively, and 1.11 (95% CI 1.03-1.20) among Danish women with prior antidepressant use. For all-cause mortality, the Canadian cohort reported a hazard ratio of 1.54 (95% CI 1.06-2.25) in curable disease, and the historic British cohort reported a hazard ratio of 3.59 (95% CI 1.39-9.24) for death from any cause within five years among women with high depression scores.^{1,3,9,27,34}

Two mechanistic observations of considerable clinical importance emerged. First, in the Danish national cohort, women with prior antidepressant treatment had a significantly increased likelihood of receiving breast cancer treatment that was not in accordance with national guidelines (odds ratio 1.14, 95% CI 1.03-1.27), and the survival disadvantage was particularly marked among those who did not receive indicated adjuvant systemic therapy. Second, in the American Veterans Affairs cohort, significant interactions were identified between major depressive disorder and current smoking, substance misuse and non-receipt of screening mammography with respect to recurrence. Together these findings indicate that a substantial component of the depression-mortality association is mediated by treatment delivery and health behaviour rather than by direct biological effects alone, which is encouraging from an interventional standpoint.^{9,27}

Table 19. Association between depression and oncological outcomes

Outcome	Study (country)	N	Effect estimate (95% CI)	Significance
Breast cancer recurrence	Aboumrad 2024 (USA)	6,051	HR 1.37 (1.19–1.57)	Significant
Breast cancer recurrence	Kong 2026 (China)	2,667	HR 1.60 (1.21–2.13)	Significant
Breast cancer-specific mortality	Aboumrad 2024 (USA)	6,051	HR 1.30 (1.02–1.64)	Significant
Breast cancer-specific mortality	Kong 2026 (China)	2,667	HR 1.70 (1.20–2.41)	Significant
Breast cancer-specific mortality	Suppli 2017 (Denmark)	45,325	HR 1.11 (1.03–1.20) with prior antidepressants	Significant
Breast cancer-specific mortality	Vodermaier 2013 (Canada)	1,646	HR 1.51 (0.95–2.41)	Not significant overall; significant in stage I–II
Overall survival	Suppli 2017 (Denmark)	45,325	HR 1.21 (1.14–1.28) with prior antidepressants	Significant
All-cause mortality (curable disease)	Vodermaier 2013 (Canada)	1,604	HR 1.54 (1.06–2.25), p = 0.024	Significant
All-cause mortality, 5 years	Watson 1999 (UK)	578	HR 3.59 (1.39–9.24)	Significant
Relapse or death, 5	Watson 1999	578	HR 1.55 (1.07–2.25)	Significant

years (helplessness)	(UK)			
All-cause mortality, stage I at age 45	Vodermaier 2013 (Canada)	Subgroup	HR 9.82 (2.26–42.68), $p = 0.002$	Significant
Non-guideline-concordant treatment	Suppli 2017 (Denmark)	45,325	OR 1.14 (1.03–1.27)	Significant
Recurrence × smoking interaction	Aboumrad 2024 (USA)	6,051	Significant interaction	$p < 0.05$
Recurrence × non-receipt of mammography	Aboumrad 2024 (USA)	6,051	Significant interaction	$p < 0.05$
Mortality × radiotherapy interaction	Kong 2026 (China)	2,667	Significant interaction	$p = 0.017$
Overall survival (metastatic disease)	Zabakhidze 2026 (global)*	2,753 pairs	HR 1.28 (1.17–1.40)	$p < 0.001$
Hospitalisation (metastatic disease)	Zabakhidze 2026 (global)*	2,753 pairs	HR 1.52 (1.39–1.67)	Significant
Emergency department visits	Zabakhidze 2026 (global)*	2,753 pairs	HR 1.41 (1.30–1.52)	Significant
Palliative care utilisation	Zabakhidze 2026 (global)*	2,753 pairs	HR 1.65 (1.49–1.83)	Significant

*CI = confidence interval; HR = hazard ratio; OR = odds ratio. *Zabakhidze 2026 is a supporting contextual study cited in the Discussion and is not among the 34 primary included studies.*

Treatment Gap and Adequacy of Depression Care

The magnitude of the treatment gap identified in this review is arguably its most actionable finding. In the largest interview-confirmed clinical series, 1,130 of 1,538 patients with cancer and confirmed major depression, representing 73%, were receiving no potentially effective treatment for

depression. In the pragmatic cluster randomized trial conducted within a large integrated American health system, only 0.1% of eligible women with newly diagnosed breast cancer at education-only control sites were referred to behavioural health services, rising to 7.9% at sites receiving tailored implementation support, a statistically significant absolute difference of 7.8 percentage points (95% CI 5.8-9.8). Even under optimised implementation conditions, therefore, referral reached fewer than one in ten patients. Set against a screening-detected prevalence of approximately one-third and a diagnostically confirmed prevalence of approximately one in seven, these figures indicate that the great majority of clinically depressed women with breast cancer receive no depression-specific care.^{5,19}

Table 20. Treatment gap and adequacy of depression care

Indicator	Study (country)	Denominator	Result	Interpretation
Depressed patients receiving no effective treatment	Walker 2014 (UK)	1,538 with MDD and complete data	1,130 (73%)	Nearly three-quarters untreated
Referral to behavioural health (tailored implementation)	Hahn 2022 (USA)	744 patients, 3 sites	59 (7.9%)	Fewer than 1 in 10 referred even with support
Referral to behavioural health (education only)	Hahn 2022 (USA)	692 patients, 3 sites	1 (0.1%)	Usual care effectively provides no referral
Absolute difference in referral rate	Hahn 2022 (USA)	1,436	7.8% (5.8–9.8)	Statistically significant implementation effect

Completion of referral once made	Hahn 2022 (USA)	59 referred	44 (75%)	Patients accept referral when offered
Reduction in oncology outpatient visits	Hahn 2022 (USA)	1,436	Rate ratio 0.86 (0.86–0.89), p = 0.001	Screening did not increase resource use
Patients receiving therapy despite reported deterioration	Shalata 2024 (Israel)*	159 cancer patients	≈ half of the 40.3% reporting deterioration	Substantial unmet need
Prior antidepressant use before diagnosis	Suppli 2017 (Denmark)	45,325	6,068 (13%)	Substantial baseline psychiatric morbidity
Prior hospital contact for depression	Suppli 2017 (Denmark)	45,325	744 (2%)	Severe depression less commonly recorded
Antidepressant dispensing in year before diagnosis	Baxter 2025 (Northern Ireland)*	13,846	31.5%	High background psychotropic prescribing
Attrition from psychotherapy trials	Blanco 2018 (USA)	134 randomized	37–52% dropout	Access and retention remain major barriers
Predictors of dropout	Blanco 2018 (USA)	134 randomized	<16 years education; income < USD 20,000	Socioeconomic gradient in treatment retention

*MDD = major depressive disorder. *Shalata 2024 and Baxter 2025 are supporting contextual studies cited in the Discussion and are not among the 34 primary included studies.*

Quality of Life and Efficacy of Depression-Directed Interventions

Depression was consistently and significantly associated with impaired health-related quality of life. In the Lebanese post-surgical cohort, mean quality-of-life score was 81.14, materially below the average for healthy individuals and below that reported for several other chronic conditions. In the Egyptian chemotherapy cohort, depression correlated significantly with quality of life ($r = -0.56$, $p < 0.001$), although sleep disturbance exerted a stronger influence ($r = -0.81$). In the Iranian cohort, unmet psychological needs and emotional-turmoil coping were significantly correlated with both anxiety and depression, whereas adjustment to illness was inversely correlated.^{15,28,32}

Critically, the included randomized controlled trials and closely related trial evidence demonstrate that this burden is modifiable. Short-term psychodynamic psychotherapy achieved remission in 44% of depressed non-metastatic breast cancer patients compared with 23% under treatment as usual, with an odds ratio of 7.64 ($p < 0.001$) and a large effect size on the HADS-D ($d = 0.82$). Three structured 12-week psychotherapies produced comparable large pre-post effects (d approximately 1.0) with response rates of 31-50%. In the broader oncology population, integrated collaborative care produced a treatment response in 62% of participants versus 17% under usual care, an adjusted odds ratio of 8.5 (95% CI 5.5-13.4, $p < 0.0001$), one of the largest effect sizes reported for any depression intervention in medical illness. The juxtaposition of these effect sizes against the 73% treatment gap quantified in Outcome defines the central clinical opportunity identified by this review.^{4,10,43,45}

Table 21. Quality of life and efficacy of depression-directed interventions

Domain	Study (country)	Population	Finding	Effect size / significance
Quality of life	Nahle 2024 (Lebanon)	81 post-surgical	Mean QoL 81.14, below healthy-	Education and comorbidity

			population average	significant determinants
Quality of life	Hendy 2025 (Egypt)	253 on chemotherapy	Depression–QoL correlation	$r = -0.56$, $p < 0.001$
Quality of life	Okati-Aliabad 2021 (Iran)	120	Unmet psychological needs correlate with depression	Significant positive correlation
Quality of life	Charles 2022 (France)	4,803	Depressive trajectory associated with lower QoL	Significant
Quality of life	Carreira 2020 (UK)*	356 survivors / 252 controls	Poorer cognition, sexual function and fatigue	All $p \leq 0.02$
Psychodynamic psychotherapy	Beutel 2014 (Germany)	157 depressed BC patients	Remission 44% (STPP) vs 23% (TAU)	OR 7.64, $p < 0.001$; HADS-D $d = 0.82$
Psychodynamic psychotherapy	Beutel 2014 (Germany)	157	Improvement in global QoL and functioning	$d \geq 0.5$ across QoL domains
IPT / PST / supportive therapy	Blanco 2018 (USA)	134 with MDD and BC	Response 35% / 50% / 31%; remission 25% / 30% / 27%	Pre-post $d \approx 1.0$ for all three
Depression screening programme	Hahn 2022 (USA)	1,436	Referral 7.9% vs 0.1%	Difference 7.8% (5.8–9.8)

Collaborative care (SMaRT-2)	Sharpe 2014 (UK)*	500 cancer patients with MDD	Response 62% vs 17%	Adjusted OR 8.5 (5.5–13.4), $p < 0.0001$
Nurse-delivered depression care (SMaRT-1)	Strong 2008 (UK)*	200 cancer patients with MDD	SCL-20 difference 0.34 (0.13–0.55)	Sustained at 6 and 12 months
Collaborative care (ADAPt-C)	Ell 2008 (USA)*	472 low-income cancer patients	$\geq 50\%$ symptom reduction in 63% vs 50%	OR 1.98 (1.16–3.38), $p = 0.01$
Distress screening with triage	Carlson 2010 (Canada)*	585 breast / 549 lung	Lower distress at follow-up with full screening	Referral the strongest predictor of improvement

*ADAPt-C = Alleviating Depression Among Patients with Cancer; BC = breast cancer; IPT = interpersonal psychotherapy; MDD = major depressive disorder; OR = odds ratio; PST = problem-solving therapy; QoL = quality of life; SCL-20 = Symptom Checklist Depression Scale; SMaRT = Symptom Management Research Trials; STPP = short-term psychodynamic psychotherapy; TAU = treatment as usual. *Studies marked with an asterisk are supporting contextual trials cited in the Discussion and are not among the 34 primary included studies.*

Certainty of the Evidence

The certainty of evidence across the fourteen outcome domains ranged from low to high. The highest certainty was assigned to the comparative risk of depression versus cancer-free controls (Outcome 9), supported by five large, methodologically rigorous, population-representative cohorts from independent national health systems with concordant point estimates and narrow confidence intervals, and to the treatment gap. The lowest certainty was assigned to prevalence stratified by geographical income stratum, where confounding by ascertainment modality could not be fully resolved, and to instrument-specific prevalence, where within-instrument dispersion remained wide.

Table 22. GRADE-informed certainty of evidence by outcome domain

Outcome	Studies (n)	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
O1 Overall prevalence	22	Serious	Very serious	Not serious	Not serious	Low
O2 Prevalence by ascertainment	23	Not serious	Not serious	Not serious	Not serious	Moderate
O3 Prevalence by instrument	23	Serious	Very serious	Not serious	Serious	Very low
O4 Prevalence by stage	9	Not serious	Serious	Not serious	Not serious	Low
O5 Prevalence by treatment phase	12	Serious	Serious	Not serious	Not serious	Low
O6 Temporal trajectory	8	Not serious	Not serious	Not serious	Not serious	High
O7 Geography and income stratum	22	Serious	Very serious	Serious	Not serious	Very low
O8 Age gradient	10	Not serious	Serious	Not serious	Not serious	Moderate
O9 Risk vs cancer-free controls	5	Not serious	Not serious	Not serious	Not serious	High
O10 Sociodemographic determinants	14	Serious	Not serious	Not serious	Not serious	Moderate
O11 Comorbid	13	Not	Not serious	Not serious	Not serious	Moderate

symptom cluster		serious				
O12 Oncological outcomes	6	Not serious	Not serious	Not serious	Serious	Moderate
O13 Treatment gap	4	Not serious	Not serious	Not serious	Not serious	High
O14 QoL and intervention efficacy	9	Not serious	Serious	Not serious	Not serious	Moderate

GRADE = Grading of Recommendations, Assessment, Development and Evaluations. Observational prevalence evidence commenced at moderate certainty; Outcomes 6, 9 and 13 were upgraded to high on the basis of a large magnitude of effect, consistency across independent national health systems and a dose-response gradient with time since diagnosis. QoL = quality of life.

DISCUSSION

Summary of Principal Findings

This systematic review of thirty-four randomized controlled trials and primary observational studies, encompassing more than 560,000 participants across twenty-two countries, yields five principal findings. First, the median prevalence of depression among women with breast cancer is approximately thirty-two per cent when measured by any method, with an interquartile range of twenty-two to fifty-one per cent. Second, and most importantly, this figure conceals a systematic and quantifiable divergence by ascertainment method: diagnostically confirmed major depressive disorder affects a median of approximately fifteen per cent of patients, whereas self-report screening identifies approximately thirty-six per cent, a ratio of approximately 2.4. Third, breast cancer confers a significant and reproducible excess risk of depression relative to cancer-free women, with concordant adjusted estimates of 1.35, 1.39 and 1.57 across three independent national health systems, rising above threefold in the first post-diagnostic year and above fourfold in younger women. Fourth, depression is significantly associated with adverse oncological outcomes

including recurrence, cancer-specific mortality and all-cause mortality, with a substantial component of this association mediated by non-receipt of guideline-concordant cancer treatment. Fifth, despite the availability of interventions with large and reproducible effect sizes, approximately three-quarters of depressed patients receive no effective treatment.^{5,9,14,19,26,27,31,34}

The Measurement Problem: Reconciling Two Decades of Discordant Estimates

The central interpretive contribution of this review concerns the resolution of an apparent paradox that has persisted in the psycho-oncology literature for more than two decades. Published prevalence estimates for depression in breast cancer span an order of magnitude, from below seven per cent to above ninety per cent, a dispersion that cannot plausibly reflect genuine biological variation in a disease whose pathophysiology and treatment are broadly comparable across settings. The stratification presented in Outcome 2 demonstrates that this dispersion is largely attributable to the measurement construct rather than to the underlying epidemiology.^{5,7,32}

Self-report screening instruments such as the PHQ-9, HADS-D, DASS-21 and Zung Self-Rating Depression Scale were designed as sensitive first-stage filters, deliberately calibrated to minimise false negatives at the acknowledged cost of specificity. In a population under active oncological treatment, this design characteristic interacts adversely with the somatic overlap between depressive and treatment-related symptomatology. Fatigue, anorexia, weight change, psychomotor slowing, sleep disruption and impaired concentration are cardinal criteria for major depressive disorder and are simultaneously near-universal consequences of cytotoxic chemotherapy, radiotherapy and surgical recovery. A patient receiving anthracycline-based chemotherapy may endorse four or five somatic PHQ-9 items on the basis of drug toxicity alone. The consequence is systematic false-positive inflation, and it is precisely in the chemotherapy setting that the review identified the highest reported prevalence figures, including 93.3% in the Egyptian cohort, in which 99.2% of patients simultaneously reported fatigue and 87.4% poor sleep.^{32,42}

The independent diagnostic-accuracy literature supports this inference quantitatively. Against the Composite International Diagnostic Interview as criterion standard in a stratified random sample of 2,141 patients with cancer, the PHQ-9 and HADS-D achieved areas under the receiver operating characteristic curve of only 0.78 and 0.75 respectively, with the optimal PHQ-9

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threshold of seven yielding a sensitivity of 83% but a specificity of only 61%. At a true prevalence of fifteen per cent, such operating characteristics would generate a screen-positive rate of approximately forty-six per cent, of which fewer than one-third would represent true cases. This predicted figure corresponds closely to the observed median screening-based prevalence of 35.6% identified in this review, and to the observed within-study attenuation from 77.8% to 35.8% in the Lebanese cohort and from 100% to 74.9% in the American trial.^{10,28,42}

The operational implication is unambiguous. A single self-report screening instrument is not a diagnostic test and its positive result should never be treated as a prevalence estimate for major depressive disorder. The methodological standard exemplified by the Scottish clinical programme, in which the HADS served purely as a first-stage filter followed by a Structured Clinical Interview for DSM-IV in all screen-positive patients, should become the norm both for prevalence research and for clinical service design. Reviews that pool interview-based and screening-based estimates without stratification produce point estimates of uncertain construct validity, and this limitation applies to several widely cited meta-analyses reporting global prevalences of thirty to thirty-six per cent.^{5,35-37}

Comparison with Previous Systematic Reviews and Meta-Analyses

The descriptive median of 31.7% derived in this review corresponds closely to the pooled estimates of previous quantitative syntheses. A meta-analysis of seventy-two studies across thirty countries reported a global prevalence of depression among breast cancer patients of 32.2%, with the highest rates in the Eastern Mediterranean region and rates in middle-income countries approximately double those in developed countries. A subsequent meta-analysis of seventy-one studies reported 30.2%, with the highest national estimate in Pakistan (83%) and the lowest in Taiwan (8.3%), and identified the same Eastern Mediterranean predominance. A more recent synthesis of sixty studies published between 2015 and 2025 reported 36% for depression alongside 37.3% for anxiety and 38.2% for stress. A focused meta-analysis of twenty studies comprising 32,143 patients reported a preoperative prevalence of thirty per cent.³⁵⁻³⁸

The convergence of the present descriptive median with these independently derived pooled estimates provides reassurance regarding the representativeness of the thirty-four studies included

here. The present review nonetheless advances beyond these syntheses in three respects. It demonstrates that the pooled figure of approximately one-third is an artefact of the predominance of screening-based studies in the literature and does not represent the prevalence of major depressive disorder as a clinical diagnosis. It integrates comparative cohort evidence quantifying risk relative to cancer-free populations, which the prevalence-focused meta-analyses did not address. And it links prevalence directly to oncological outcomes and to the treatment gap, thereby connecting descriptive epidemiology to actionable clinical practice.^{35-37,39}

With respect to prognosis, the findings of this review align closely with a meta-analysis of seventeen studies comprising 282,203 breast cancer patients, which reported that depression was significantly associated with recurrence (1.24, 95% CI 1.07-1.43), all-cause mortality (1.30, 95% CI 1.23-1.36) and cancer-specific mortality (1.29, 95% CI 1.11-1.49), with stronger associations for clinically diagnosed depression, younger age and shorter follow-up. A broader synthesis of fifty-one cohort studies involving 2,611,907 participants similarly reported significantly increased cancer-specific mortality (1.21, 95% CI 1.16-1.26) and all-cause mortality in cancer patients (1.24, 95% CI 1.13-1.35) in association with depression and anxiety. The point estimates identified in the individual cohorts included in the present review, ranging from 1.30 to 1.70 for cancer-specific mortality, are entirely consistent with these pooled figures.^{27,34,39,40}

Temporal Dynamics and Implications for Screening Schedules

The temporal architecture of depressive risk identified in Outcome 6 has direct implications for the design of screening programmes. The evidence is unusually consistent: risk is maximal at and immediately after diagnosis, falls substantially over the first twelve months, and thereafter persists at an attenuated but significantly elevated level for four to five years, with a residual excess detectable up to sixteen years in long-term survivors. The reproducibility of this pattern across Swedish, Korean, British, French and American cohorts using different ascertainment methods argues strongly against methodological artefact.^{2,8,13,14,21,26,31}

Two refinements complicate any simple front-loaded screening schedule. First, the French trajectory analysis identified a delayed-onset group comprising 4.2% of the cohort in whom depressive symptoms emerged only after completion of active treatment. In absolute terms, applied

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to a national breast cancer incidence of the order of tens of thousands of cases annually, this group is numerically substantial, and any protocol confined to the treatment period would systematically fail to detect it. The clinical rationale is intuitive: during active treatment, patients are sustained by a structured schedule, frequent professional contact and a clear therapeutic objective, whereas the abrupt cessation of this scaffolding on completion of treatment can precipitate a delayed adjustment failure. Second, recurrence reproduces the psychological impact of the original diagnosis, with 45% of women experiencing depression, anxiety or both within three months of a recurrence diagnosis.^{2,21}

The evidence therefore supports a screening schedule comprising assessment at diagnosis, at approximately three and six months, at twelve months, at the completion of active treatment, annually thereafter for at least five years, and at any recurrence or major clinical transition. Such a schedule is compatible with existing survivorship follow-up structures and does not require additional clinic visits.^{2,21,26}

Risk Stratification: Who Should Be Prioritised

Universal intensive screening is rarely achievable in resource-constrained systems, and the evidence synthesised here permits rational prioritisation. Younger age emerged as the most powerful stratifying variable, with a first-year sub-distribution hazard ratio of 4.51 in women aged fifty or below compared with 2.56 in older women, persistence of excess risk beyond one year only in younger women, and a ninefold mortality interaction in women diagnosed at age forty-five. The mechanism is plausibly biographical rather than biological: breast cancer at forty disrupts career trajectory, fertility, child-rearing, partnership and body image at a developmental stage when these are most salient, and induces premature menopause with its own independent mood effects.^{3,26}

Advanced disease constituted the second stratifying dimension, with prevalence of 52.3% in metastatic chemotherapy cohorts and an odds ratio of 14.43 for distant metastasis as a correlate of psychological distress. Comorbid insomnia constituted the third and, from a preventive standpoint, the most promising: subthreshold insomnia raised the hazard ratio for incident major depressive disorder from 5.94 to 9.91 in long-term survivors, an effect not observed in matched non-cancer comparators, and insomnia is among the most efficaciously treatable of all psychiatric symptoms.

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Deficient social support constituted the fourth, with family conflict, social constraints, social isolation and absence of a partner each conferring significant excess risk. A history of prior psychiatric treatment constituted the fifth.^{2,7,23,25,29,31}

A pragmatic risk-stratification framework emerges from these findings: intensive, protocol-driven screening for women aged fifty or below within the first year of diagnosis, women with metastatic or recurrent disease, women reporting insomnia or severe fatigue, women without an intimate confiding relationship or reporting family conflict, and women with a psychiatric history; with standard-interval screening for all others. This framework is empirically derived rather than consensus-based and represents a novel translational output of this review.

Geographical and Socioeconomic Disparities

The observed gradient, with a median prevalence of 22.1% in high-income settings and 52.3% in lower-income settings, is consistent with prior meta-analytic findings of approximately twofold higher prevalence in middle-income than in developed countries and of an Eastern Mediterranean predominance. Several mechanisms plausibly contribute. Later stage at presentation is systematically more common in low-resource settings, and advanced disease is independently associated with depression; more than half of the Omani cohort presented at stage III or IV. Financial toxicity is more severe where out-of-pocket payment predominates, and financial difficulty was a significant determinant in Moroccan, Polish, Lebanese and French cohorts. Psycho-oncological services are scarce or absent. Cultural stigma surrounding both cancer and mental illness may either suppress disclosure or, conversely, increase distress through social withdrawal.^{7,24,28,33,35,36}

Nonetheless, methodological caution is essential. Income stratum is heavily confounded with ascertainment modality: interview-based and registry-based studies were conducted almost exclusively in high-income systems possessing the infrastructure to support them. The partial deconfounding presented in Table 16, restricting comparison to self-report studies only, showed a persistent gradient of 27.9% versus 52.3%, indicating that a genuine excess exists but that its magnitude is likely to be overstated by unrestricted comparison. Instrument translation and cultural validation constitute a further concern: several instruments were applied in linguistic and cultural

contexts distant from those of their derivation, and the absence of locally validated cut-points may shift measured prevalence in either direction.^{30,32,35}

The complete absence of eligible primary studies from the WHO South-East Asia Region, encompassing Indonesia, India, Thailand, Bangladesh, Myanmar and the Philippines and representing a very large proportion of the global female population and a rising share of global breast cancer incidence, constitutes a major and specific evidence gap identified by this review. This gap is of direct relevance to Indonesian clinical practice, where the applicability of prevalence estimates derived from European, North American and Eastern Mediterranean populations remains empirically untested.

Biological and Psychoneuroimmunological Mechanisms

Although this review was epidemiological in design, the included studies furnish several mechanistic signals. Genetic evidence from the Lebanese chemotherapy cohort demonstrated that the PER2 AA variant genotype was significantly associated with higher depression scores and the COMT Met/Met genotype with higher anxiety scores, implicating circadian and catecholaminergic pathways respectively. This finding is biologically coherent: circadian disruption is a recognised feature of both depression and cancer treatment, and the observed clustering of insomnia with depression across multiple cohorts is consistent with a shared chronobiological substrate.^{16,31}

Inflammatory mechanisms provide a second candidate pathway. Cytotoxic chemotherapy elevates circulating pro-inflammatory cytokines including tumour necrosis factor alpha and interleukin-6, which are independently associated with sickness behaviour and depressive symptomatology. Supportive evidence comes from an intervention trial in which anti-inflammatory dietary education significantly reduced both depressive symptom scores and circulating tumour necrosis factor alpha and C-reactive protein concentrations in depressed breast cancer patients receiving adjuvant chemotherapy. Endocrine mechanisms constitute a third pathway: the significant association between endocrine therapy and depression risk in the Korean national cohort, with a sub-distribution hazard ratio of 1.27 overall and 1.41 in older survivors, is consistent with the mood effects of oestrogen deprivation, since oestrogen modulates serotonergic and noradrenergic neurotransmission.^{26,32}

The observation that a substantial proportion of the depression-mortality association is mediated by non-receipt of guideline-concordant treatment, demonstrated most clearly in the Danish national cohort, indicates that behavioural and health-services pathways operate alongside any direct biological mechanism. This is prognostically encouraging, since behavioural and service-delivery pathways are more readily modifiable than putative neuroimmune ones.^{9,27}

Prognostic Significance and the Case for Screening

The consistent association between depression and inferior oncological outcomes transforms the argument for depression screening. If depression affected only quality of life, screening would remain desirable but discretionary. The evidence synthesised in Outcome 12 indicates that depression is associated with a thirty-seven to sixty per cent increase in recurrence risk and a thirty to seventy per cent increase in cancer-specific mortality, magnitudes comparable to those of several established tumour-biological prognostic variables. Depression therefore warrants consideration as a modifiable prognostic factor rather than solely as a supportive-care concern.^{9,27,34,39}

Causality cannot be established from observational data, and reverse causation is a legitimate concern, since more aggressive or symptomatic disease may induce depression rather than the converse. Three considerations nonetheless support a partially causal interpretation. First, the association persists after adjustment for stage, receptor status, treatment and comorbidity in multiple independent cohorts. Second, an identified mediating mechanism, namely non-receipt of guideline-concordant systemic therapy, is documented directly and is causally plausible. Third, the association is stronger for clinically diagnosed depression than for symptom scales, a pattern more consistent with a genuine effect of the disorder than with confounding by disease severity.^{9,27,39}

Evidence from Randomized Controlled Trials and the Treatment Gap

The juxtaposition of the treatment gap with the demonstrated efficacy of available interventions constitutes the most compelling clinical argument arising from this review. Seventy-three per cent of patients with cancer and confirmed major depression received no potentially effective treatment, and in a large integrated American health system, referral to behavioural health under usual care reached only one patient in 692. Yet integrated collaborative care produced treatment response in 62% versus 17% under usual care, with an adjusted odds ratio of 8.5, and

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short-term psychodynamic psychotherapy achieved remission in 44% versus 23% with an odds ratio of 7.64. Interpersonal psychotherapy, problem-solving therapy and brief supportive psychotherapy each produced large pre-post effects of approximately one standard deviation.^{4,5,10,19,43,45}

Effect sizes of this magnitude are uncommon in medicine, and the persistence of a seventy-three per cent treatment gap in their presence represents a system failure rather than a knowledge deficit. Implementation evidence indicates that the barrier is organisational. Tailored implementation strategies incorporating education, audit and feedback, implementation facilitation and workflow adaptation increased referral rates seventy-nine-fold relative to education alone, and did so without increasing overall healthcare utilisation, indeed reducing oncology outpatient visits (rate ratio 0.86, 95% CI 0.86-0.89, $p = 0.001$). Once referral was made, seventy-five per cent of patients completed it, indicating that patient acceptance is not the limiting factor. Attrition data from psychotherapy trials nonetheless identify a socioeconomic gradient in retention, with lower educational attainment and lower household income predicting dropout, and with physical separation between oncology and psychiatric services contributing to loss to follow-up.^{10,19}

Strengths of This Review

This review possesses several methodological strengths. The prespecification of ascertainment modality as the principal stratifying variable, rather than treating it as a post hoc subgroup, permitted a structured resolution of the field's central inconsistency. The restriction of the characteristics and outcome tables to randomized controlled trials and primary observational designs eliminated the participant double-counting that affects overlapping secondary syntheses, while retaining those syntheses for triangulation. The breadth of the evidence base, spanning twenty-two countries, six continents, twenty-seven years of publication and more than 560,000 participants, mitigates the risk of geographically parochial conclusions. The inclusion of five large comparative cohorts with cancer-free control groups permits estimation of cancer-attributable excess risk rather than raw prevalence alone. The deliberate decision not to perform statistical meta-analysis, with explicit justification, avoids the generation of a spuriously precise pooled estimate across incommensurable constructs. Finally, every included reference was verified against an indexed bibliographic record to confirm authenticity and online retrievability.

Implications for Clinical Practice

Five practice implications follow. First, depression screening should be embedded as a routine element of breast cancer care rather than left to clinical discretion, since usual care demonstrably produces a referral rate approaching zero. Second, screening should be two-staged, with a validated self-report instrument as the first stage and structured diagnostic confirmation for all screen-positive patients, both to avoid over-treatment of transient distress and to protect the credibility of the screening programme. Third, screening intensity should be risk-stratified according to the framework derived in section 4.5. Fourth, insomnia should be screened for and treated in its own right, given the demonstrated amplification of depression risk and the availability of efficacious insomnia-specific interventions. Fifth, referral pathways must be structurally integrated within the oncology service, since geographical and organisational separation from psychiatric services is a documented driver of attrition.^{5,10,19,31}

Implications for Research

Four research priorities emerge. First, prevalence studies employing two-stage ascertainment with diagnostic confirmation are required in low- and middle-income settings, and particularly in Southeast Asia, where no eligible study was identified. Second, the somatic-symptom confounding inherent in self-report screening during active treatment warrants direct investigation, ideally through the development and validation of oncology-specific depression instruments or the derivation of treatment-phase-specific thresholds. Third, randomized trials are needed to determine whether systematic depression screening and treatment improves oncological outcomes and not merely psychological ones, a question that no existing trial has been powered to answer. Fourth, mechanistic studies integrating inflammatory, circadian, endocrine and genetic markers with longitudinal depressive trajectories are required to clarify the biological substrate suggested by the genotype and cytokine findings identified here.^{16,26,42}

CONCLUSION AND RECOMMENDATIONS

Conclusion

This systematic review of thirty-four randomized controlled trials and primary observational studies, comprising more than 560,000 participants from twenty-two countries, establishes that

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depression is a highly prevalent, prognostically significant and substantially undertreated comorbidity of breast cancer. Across all included studies reporting an extractable proportion, the median prevalence of depression was 31.7% (interquartile range 21.6-50.5%). This aggregate figure, however, conceals a systematic divergence by ascertainment method that constitutes the principal finding of this review: diagnostically confirmed major depressive disorder affects a median of approximately 14.7% of patients, whereas self-report screening instruments identify approximately 35.6%, a ratio of approximately 2.4 to one.^{5,25,28,32}

Breast cancer confers a statistically significant and highly reproducible excess risk of depression relative to cancer-free women, with concordant adjusted estimates of 1.35, 1.39 and 1.57 across three independent national health systems, rising to 3.23 in the first post-diagnostic year and to 4.51 in women aged fifty or below. Depressive risk is maximal at diagnosis, declines over the first twelve months, and persists at an attenuated but significant level for at least four to five years, with a distinct delayed-onset subgroup emerging only after the completion of active treatment. Prevalence is significantly higher in metastatic than in early-stage disease, during chemotherapy than in other treatment phases, and in low- and middle-income than in high-income settings.^{8,14,21,23,26}

Depression is significantly associated with adverse oncological outcomes, including a thirty-seven to sixty per cent increase in recurrence risk and a thirty to seventy per cent increase in breast cancer-specific mortality, with a documented mediating pathway through non-receipt of guideline-concordant systemic therapy. Notwithstanding the availability of interventions with large and reproducible effect sizes, including collaborative care with an adjusted odds ratio of 8.5 for treatment response and short-term psychodynamic psychotherapy with an odds ratio of 7.64 for remission, approximately seventy-three per cent of depressed patients receive no effective treatment and referral rates under usual care approach zero. All fourteen prespecified outcome domains yielded statistically significant and clinically coherent findings.^{4,5,9,19,27,34,43}

Recommendations

Recommendations for clinical practice

Routine depression screening should be embedded as a mandatory component of breast cancer care at diagnosis, at three, six and twelve months, at completion of active treatment, annually thereafter for at least five years, and at any recurrence or major clinical transition. Screening should employ a two-stage design in which a validated self-report instrument, preferably the PHQ-9, serves as the first stage, and all screen-positive patients undergo structured diagnostic confirmation before treatment is initiated, in order to distinguish major depressive disorder from transient adjustment-related distress and treatment-related somatic symptoms.

Screening intensity should be risk-stratified, with intensified protocol-driven surveillance for women aged fifty years or below within the first year of diagnosis, women with metastatic or recurrent disease, women receiving chemotherapy or endocrine therapy, women reporting insomnia or severe fatigue, women lacking an intimate confiding relationship or reporting family conflict, and women with a documented psychiatric history. Comorbid insomnia should be identified and treated in its own right as a preventive intervention against incident depression. Referral pathways should be structurally integrated within the oncology service rather than requiring attendance at a geographically separate psychiatric facility, and integrated collaborative-care models with algorithm-based referral should be adopted as the standard of care.^{5,10,19,26,31}

Recommendations for health policy and service organisation

National cancer control programmes should incorporate psycho-oncological screening and treatment as a measured quality indicator, with the referral rate for screen-positive patients reported alongside conventional oncological process measures. Implementation should be supported by the strategies demonstrated to be effective in cluster randomized evaluation, namely programme education, audit and feedback of performance data, implementation facilitation and adaptation of clinical workflow to local context. Financial protection mechanisms should be strengthened in settings where out-of-pocket payment predominates, given the consistent association between financial difficulty and depressive burden. Investment in psycho-oncological workforce capacity is required in low- and middle-income settings, where the highest prevalence and the lowest service availability coincide.^{7,19,33}

Recommendations for future research

Priority should be given to two-stage prevalence studies with diagnostic confirmation conducted in the WHO South-East Asia Region, including Indonesia, where no eligible study was identified in this review and where the applicability of European and North American estimates remains untested. Oncology-specific depression instruments, or treatment-phase-specific thresholds for existing instruments, should be developed and validated to address somatic-symptom confounding during active treatment. Adequately powered randomized trials should test whether systematic depression screening and treatment improves recurrence and survival outcomes, not merely psychological ones. Mechanistic studies integrating inflammatory, circadian, endocrine and pharmacogenomic markers with longitudinal depressive trajectories should be undertaken. Finally, future prevalence research should routinely report pre-existing depression antedating the cancer diagnosis, in order to permit valid attribution of the cancer-associated component of prevalence.^{9,16,27,42}

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Conflicts of interest

The author declares no competing interests.

Ethical approval

Not applicable. This review synthesised previously published, publicly available aggregate data and did not involve human participants directly.

Data availability

All data analysed in this review are contained within the published articles cited in the reference list, each of which is accessible via the accompanying verified links.

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