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Prevalence and risk factors of anxiety and depression among patients with breast cancer: a protocol for systematic review and meta-analysis

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ABSTRACT

Background Patients with breast cancer often experience severe psychological distress, especially anxiety and depression, leading to poorer quality of life, shortened survival time and increased mortality.
The objective of the review will be to summarise data on the prevalence and risk factors of anxiety and depression in patients with breast cancer.

Methods and analysis Two reviewers will be applied in seven databases, including Web of Science, PubMed, EMBASE, Wan Fang Data Knowledge Service Platform, Chinese Biomedical Literature Database, Chinese Scientific Journal Database (VIP database), China National Knowledge Infrastructure and for studies on the prevalence and risk factors of depression in patients with breast cancer, which should be published from inception to Feb 2020 in English, Chinese, French and Spanish. The selection of studies, data extraction and risk of bias assessment will be done independently by two reviewers. Data synthesis will be carried out using RevMan V.5.3 software. The heterogeneity will be determined by the I^2 test. Publication bias will be evaluated by generating a funnel plot and performing the Begg and Egger test. The quality of the systematic review will be assessed using the Grading of Recommendations Assessment, Development and Evaluation Tool criteria.

Ethics and dissemination No ethical approval is required. This protocol will not involve individual patient information and endangering participant rights. The results will be reported in a peer-reviewed journal or disseminated in relevant conferences.

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Strengths and limitations of this study

- The study aims to summarise data on the prevalence and risk factors of anxiety and depression in patients with breast cancer.
- The selection of studies, data extraction and risk of bias assessment will be done independently by two reviewers.
- The quality of the systematic review will be assessed using the Grading of Recommendations Assessment, Development and Evaluation criteria.
- In this review, only studies published in English or Chinese will be considered, which may cause a potential risk of publication bias.
- Different measurements and tools might lead to inconsistent levels of outcomes.

INTRODUCTION

Breast cancer in women is increasing worldwide. The Cancer Statistics[1] produced the three most common cancers, including breast cancer, lung cancer and colorectal cancer, accounting for 50% of all new diagnoses. Prevalence of breast cancer alone accounts for 30% of female cancers and has been listed as the most frequent cancer diagnosis of female malignancy. It is known as global cancer statistics[2]; 2 088 849 new cases were reported in 2018.

Published epidemiological reports around the world[3] show that there is a significant increase in the death rate from breast cancer over the past two decades. Approximately 0.5 million people worldwide die from metastatic breast cancer every year even after receiving many therapies. Patients with breast cancer suffer from psychological and physical cancer-related stressors, which may affect patients for many years after treatment.[4] Women with breast cancer may suffer from treatment-related side effects, such as surgical trauma, scarring, mastectomy and lymphedema. According to the medical data,[5 6] these effects will easily lead to body image distortion, sexual dysfunction/intimacy problems as well as low self-esteem. Compared with the general population, when these patients are diagnosed with breast cancer, these effects will cause nearly 50% of patients with breast cancer to experience more considerable psychological distress, such as depression and anxiety, the prevalence of depression and anxiety in the

year after diagnosis is around twice as high as in the general female population.[7 8] Besides, lack of intimate confiding support will also lead to chronic depression and anxiety. The quality of life of patients with psychological symptoms is poor and the risk should not be ignored,[9–11] the depressive symptoms in patients with breast cancer can lead to physical deterioration and increased mortality.[12 13] Early screening for depression is essential because of its severity.

However, complete screening for depression is difficult due to its complex aetiology and pathogenesis. Some previous studies have linked the prevalence of depression to the following factors, such as physical symptom burden, marital status, age, level of education, financial status and the number of therapies.[14 15] However, some of the results are inconsistent. Some researchers have shown that the chemotherapy can reduce the risk of depression,[14] while others have found that the risk of depression is not affected by clinical factors such as prognosis, type of surgery or adjuvant radiotherapy, they consider that adjuvant chemotherapy may increase the risk of depression, anxiety or both during.[16–20] Only after screening out unified risk factors, and looking for high-risk patients can we effectively provide more targeted treatment strategies and improve quality of life in patients with breast cancer and survivors. To provide strong evidence on the risk factors related to depression, we will conduct a systematic review of evidence-based medicine and a meta-analysis. The validated findings will give recommendations for physicians to identify patients with breast cancer with depression and the management of emotional problems for patients, and we can also give some suggestions on improving the quality of life of these patients.

METHODS

This study consists the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Inclusion criteria for study selection

Types of studies

Observational studies with available data on the prevalence and risk factors associated with anxiety and depression among patients with breast cancer will be considered. For study selection, we will exclude cross-sectional, cohort studies, case–control studies, case reports, case series, opinion papers, qualitative research, letters to the editor, comments, conference proceedings, policy documents, reviews and meta-analyses, study protocols without baseline data and animal studies.

Types of patients

Study population inclusion criteria will be all patients diagnosed with breast cancer, regardless of demographic age, race and education status.

Types of outcome measures

(1) Prevalence of anxiety and depression among patients with breast cancer; (2) Risk factors associated with anxiety and depression in patients with breast cancer and (3) The strength of the correlation between each risk factor and anxiety and depression.

Search methods for the identification of studies

Data sources

The following databases will be used: Web of Science, PubMed, EMBASE, Wan Fang Data Knowledge Service Platform, Chinese Biomedical Literature Database, Chinese Scientific Journal Database (VIP database), China National Knowledge Infrastructure. We will also conduct unpublished academic research data, contacting authors in the field for information. Two systematic reviews will be carried out from inception to February 2020. The reference lists of review articles will be conducted and the following search terms will be used: breast cancer, breast carcinoma, breast tumour, mammary cancer, mammary adenocarcinoma, anxiety, depression and depressive disorder. And we will use the search strategy provided in table 1 for searching the database. The authors will also search relevant trials from Clinical Trials.gov, Google Scholar and WHO International Clinical Trials Registry Platform.

Study selection

Studies imported into Endnote X9 software after deleting duplicates will be independently reviewed by two authors (JL and FZ) based on the exclusion and inclusion criteria. The researcher (WW) will read the full text of relevant articles to confirm the final inclusion of studies. For unclear study, the researcher (RP) will contact the author for details to determine whether this literature would be included. Any disagreement between reviewers will be resolved by discussion or a researcher (LJC). The study screening process is shown in figure 1. The documents selection will be demonstrated on a PRISMA flow chart.

Risk of bias assessment

The risk of bias will be assessed applying the Cochrane's 'Risk of bias' tool. The quality of the included studies will be assessed independently by two authors (QM and AZ) at the study and outcome levels. Any disagreements will be settled by discussion or with the arbitrament of the third author (LJ). In this study, we will use the Newcastle-Ottawa Scale to evaluate the quality of studies. This scale is a quality assessment tool for non-randomised controlled trials, with scores ranging from 0 to 9; scores of 0–4 and 5–9 mean low quality and high quality, respectively.

Statistical collection and analysis

Data extraction and management

Extracted information include the first author's name, date of publication, journal, country and region, sample size (N and male/female), duration of the study, baseline age, diagnostic criteria for breast cancer and anxiety and depression, incidence of anxiety and depression/mean and SD for anxiety and depression score, variables, OR values, 95% CI, and other relevant data for quality evaluation and risk of bias assessment. And the reasons

Table 1 Search strategy in PubMed database

No	Search items
1	observational study. Mesh.
2	observational. ti.ab.
3	observe. ti.ab.
4	study. ti.ab.
5	1 or 2–4
6	breast cancer. Mesh.
7	breast carcinoma. ti.ab.
8	breast tumor. ti.ab.
9	mammary cancer. ti.ab.
10	mammary adenocarinoma. ti.ab.
11	6 or 7–10
12	anxiety. Mesh.
13	anxious. ti.ab.
14	hypervigilance. ti.ab.
15	nervousness. ti.ab.
16	social anxiety. ti.ab.
17	anxieties, social. ti.ab.
18	anxiety, social. ti.ab.
19	social anxieties. ti.ab.
20	12 or 13–19
21	depression. Mesh.
22	depressions. ti.ab.
23	depressive symptoms. ti.ab.
24	depressive symptom. ti.ab.
25	symptom, depressive. ti.ab.
26	symptoms, depressive. ti.ab.
27	emotional depression. ti.ab.
28	depression, emotional. ti.ab.
29	depressions, emotional. ti.ab.
30	emotional depressions. ti.ab.
31	21 or 22–30
32	5 and 11 and 20 and 31

for the exclusion of studies while extracting will also be recorded. The extraction of possible risk factors will be included gender, age, occupation, marital status, education level, social support, alcohol status, smoking status, pathological type, cancer clinical stage, disease course and therapy method. The extracted variables will be adjusted during the process, as it is likely that more and more variables that need to be included will turn up. Data collection will be done by two reviewers (JL and FZ) independently using Review Manager software. And if they are inconsistent in the process, they will discuss the results. A third reviewer will be consulted to resolve the doubts. For unclear details, the researchers will contact the corresponding authors by email for detailed information.

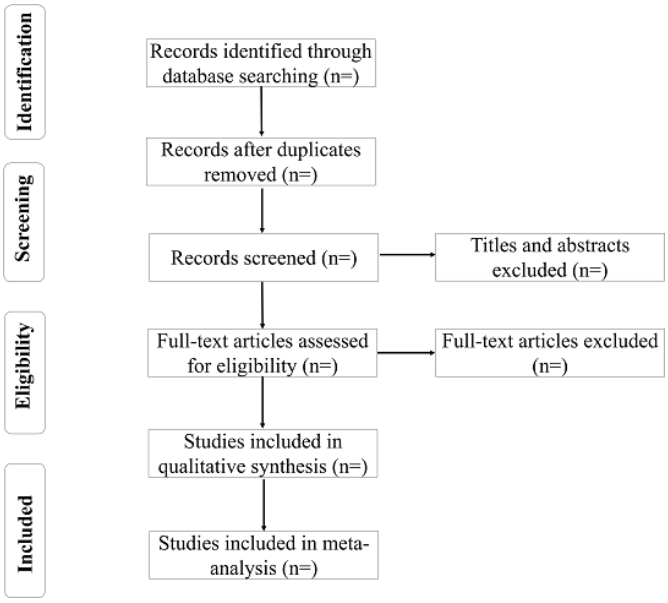

Figure 1 Flow diagram of the trial selection process.

Measurements of prevalence and risk factors

RevMan V.5.3 will be used to calculate the OR values and 95% CIs of the reported risk factors for anxiety and depression in breast cancer. When the CI for the OR does not include 1, it is considered statistically significant. The prevalence estimates reported by the individual studies will be extracted or converted into prevalence percentages, and their respective SEs will be calculated. For the anxiety and depression scores, standardised mean difference will be used for analysis. We will use the Freeman-Tukey double arcsine transformation to stabilise the variance of study-specific prevalence. The prevalence of each study will be recalculated to confirm numerators and denominators, and adjustments as necessary.

Assessment of heterogeneity

The I^2 test will be used to determine the extent of heterogeneity. When the I^2 value is less than 50%, the fixed-effects model will be used. If the I^2 value is higher than 50%, the random-effects model will be used. In this study, factors of high heterogeneity will be removed one by one to identify the source of any observed heterogeneity. The causes of heterogeneity may include differences in study design, statistical methods and participants.

Data synthesis

We will use RevMan V.5.3 software for analysis. Meta-analysis will be performed when the heterogeneity is low or the source could be found, although heterogeneity is high. A systematic narrative synthesis will be conducted if it is impossible to complete any meta-analysis. If there is significant heterogeneity, we will use the subgroup analysis.

Subgroup analysis

Subgroup analysis will be done when data are available. The groups may be designed based on country or region,

diagnostic criteria for anxiety and depression, bias score, time since diagnosis (long-term vs short-term survivors), severity/staging of breast cancer and study design.

Meta-regression analysis

Meta-regression analysis will be used to evaluate important factors (gender, age, occupation, marital status, education level, social support, alcohol status, smoking status, pathological type, cancer clinical stage, disease course and therapy method) on our study, which may explain heterogeneity across studies in the pooled effect size.

Assessment of reporting biases

Funnel plots will be used to assess publication bias. We will evaluate publication bias by performing the Begg's and Egger's tests. The significant p value (<0.05) indicates the existence of publication bias.

Quality control of the systematic review and meta-analysis

The methodological quality of the systematic review will be evaluated using the Measurement Tool to Assess Systematic Reviews. The Grading of Recommendations Assessment, Development and Evaluation will also be used to evaluate the strength of evidence produced by the systematic review (JL and FZ).

DISCUSSION

This study will review current researches to provide effective evidence on the risk factors related to depression and anxiety, and the results of systematic review and meta-analysis will provide significant help in identifying high-risk groups. These unified risk factors of depression will be screen out to advise on the management of emotional issues for patients. There may be some limitations to this review. First, a limitation will be the high heterogeneity studies may not be appropriate to be used in meta-analysis. Second, there may be heterogeneity in the diagnostic criteria for different types of anxiety and depression, as well as in the staging of cancer and depression. Different measurements and tools might lead to inconsistent levels of outcomes.

Contributors JL and FZ will identify eligible studies after reading titles and abstracts. WW will read the full texts to perform further selection. Several studies from different opinions will be determined by the RP. Data will be extracted from the original reports by LJC. The assessment of the risk of bias will be carried out by QM, AZ and JL. Any discrepancies will be resolved by discussion with a third AZ. JL and FZ will use the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. JL conceived the review protocol and drafted the manuscript. FZ will monitor each procedure of the review. All authors read and approved the publication of the protocol.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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