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Psychological distress and coping strategies in breast cancer patients under neoadjuvant therapy: A systematic review

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Abstract

Background: During neoadjuvant therapy (NAT), patients with locally advanced breast cancer (LABC) experience psychological distress (PD) and adopt appropriate coping strategies.

Objective: This systematic review aimed to examine the prevalence and changes in PD and coping strategies in patients with LABC during NAT and to evaluate effective interventions to reduce their PD.

Design: Quantitative (cross-sectional, longitudinal, and interventional) and qualitative studies reporting PD and coping strategies related to NAT during LABC were included.

Data sources and methods: PubMed, Cochrane Library, Scopus, ScienceDirect, Wiley Online Library, and Web of Science databases were consulted to gather relevant literature from the first publications until July 25, 2023. Selection was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Results: A total of 41 articles were included, of which four were qualitative. The main results showed that the prevalence of depression before NAT ranged from 0% to 46% and that of anxiety from 5.5% to 54%. After NAT, the prevalence of depression ranged from 40% to 78.5% and anxiety accounted for 27%. Additionally, PD decreased during NAT. The main determinants of PD were perceived social support, living in joint families, being affected by COVID-19 infection, delays in diagnosis, and starting neoadjuvant treatment. For coping strategies, after NAT, "resigned coping" decreased, whereas

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"social support" increased, and active coping strategies were correlated with better PD. Some interventions found a reduction in PD, such as a mobile health application, fasting-mimicking diet, relaxation training, and guided imaging.
Conclusion: These findings highlight the importance of considering PD and coping strategies in patients with LABC from diagnosis to the end of NAT. The results suggest that effective psychological interventions should be implemented.

Keywords
locally advanced breast cancer, neoadjuvant therapy, psychological distress, coping strategies, prevalence, determinants, psychological intervention

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Introduction

Breast cancer (BC) is the most common cancer in women worldwide, and its prevalence continues to increase annually. As indicated by the International Agency for Research on Cancer, the incidence of BC increased by 24.3% between 2012 and 2020.[1] Locally advanced breast cancer (LABC) is a group of breast tumors characterized by advanced progression without distant metastases. It includes tumors surpassing 5 cm in size with regional lymph node involvement, as well as tumors of any size with invasion of the skin or chest wall, regardless of the lymph node regional involvement.[2]

Neoadjuvant therapy (NAT) is commonly used for the treatment of LABC. Neoadjuvant chemotherapy (NACT) was originally administered to increase the rate of conservative surgery in patients with LABC who were initial candidates for mastectomy.[3] Subsequent research has revealed a correlation between obtaining a pathological complete response and good long-term clinical outcomes.[4,5] NACT has the most significant benefits in patients with human epidermal growth factor receptor 2 (HER2)-positive and triple-negative BC.[6–8] However, there is a growing trend in the use of neoadjuvant endocrine therapy (NET) for estrogen receptor positive tumors.[3]

Diagnosis and treatment of cancers such as NET in LABC can become a high and chronic stressor and thus contribute to persistent psychological distress (PD).[9] Owing to the seriousness of the disease, a significant number of women experience psychological disturbances during or after treatment. The most common symptoms include fatigue, depression, psychological stress, anxiety, and fear.[10] PD levels tend to be the highest at the time of diagnosis when patients are confronted with the initial shock and the consequences of their condition. Thereafter, these levels tend to decrease progressively as the patients begin treatment.[11] According to a meta-analysis, 32% of women with BC experienced depression.[12] In another study,[13] among women who underwent chemotherapy, the level of anxiety was highest before the first infusion session.[13] Women with BC develop PD for various reasons. These include treatment uncertainty; physical symptoms; fear of progression, recurrence, and death; body image; changes in female identity; sexual problems; difficulties in daily activities; family problems; and lack of emotional support.[14]

Several publications[15–18] have shown that PD is a concept that covers different alterations, such as depression (hopelessness, sadness, lost interest), anxiety (feeling tense, restlessness), fear, the inability to cope positively with stress, and emotional disorders. The choice of the term "PD" to the detriment of other concepts takes its strength from the National Comprehensive Cancer Network (NCCN) Guideline,[17] which considers it less stigmatizing and more acceptable. Commonly, psycho-oncology researchers have turned to the NCCN guidelines to define PD as "a multifactorial unpleasant experience of a psychological (cognitive, behavioral, emotional), social, spiritual, and/or physical nature that may interfere with one's ability to cope effectively with cancer, its physical symptoms, and its treatment."[17] The concept of PD can also be extended to dimensions encompassing the quality of life (QoL) in patients with BC. Among these dimensions, emotional functioning (EF)[19–21] and emotional well-being (EWB)[21,22] are examples that have been sufficiently mentioned in the literature.

Furthermore, women adopt coping strategies as a result of LABC. Indeed, women with this diagnosis must cope with the alterations in PD, deal with the side effects of treatment and surgery, and adapt to new life circumstances.[23,24] In a systematic review[25] of 20 articles aiming to investigate coping responses following a diagnosis of different stages of BC, the most common coping strategies that patients used were seeking social support, positive reframing, reappraisal behaviors, religion/spirituality, emotional expression, avoidance, and distraction.

To the best of our knowledge, no systematic review has specifically examined PD and coping strategies or their determinants during NAT in patients with LABC. However, a recent publication focusing on QoL[26] attempted to present some results without covering all aspects of PD.[26] With the increased use of NACT in LABC, research has focused on understanding PD and coping strategies to provide more effective care for patients from diagnosis to survival. Therefore, we are convinced that an in-depth systematic review of PD and coping strategies in LABC patients receiving NAT should be carried out. A protocol for this systematic review[27] has already been published. Consequently, the main objectives were (a) to present the prevalence of PD and its different forms during NAT and its evolution, to describe

Table 1. Summary of the PICOS elements that make up the systematic review.

PICOS	Inclusion criteria	Exclusion criteria
Population	- Women with breast cancer under NAT	Breast cancer man
Interventions	- Any intervention used to evaluate psychological distress and coping strategies, also other psychological symptoms correlates - Any intervention applied to menage these different psychological variables	
Comparators	- Changes in the psychological distress and coping strategies in the different before, during and after NAT - Comparison between different groups of patients compared to patients undergoing the adjuvant chemotherapy or compared to other cancer	
Outcomes	*Primary main outcomes* - Psychological distress - Depression and anxiety - Coping strategies - Psychological domains of quality of life *Secondary main outcomes* - Patient information - Cancer symptoms - Social support - Patient experiences and perception	
Type of studies	Observational studies (cross-sectional, longitudinal, case-control, and retrospective designs, with a qualitative or quantitative design) and interventional studies related to the psychological distress	Abstracts, conference abstracts, literature reviews, letter, books, editorials, case reports, and unpublished studies, gray literature
General	Limited to English language No deadline will be applied for publication dates	Not written in English

NAT, neoadjuvant therapy; PICOS, population, intervention, comparison, outcome, and study type.

the coping strategies adopted, (b) to examine the determinants of PD and coping strategies during NAT, and (c) to evaluate the interventions carried out to reduce PD.

Methods

This systematic review was designed according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (Appendix A in the Supplemental Material). This review presented an objective procedure for extracting the maximum information from studies on PD and coping strategies for patients undergoing NAT. The protocol was registered at International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42021230300. We worked to ensure the integrity of this systematic review from 2022 to the end of 2023.

Inclusion and exclusion criteria

We based our inclusion and exclusion criteria on PICOS (population, intervention, comparison, outcome, and study type). A summary of the PICOS elements constituting the systematic review is presented in Table 1. The following databases were searched to identify relevant articles: PubMed, Cochrane Library, Scopus, ScienceDirect, Wiley Online Library, and Web of Science. The search strategy used Boolean operators for the medical subject heading (MeSH) terms (Table 2). We also created alerts in the databases corresponding to our search equation to identify articles suitable for our review. We extended the bibliographic research to other sources, specific journals, and manual searches of articles using Google. As this is the first systematic review of the variables in question, we conducted a comprehensive search of studies spanning more than 20 years until July 25, 2023.

Data extraction

Two authors independently reviewed the inclusion and exclusion criteria of each study. All articles were collected using the Zotero reference management software, which allowed them to organize and read their titles and abstracts. Among the data extracted from each quantitative study were the first author's name; year of study; sitting; study design; mean age; sample size; variables of interest and instrument; prevalence and mean of variables before, after, and during the NAT cycle; and the main significant changes and associates. For the qualitative studies, two reviewers listed the main findings for each theme.

Table 2. Search strategy until July 25, 2023.

Search number	PubMed	Result
#15	#14 AND #13 ((“breast neoplasms” [MeSH Terms] OR (“breast” [All Fields] AND “neoplasms” [All Fields]) OR “breast neoplasms” [All Fields]) AND (“neoadjuvant therapy” [MeSH Terms] OR (“neoadjuvant” [All Fields] AND “therapy” [All Fields]) OR “neoadjuvant therapy” [All Fields] OR (“therapy” [All Fields] AND “neoadjuvant” [All Fields]) OR “therapy neoadjuvant” [All Fields])) AND ((((((((((“psychological distress” [MeSH Terms] OR (“psychological” [All Fields] AND “distress” [All Fields]) OR “psychological distress” [All Fields]) OR (“mental disorders” [MeSH Terms] OR (“mental” [All Fields] AND “disorders” [All Fields]) OR “mental disorders”[All Fields])) OR (“depressed” [All Fields] OR “depression” [MeSH Terms] OR “depression” [All Fields] OR “depressions” [All Fields] OR “depression s” [All Fields] OR “depressive disorder” [MeSH Terms] OR (“depressive” [All Fields] AND “disorder” [All Fields]) OR “depressive disorder” [All Fields] OR “depressivity” [All Fields] OR “depressive” [All Fields] OR “depressively” [All Fields] OR “depressiveness” [All Fields] OR “depressives” [All Fields])) OR (“anxiety disorders” [MeSH Terms] OR (“anxiety” [All Fields] AND “disorders” [All Fields]) OR “anxiety disorders” [All Fields])) OR (“adaptation, psychological” [MeSH Terms] OR (“adaptation” [All Fields] AND “psychological” [All Fields]) OR “psychological adaptation” [All Fields] OR (“adaptation” [All Fields] AND “psychological” [All Fields]) OR “adaptation psychological” [All Fields])) OR (“adaptation, psychological” [MeSH Terms] OR (“adaptation” [All Fields] AND “psychological” [All Fields]) OR “psychological adaptation” [All Fields] OR (“behavior” [All Fields] AND “coping” [All Fields]) OR “behavior coping” [All Fields])) OR (“social adjustment” [MeSH Terms] OR (“social” [All Fields] AND “adjustment” [All Fields]) OR “social adjustment” [All Fields] OR (“adjustment” [All Fields] AND “social” [All Fields]) OR “adjustment social” [All Fields])) OR (“Access to Information” [Mesh])) OR (“decision support techniques” [MeSH Terms] OR (“decision” [All Fields] AND “support” [All Fields] AND “techniques” [All Fields]) OR “decision support techniques” [All Fields])) OR (“quality of life” [MeSH Terms] OR (“quality” [All Fields] AND “life” [All Fields]) OR “quality of life” [All Fields]))	413
#14	(#3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11) AND #12: (((((((((“psychological distress” [MeSH Terms] OR (“psychological” [All Fields] AND “distress” [All Fields]) OR “psychological distress” [All Fields]) OR (“mental disorders” [MeSH Terms] OR (“mental” [All Fields] AND “disorders” [All Fields]) OR “mental disorders” [All Fields])) OR (“depressed” [All Fields] OR “depression” [MeSH Terms] OR “depression” [All Fields] OR “depressions” [All Fields] OR “depression” [All Fields] OR “depressive disorder” [MeSH Terms] OR (“depressive” [All Fields] AND “disorder” [All Fields]) OR “depressive disorder” [All Fields] OR “depressivity” [All Fields] OR “depressive” [All Fields] OR “depressively” [All Fields] OR “depressiveness” [All Fields] OR “depressives” [All Fields])) OR (“anxiety disorders” [MeSH Terms] OR (“anxiety” [All Fields] AND “disorders” [All Fields]) OR “anxiety disorders” [All Fields])) OR (“adaptation, psychological” [MeSH Terms] OR (“adaptation” [All Fields] AND “psychological” [All Fields]) OR “psychological adaptation” [All Fields] OR (“adaptation” [All Fields] AND “psychological” [All Fields]) OR “adaptation psychological” [All Fields])) OR (“adaptation, psychological”[MeSH Terms] OR (“adaptation” [All Fields] AND “psychological” [All Fields]) OR “psychological adaptation” [All Fields] OR (“behavior” [All Fields] AND “coping” [All Fields]) OR “behavior coping” [All Fields])) OR (“social adjustment” [MeSH Terms] OR (“social” [All Fields] AND “adjustment” [All Fields]) OR “social adjustment” [All Fields] OR (“adjustment” [All Fields] AND “social” [All Fields]) OR “adjustment social” [All Fields])) OR (“Access to Information” [Mesh])) OR (“decision support techniques” [MeSH Terms] OR (“decision” [All Fields] AND “support” [All Fields] AND “techniques” [All Fields]) OR “decision support techniques” [All Fields])) OR (“quality of life” [MeSH Terms] OR (“quality” [All Fields] AND “life” [All Fields]) OR “quality of life” [All Fields])	2,547,252
#13	#1 AND #2 = (“breast neoplasms”[All Fields] OR “breast neoplasms”[MeSH Terms] OR (“neoplasms”[All Fields] AND “breast”[All Fields])) AND ((“neoadjuvant”[All Fields] AND “therapy”[All Fields]) OR “neoadjuvant therapy”[All Fields OR “neoadjuvant therapy”[MeSH Terms] OR (“therapy”[All Fields] AND “neoadjuvant” [All Fields]) OR “therapy neoadjuvant” [All Fields])	10,741

(Continued)

Table 2. (Continued)

Search number	PubMed	Result
#12	("quality" [All Fields] AND "life"[All Fields]) OR "quality of life"[MeSH Terms] OR "quality of life" [All Fields]	538,859
#11	"decision support techniques" [MeSH Terms] OR "decision support techniques" [All Fields] OR ("decision" [All Fields] AND "support" [All Fields] AND "techniques" [All Fields])	93,157
#10	"Access to Information" [Mesh]	8,185
#9	("social" [All Fields] AND "adjustment" [All Fields]) OR "social adjustment" [MeSH Terms] OR "social adjustment" [All Fields] OR "adjustment social" [All Fields] OR ("adjustment" [All Fields] AND "social" [All Fields]) OR	46,581
#8	("adaptation" [All Fields] AND "psychological" [All Fields]) OR "adaptation, psychological" [MeSH Terms] OR "psychological adaptation" [All Fields] OR "behavior coping" [All Fields] OR ("behavior" [All Fields] AND "coping" [All Fields])	155,986
#7	("adaptation" [All Fields] AND "psychological" [All Fields]) OR "adaptation, psychological" [MeSH Terms] OR "psychological adaptation" [All Fields] OR "adaptation psychological" [All Fields] OR ("adaptation" [All Fields] AND "psychological" [All Fields])	149,605
#6	"anxiety disorders" [MeSH Terms] OR ("anxiety" [All Fields] AND "disorders" [All Fields]) OR "anxiety disorders" [All Fields]	172,275
#5	"depression" [MeSH Terms] OR "depressed" [All Fields] OR "depression" [All Fields] OR "depressive disorder" [MeSH Terms] OR "depressions" [All Fields] OR "depression" [All Fields] OR ("depressive" [All Fields] AND "disorder" [All Fields]) OR "depressive disorder" [All Fields] OR "depressivity" [All Fields] OR "depressive" [All Fields] OR "depressives" [All Fields] OR "depressively" [All Fields] OR "depressiveness" [All Fields]	616,994
#4	("mental" [All Fields] AND "disorders" [All Fields]) OR "mental disorders" [MeSH Terms] OR "mental disorders" [All Fields]	1,492,561
#3	("psychological" [All Fields] AND "distress" [All Fields]) OR "psychological distress" [MeSH Terms] OR "psychological distress" [All Fields]	57,519
#2	("neoadjuvant" [All Fields] AND "therapy" [All Fields]) OR "neoadjuvant therapy" [MeSH Terms] OR ("therapy" [All Fields] AND "neoadjuvant" [All Fields]) OR "therapy neoadjuvant" [All Fields] OR "neoadjuvant therapy" [All Fields]	47,357
#1	("breast" [All Fields] AND "neoplasms" [All Fields]) OR "breast neoplasms" [MeSH Terms] OR "breast neoplasms" [All Fields]	401,545
	Library Cochrane	Results
#12	#3 AND #10	42
#11	#4 OR #5 OR #6 OR #7 OR #8 OR #9	78,606
#10	MeSH descriptor: [Quality of Life] explode all trees	43,718
#9	MeSH descriptor: [Decision Support Techniques] explode all	3982
#8	MeSH descriptor: [Psychological Distress] explode all trees	415
#7	MeSH descriptor: [Social Support] explode all trees	4317
#6	MeSH descriptor: [Depression] explode all trees	18,466
#5	MeSH descriptor: [Anxiety Disorders] explode all trees	9038
#4	MeSH descriptor: [Adaptation, Psychological] explode all trees	6349
#3	#1 AND #2	688
#2	MeSH descriptor: [Breast Neoplasms] explode all trees	17,876
#1	MeSH descriptor: [Neoadjuvant Therapy] explode all trees	2175

(Continued)

Table 2. (Continued)

Search number	PubMed	Result
	Web of science	Results
#4	**#1 AND #2**	957
#3	TS = ("psychological distress" OR anxiety OR depression OR "anxiety disorders" OR "depressive disorder" OR "mental disorders" OR "mental health" OR "psychotherapy health" OR coping OR adjustment OR adaptation OR "mental adaptation" OR "mental adjustment" OR "Psychological adaptation" OR "psychological adjustment" OR "coping behavior" OR "social support" OR "social adjustment" OR "social adaptation" OR "family support" OR "informational support" OR "patient information" OR "aid decision" OR "decision support techniques" OR "access to information" OR "quality of life" OR "life quality" OR "health-related quality of life" OR "health-related quality of life" OR HRQOL OR QOL)	2,674,890
#2	**TS = ("neoadjuvant therapy" OR neo-adjuvant OR neoadjuvant OR "preoperative chemotherapy" OR "primary systemic chemotherapy" OR "neoadjuvant endocrine" OR "neo-adjuvant endocrine")**	76,388
#1	TS = (breast AND (neoplasms OR cancer))	666,640
	Scopus	Results
	(TITLE-ABS-KEY ({Breast cancer} OR {Breast Neoplasms})) AND (TITLE-ABS-KEY ({neoadjuvant chemotherapy } OR {neoadjuvant therapy } OR {neo-adjuvant chemotherapy} OR {Primary systemic chemotherapy} OR {Preoperative chemotherapy} OR {neo-adjuvant endocine} OR {neoadjuvant endocine})) AND (TITLE-ABS-KEY ({psychological distress} OR anxiety OR depression OR {anxiety disorders} OR {Mental Disorders} OR{depressive disorder}OR coping OR {adaptation psychological} OR adaptation OR adjustment OR {behavior coping} OR {family support} OR {Social support} OR {informational support} OR {Patient information} OR {aid decision} OR {quality of life} OR {Health-Related QOL} OR {life quality} OR{Health-Related Quality Of Life} OR {Health Related Quality Of Life} OR {Health Related QOL} OR hrqol)) AND (LIMIT-TO (DOCTYPE, "ar"))	749
	Sciencedirect	Results
	("breast neoplasms" AND ("neoadjuvant OR "neo-adjuvant")) AND ("psychological distress" OR "depression" OR "anxiety" OR "Coping" OR "adjustment" OR "quality of life") ("breast neoplasms" AND ("neoadjuvant OR "neo-adjuvant")) AND ("psychological distress" OR "depression" OR "anxiety" OR "Coping" OR "adjustment" OR "quality of life") Filtrs limited "research articles"	199
	Wiley Online library	Results
	"breast OR "breast neoplasm" OR "breast cancer"" in Title and ""neoadjuvant therapy" OR neoadjuvant OR "neo-adjuvant therapy" OR neo-adjuvant OR "preoperative chemotherapy" OR "primary systemic chemotherapy" OR "neoadjuvant endocrine" OR "neoadjuvant endocrine"" in Keywords and ""psychological distress" OR anxiety OR depression OR "anxiety disorders" OR "depressive disorder" OR "mental disorder" OR "mental health" OR "psychotherapy health" OR coping OR adjustment OR adaptation OR "mental adaptation" OR "mental adjustment" OR "psychological adaptation" OR "psychological adjustment" OR "coping behavior" OR "social support" OR "social adjustment" OR "social adaptation" OR "family support" OR "informational support" OR "patient information" OR "aid decision" OR "decision Support Techniques" OR "access to information" OR "life quality" OR "quality of life" OR "health-related quality of life" OR HRQOL OR "health related quality of life" OR QOL" anywhere	156
	Results of research in others resources	08

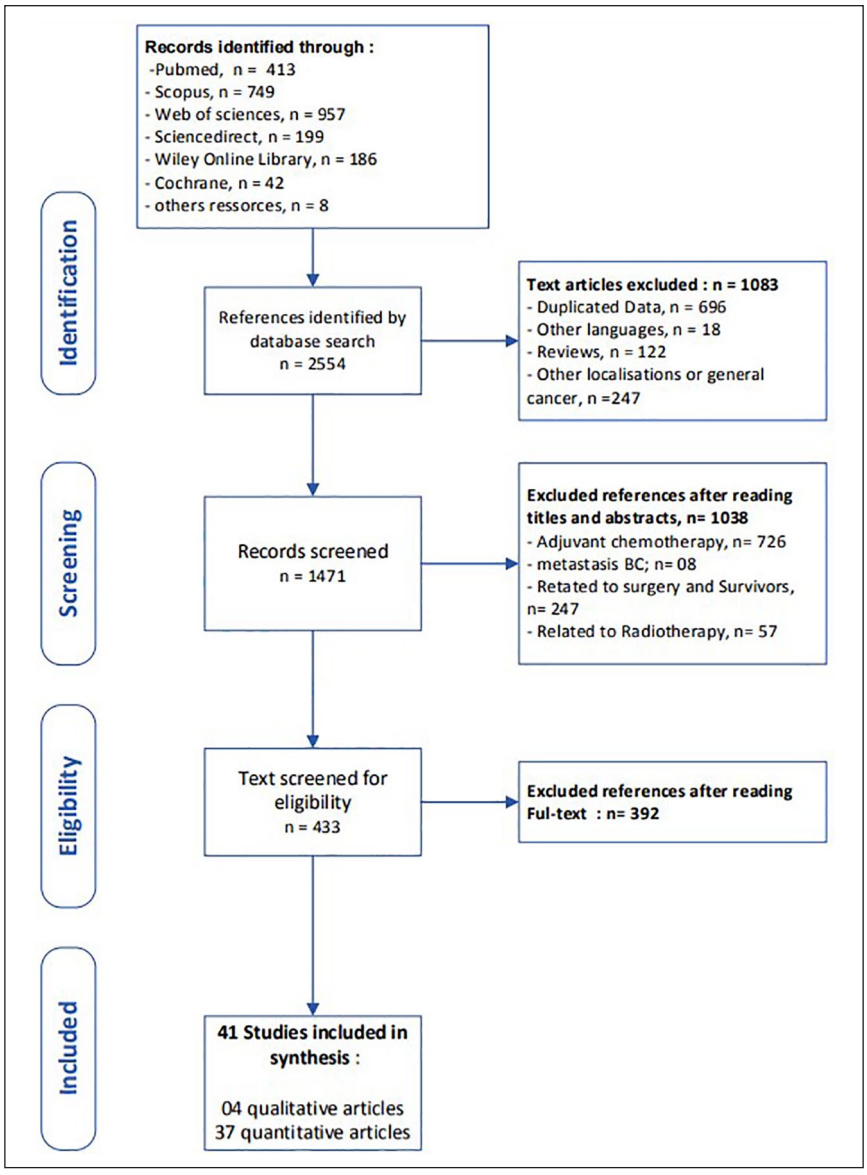

Figure 1. Flow diagram of the process of systematic literature search in accordance with PRISM guidelines.

Quality assessment

Two reviewers assessed the quality of the included studies using the QualSyst tool, which is generally preferred for both quantitative and qualitative studies. The QualSyst tool enables the evaluation of quantitative studies using 14 items, whereas 10 items are used for qualitative studies.[28] We noted each item was scored 2 for "Yes," 1 for "Partial," and 0 for "No"; items not suitable for the specified study design were labeled "NA" and eliminated while calculating the final score. Quality assessment for each quantitative study was performed by dividing the total possible score by the aggregate score, which was calculated by adding the relevant items. We calculated the scores of the qualitative studies using the same method.[28]

Results

Description of included studies

A total of 2554 articles were found in the initial pool of articles. A total of 41 studies were included in this review. Figure 1 shows the selection procedure used in this study. In our systematic review, 4268 participants were included, resulting in original studies published between 1999 and 2023. Figure 1 presents a flow diagram of the process of this systematic review search, in accordance with the PRISMA guidelines. Tables 3 and 4 show the characteristics of the observational and interventional quantitative studies included in this systematic review, respectively, and Table 5 shows the qualitative studies.

Table 3. Characteristics of included observational studies.

Author (year), Citation; Country	Study design, assessment timepoints comparison	Sample	Mean age, ±standard deviation, (range)	Variable of interest; Measuring instruments	Main fundings	QualSyst score
Tschuschke et al. (2017)[29]; Germany	Prospective Before and after NACT	$n=53$	50.2 (34–74)	Depression; HADS-D and POMS-D	- At $t-1$, mean of HADS-D = 5.80 (4.86) - At $t-1$, mean of POMS-D = 2.47 (0.63) - At $t-2$, mean of HADS-D = 4.76 (3.89) - At $t-2$, mean of POMS-D = 1.66 (0.62) - POMS-D experienced a significant reduction between $t-1$ and $t-2$, but the change in HADS-D was not significant	91%
				Anxiety; HADS-A	- At $t-1$, mean of HADS-A = 9.16 (4.37) - At $t-2$, mean of HADS-A = 5.33 (3.72) - Anxiety showed a significant reduction between $t-1$ and $t-2$	
				Psychological distress; BSI	- At $t-1$, Mean of psychological distress = 0.65 - At $t-2$, Mean of psychological distress = 0.49 - Patients had significantly elevated levels of psychological distress at $t-1$ compared to $t-2$	
				Coping strategies; Ulm Coping Manual	- "Resigned coping" decreased, whereas "seeking social support" increased significantly during the NACT - The reduction in "distraction" and "fighting spirit" was not significant during the NACT - At $t-2$, "active coping strategies" ("fighting spirit," "social support"; "cognitive restructuring" and "complying to treatment") were associated with better psychological adjustment - At $t-1$, higher "cognitive restructuring" associated with lower psychological stress - At $t-1$, "fighting spirit" was negatively correlated with "resigned coping" and positively correlated with "social support" - At $t-1$, patients with no or low "resignation" scores tend to adopt a "fighting spirit" - At $t-2$, a higher "fighting spirit" score was associated with better adaptation to the NACT - At $t-2$, "Resigned adaptation" was associated with poorer psychological adjustment	
Chintamani et al. (2011)[30]; India	- Prospective - Women were interviewed at each stage of disease management	$n=84$	NR	Depression; HADS-D (cut-off $\geqslant 11$)	- At $t-1$, prevalence of depression was 0%, and mean was 4.9 - At $t-2$, prevalence of depression was 41% - The rate of depression was significantly higher in patients who did not respond to NACT than in those who responded to therapy - Lower rates of depression are associated with a higher percentage of patients living in mixed families, in contrast to patients in nuclear families	64%
Miranda et al. (2002)[31]; Brazil	Prospective Before and after NACT; Breast cancer patients versus patients with cervical cancer	$n=43$ - $n=21$ BC patients - $n=22$ cervical cancer patients.	- BC patients = 49.8 (36–62) - Cervical cancer patients = 40.8 (29–57)	Depression; BDI	- At $t-1$, prevalence of depression was 30% - At $t-2$, prevalence of depression was 45% - The change of depression was not significant during the NACT - There is no significant association between depression and response to NACT, but patients who responded to NACT were less depressed at the end of treatment	73%

(Continued)

Table 3. (Continued)

Author (year), Citation; Country	Study design, assessment timepoints comparison	Sample	Mean age, ±standard deviation, (range)	Variable of interest; Measuring instruments	Main fundings	QualSyst score
Oh et al. (2020)[32]; Korea	- Prospective - 8 cycles of NACT - Group with low PSS versus group with "Moderate to High" PSS	*n* = 184	- Group with low PSS = 46.9 ± 8.6; - Group with "Moderate to High" PSS = 43.9 ± 7.4	Depression; HADS-D (cut-off ⩾8) Anxiety; HADS-A (cut-off ⩾8) Cancer reported symptoms; MDASI	- At *t* − 1, prevalence of depression was 46% - At *t* − 1, low PSS score associated with more depression compared to "moderate to high" PSS - At *t* − 1, prevalence of anxiety was 54% - At *t* − 1, there was no difference in anxiety between the "moderate to high" PSS group and the low PSS group - During NACT, memory loss, distress, insomnia, and sadness were worsened during NACT - Patients in the "moderate to high" PSS group had significantly lower scores of distress, insomnia, and memory loss	86%
Taira et al. (2014)[33]; Japan	- Prospective - Baseline, 4 weeks, and 16 weeks.	*n* = 497	63 (46–75)	Depression; HADS-D (cut-off ⩾11) Anxiety; HADS-A (cut-off ⩾11) HADS total EWB; FACT-B	- At *t* − 1, the mean of depression was 4.3 (3.2) - At *t* − 1, the mean of anxiety was 6.1 (3.4) - At *t* − 1, the mean of HADS total was 10.4 (6.0) - At *t* − 1, the prevalence of the score total of HADS was 42% - After 4 weeks, 30% of patients had a high HADS total score - After 16 weeks,31% have a high HADS total score - Significant improvement in depression, anxiety, and HADS total during TEN - At *t* − 1, the prevalence of loss of interest in sex was 42%, irritability was 5.7%, and mood swings was 5.5% - After 4 weeks, the mean of EWB was 60.1 (10.0) - After 16 weeks, the mean of EWB was 59.7 (9.6) - Significant improvement in EWB (FACT-B) during neoadjuvant LET	86%
Chellappan (2018)[53]; India	- Cross-sectional - Three weekly group versus weekly group;	*n* = 100 - 50 three weekly patients - 50 weekly patients	NR	Depression; HAMD EWB; FACT-B	No statistically significant difference in depression between weekly patients and three weekly patients - QoL was improved in three weekly NACT patients due to significantly higher score of EWB	73%
LeVasseur et al. (2020)[35]; Canada	- Prospective - Low anxiety versus high anxiety	*n* = 203	58	Anxiety; ESAS-A; CPC; PSSCAN-R	- At *t* − 1, the rate of low anxiety was 45.8% had, whereas 54.2% had high anxiety - Patients in the high anxiety score at *t* − 1 were significantly younger compared with those in the low anxiety level - Patients with high scores of anxiety at *t* − 1 were significantly 9 times more susceptible to receive mastectomy compared with anxious patients	91%
Lee et al. (2018)[36]; Korea	- Prospective	*n* = 111	44.48 ± 7.48 (26°–60°)	Depression; HADS-D (cutoff ⩾8) Anxiety; HADS-A (cutoff ⩾8) Sleep; PSQI (cutoff ⩾8)	- At *t* − 1, the prevalence of depression was 39.6% - At *t* − 1, the prevalence of anxiety was 31.5% - At *t* − 1, the anxiety was associated with peripheral neuropathy - At *t* − 1, the prevalence of poor sleep quality was 16.2% - Anxiety was significantly related with persistent CIPN	91%

(Continued)

Table 3. (Continued)

Author (year), Citation; Country	Study design, assessment timepoints comparison	Sample	Mean age, ±standard deviation, (range)	Variable of interest; Measuring instruments	Main fundings	QualSyst score
Aprilianto et al. (2021)[52]; Indonesia	- Cross-sectional - During NACT	*n* = 56		Family social support; Family social support questionnaire Self-esteem; RSES	- 48.2% of patients reported a moderate level of self-esteem - When the social support provided by the family was better, the patients had a higher level of self-esteem	77%
Yao et al. (2016)[37]; Canada	- Cross-sectional - At *t* − 1 PCG versus HCG	*n* = 56 - *n* PCG = 31 - *n* HCG = 25	- PCG = 46.1 (8.7) - HCG = 46.1 (11.0)	Depression; HADS-D (cutoff ⩾8) Anxiety; HADS-A (cutoff ⩾8) HADS total	- At *t* − 1, the prevalence of depression was 13%, whereas the mean of depression was 4.2 (3.9) - At *t* − 1, the prevalence of anxiety was 5.5%; while its mean was 8.5 (4.8) - At *t* − 1, the mean of HADS total was 12.7 (7.4) - HADS-A subscale and total HADS scores were higher for PCG compared to HCG at *t* − 1 - PCG reported a greater prevalence of anxiety, depressive, and fatigue, they also stated more problems of cognitive status	91%
Yao et al. (2016)[39]; Canada	-Prospective - At *t* − 1 1 month after NACT after surgery PCG versus HCG	*n* = 48 - *n* PCG = 28 - *n* HCG = 20	Patient group = 45.3 (8.5) HCG = 45.7 (11.3)	Anxiety; HADS-A (cutoff ⩾8)	At *t* − 1, PCG tended to report more anxiety than the HCG	95%
Lee et al. (2021)[40]; Korea	- Prospective - *t* − 1, *t* − 2; 6 months after end of NACT	*n* = 193	44.89 ± 7.9	Depression; HADS-D (cutoff ⩾8) Anxiety; HADS-A (cutoff ⩾8) QoL; FACT-B Resilience; CD-RISC	- At *t* − 1, the prevalence of depression was 36.5%, whereas at *t* − 2 it was 40% At *t* − 1, the prevalence of anxiety was 34,9%; while at *t* − 2 it was 27% - Anxiety at *t* − 2 of the participants under 50 years of age and who underwent BCS was significantly higher - Depression and anxiety moderately correlated with the QoL at each time point - Resilience at *t* − 1 was moderately correlated with depression and anxiety and QoL at each time point	75%
Sanghyup et al. (2022)[41]; Korea	- Prospective - *t* − 1: baseline and after each cycle of Doxorubicin and Cyclophosphamide	*n* = 203	45.1 ± 8.0	Depression; HADS-D (cut-off ⩾8) Anxiety; HADS-A (cut-off ⩾8) Sleep; PSQI (cut-off ⩾8)	- At *t* − 1, the prevalence of depression was 35% - At *t* − 1, the prevalence of anxiety was 34.5% - At *t* − 1, the prevalence of poor sleep quality was 18.2% - At *t* − 1, late chronotype was significantly associated with anxiety	82%

(Continued)

Table 3. (Continued)

Author (year), Citation; Country	Study design, assessment timepoints comparison	Sample	Mean age, ±standard deviation, (range)	Variable of interest; Measuring instruments	Main fundings	QualSyst score
Lee et al. (2017)[42]; Korea	- Prospective - Baseline and after the first cycle of NACT	$n=134$	49	Depression; HADS-D (cut-off ⩾8) Anxiety; HADS-A (cut-off ⩾8) Poor sleep quality; PSQI (cut-off >5) Chronotype; MCTQ	- At $t-1$, the prevalence of depression was 36.6%, and its mean was 6.60 ± 4.15 - At $t-1$, the prevalence of depression was 29.9%, and its mean was 6.66 ± 3.58 - At $t-1$, the prevalence of Poor Sleep quality was 16.4% and its mean was 2.90 - At $t-1$, the rate of late chronotype was 20.9%, of the early chronotype was 20.1%, and for intermediate chronotype was 59.0% - Anxiety was not associated to CINV	91%
Kemer et al. (2022)[54]; Brazil	Cross-sectional	$n=67$ - Non-metastatic HER2-negative patient	NR	Depression; BDI Anxiety; BAI EWB; FACT-G	- No significant differences between ages, level of education, or economic situation with anxiety and depression levels were observed - No significance between patients affected with COVID-19 and depression and anxiety scores - Lower levels of severe depression observed in patients who had sons or daughters - Delays in diagnosis or in the beginning of NACT were associated to greater levels of depression and anxiety - Higher rates of sex interest loss in patients who had delays in diagnosis of BC and systemic treatment development - Women who had social support by family/friends reported better EWB - Patients who were not diagnosed with COVID-19 showed greater impairment EWB - Patients who acquired COVID-19 infection had poorer EWB	91%
Zhou et al. (2022)[34]; China	- Prospective	$n=45$	50.47 ± 9.08 (29–68)	Depression; SDS Anxiety; SAS	- At $t-1$, the mean score of depression was 29.89 ± 6.32 - At $t-1$, the mean score of anxiety was 29.13 ± 6.87	91%
Takada et al. (2018)[68]; Japan	- Retrospective - Comparison of high and low QoL groups on subscales	$n=300$	55 (range 27–90)	Dress, sexual aspect, other; QoL-ACD-B Satisfaction with treatment and coping with disease; QoL-ACD-B	- At $t-1$: the low QoL group had a significant lower score of "dress, sexual aspect, other" than the high QoL group - At $t-1$: the high and low QoL groups had no change ($p=0.253$) for "Satisfaction with treatment and coping with disease" - Satisfaction with treatment and coping with disease did not change between pre- and post-NACT, but "Dress, sexual aspect, and other" displayed significant increases	82%
Rezapour et al. (2018)[57]; Iran	Prospective study	$n=100$ women - $n=50$ for patients received Paclitaxel and Gemcitabine - $n=50$ for patients received Doxorubicin and Cyclophosphamide		EF; EORTC-QLQ-C30	- At $t-2$, the patients received Paclitaxel and Gemcitabine had a higher significant mean score for EF compared to those received the Doxorubicin and Cyclophosphamide	82%

(Continued)

Table 3. (Continued)

Author (year), Citation; Country	Study design, assessment timepoints comparison	Sample	Mean age, ±standard deviation, (range)	Variable of interest; Measuring instruments	Main fundings	QualSyst score
Hermelink, (2007)[70]; Germany	- Longitudinal study - At $t-1$ and $t-2$	$n=101$	48.6 ± 9.7	Depression; HADS-D Anxiety; HADS-A Self-reported cognitive complaints; FEDA EORTC-QLQ-C30	- At $t-1$, deteriorated cognitive test was not correlated significantly with anxiety and depression - At $t-2$, anxiety and depression were significantly associated with self-reported cognitive complaints	91%
Lacourt et al. (2023)[66]; USA	- Retrospective and longitudinal study	$n=252$	49.4, 11.83 (23–81)	Psychological distress; Distress Thermometer	- The level of distress peaked a month before treatment onset and fell steadily during NACT - The distress level of individuals receiving NACT was lower than that of individuals not receiving NACT	95%
Reinertsen et al. (2017)[46]; Norvège	- Prospective - $t-1$ - after FEC 100, - $t-2$: after taxanes before surgery	$n=84$	50.0 (25–68)	EF; EORTC-QLQ-C30	- At $t-1$, the mean score of EF was 52.22 (45.33–59.11) - After FEC 100 12 weeks) the mean score of EF was 54.93 (48.05–61.81) - At $t-2$, the mean score of EF was 54.93 (48.05–61.81) - EF improves significantly from the start of the study to the end of the FEC 100 (after 12 weeks) - The change in EF from baseline to end of NACT was not significant	95%
				Sleep duration; hours of sleep during the past 24 h	- Significant increase in sleep duration from the start of the study to the end of the FEC 100 (after 12 weeks) and from the start of the study to the end of the NACT sleep period	
Hu et al. (2022)[47]; China	- Prospective - Before et after NACT - PCG versus HCG	- $n=35$ in the PCG - $n=30$ in HCG	50:11 ± 9:19 in the PCG 50:77 ± 9:55 in the HCG	Depression; SDS Anxiety; SAS	- At $t-1$, the mean of depression in the PCG was 26.00 (25.00–31.00) - At $t-2$, the mean of depression in the PCG was 27.00 (25.00–31.00) - At $t-1$, the mean of anxiety in the PCG was 30.00 (26.00–32.00) - At $t-2$, the mean of anxiety in the PCG was 26.00 (25.00–27.50) - The difference between mean depression scores from baseline to end of the NACT was not significant - Anxiety decreased significantly between the start of the study and the end of the NACT - The difference in depression and anxiety scores between the PCG and the HCG at baseline was not significant	95%
Yang et al. (2023)[49]; China	-Prospective - $t-1$ after the first cycle of NACT.	$n=47$	51.50 ± 9.36 (30–70)	Depression; SDS Anxiety; SAS	- At $t-1$, the mean score of depression was 23.47 ± 4.89 - After the first cycle of NACT, the mean score of depression was 22.47 ± 3.22 - At $t-1$, the mean score of depression was 24.10 ± 4.59 - After the first cycle of NACT, the mean score of depression was 22.28 ± 3.05 - The difference in mean depression scores from baseline to after the first cycle of NACT was not significant - Anxiety decreased significantly from baseline to after NACT Cycle 1	95%

(Continued)

Table 3. (Continued)

Author (year), Citation; Country	Study design, assessment timepoints comparison	Sample	Mean age, ±standard deviation, (range)	Variable of interest; Measuring instruments	Main fundings	QualSyst score
Chen et al. (2017)[50]; Chine	- Prospective	- $n=34$ in HCG - $n=31$ in PCG	HCC = 46.29 (4.09) PCG = 47.10 (4.53)	Anxiety; HAMA Depression; HAMD	- At $t-1$, in the PCG, the mean score of anxiety was 5.19 (1.05) and at $t-2$, it was 4.23 (0.96) - At $t-2$, in the PCG, the mean score of depression was 4.94 (0.93) and at $t-2$, it was 4.52 (1.24) - In the PCG, the reduction in mean scores for anxiety before and after NACT was significant, whereas the difference between mean scores for depression before and after NACT was not significant	95%
Xiao et al. (2023)[51]; China	- Prospective	$n=121$	50.74 ± 10.77 years in the depressive group; 51.22 ± 9.10 years in the non-depressive group	Depression; SDS (cut-off ⩾53)	- At $t-1$, the prevalence of depression was 38.84% - At $t-2$, the number of patients with a BMI less than 18.5 in the depression group was higher than in the non-depressed group - Women with depressive status experienced a significant reduction in K+/ potassium levels after their treatment - At $t-2$, the total cholesterol and total protein scores of depressed patients were lower than those of patients without depression - At $t-1$; Fasting blood glucose levels have been shown to have lower levels in depressed patients, compared to those who did not suffer from depression	95%
Nie et al. (2022)[63]; China	- Prospective - At $t-1$ and $t-2$	$n=70$	38.78 ± 2.64 (27–56)	Dépression; Score de HADS-D et de PHQ-9 Psychological symptoms; MDASI	- At $t-2$, the prevalence of depression was 78.5%; and the sadness was 90.4% - At $t-2$, sadness (4.15 ± 2.08) and worry (3.87 ± 1.66) were the highest symptom scores - At $t-2$, adverse symptoms such as sadness, worry, and "vertigo and nausea" had a statistically significant in the development of depression - At $t-2$, when the level of pain augmented by one point, the risk of having depressive mood was augmented by 1.123 times	95%

CD-RISC, Connor–Davidson Resilience Scale; FACT-B, Functional Assessment of Cancer Therapy-Breast; PR, prevalence; M, mean; EF, emotional functioning; $t-1$, at baseline; $t-2$, at end of NACT; NACT, neoadjuvant chemotherapy; HADS, Hospital Anxiety and Depression Scale; HADS-D, HADS-depression; HADS-A, HADS-anxiety; POMS-D, Profile of Mood State-Depression; NR, not reported; BSI, Brief Symptom Inventory; BC, breast cancer; UC, uterine cervix cancer; LET, Letrozole; BDI, Beck Depression Inventory; HAMD, Hamilton Depression Rating Scale; HAMA, Hamilton Anxiety Rating Scale; HER2, human epidermal growth factor receptor 2; ESAS-A, Edmonton Symptom Assessment Scale-Anxiety; CPC, Canadian Problem Checklist; PSSCAN-R, Psychosocial Screen for Cancer; HCG, healthy control group; PG, patient group; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; SDS, self-rating depression scale; SAS, self-rating anxiety scale; DT, Distress Thermometer; DA, decision aid; PSS, perceived social support; CRS, chemotherapy-related symptoms; PCG, patient cancer group; MDASI, M.D. Anderson Symptom Inventory; PSQI, Pittsburgh Sleep Quality Index; RSES, Rosenberg Self-Esteem scale; FEC 100, 5Fluorouracile-Epirubicine-Cyclophosphamide.

Table 4. Characteristics of included interventional studies.

Citation, author, year, and country	Study design, assessment timepoints Comparison	Sample	Mean age, ±standard deviation, (range)	Variable of interest; Measuring instruments	Main fundings	QualSyst score
Zdenkowski et al. (2019)[55]; Australia	- RCT - Decision Aid Program - NACT group versus Adjuvant group	*n* = 59 -NACT group (*n* = 51) -Adjuvant group (*n* = 7)	NR	Anxiety; STAI	- At *t* − 1, the mean score of anxiety was 54.7 in the NACT group, it was 65.7 in the adjuvant group - A higher mean score of anxiety at *t* − 1 in the adjuvant group compared with NACT group - Anxiety decreased at each follow-up in a comparable way for patients who had surgery first compared with NACT, but were not significant	91%
				Distress; Distress Thermometer	- Mean scores pf distress was not different between the adjuvant group and the neoadjuvant group ($p = 0.56$)	
Zdenkowski et al. (2018)[56]; Australia	- RCT - Decision Aid program *t* − 1: baseline *t* − 1′: after decision was made about undergoing NACT or surgery first *t* − 2 : end of NACT	*n* = 59	52 (8.9)	Anxiety; Spielberger STAI Distress; Distress Thermometer Fear; FoP-Q-SF Fear; FCRI-SF	- At *t* − 1, the mean score of anxiety before decision aid program was 55.4/100, and just after it, the mean was 49.4/100 - At *t* − 2, the mean score was 40.1/100 - At *t* − 1, the mean score of distress before decision aid program was 5.9 (2.9), and just after it, the mean was 5.0 (2.5) - At *t* − 2, the mean score of distress was 3.2 (2.5) - At *t* − 1, the mean score of fear was 33.4 (7.2), whereas at *t* − 2, it was 29.9 (7.2) - At *t* − 1, after Decision Aid program, low level of Fear in 76.5%, moderate level in 19.6% and severe level if fear in 3.6% - At *t* − 2, Low level of fear in 88.2%, and Moderate level in 11.8% - The Decision Aid program was found to be feasible and acceptable - In post-Decision Aid program, anxiety, distress and fear of progression decreased significantly	91%
Walker et al. (1999)[38]; UK	- RCT - Relaxation training- guided imaging.	*n* = 96	50 (30–73)	Depression; HADS-D (cut-off ⩾8) Anxiety; HADS-A (cut-off ⩾8)	- The higher score of depression indicates poor pathological response to NACT - The higher score of anxiety shows worse clinical response of NACT	71%
Walker et al. (1999)[43]; UK	- RCT - Relaxation training-guided imaging Six cycles of NACT CG versus IG	*n* = 96 - *n* = 48 for each group Intervention group and Control group.	- Control group = 50.1 (11.3) - Interventional group = 49.3 (10.8).	Depression; HADS-D (cut-off ⩾8) Anxiety; HADS-A (cut-off ⩾8)	- At *t* − 1, the prevalence of depression was 3.1% - At *t* − 2, the prevalence of anxiety was 37.5% - Control group and Interventional Group didn't diverge at *t* − 1 (anxiety ($p = 0.32$): depression ($p = 0.56$)) or at *t* − 2 (anxiety ($p = 0.85$), depression ($p = 0.75$)) - Depression augmented until sequence 5 and then decreased ($F = 4.89$, $p = 0.001$), whereas anxiety decreased in both groups prior to the second cycle of NACT and endured at a low level ($F = 2.66$, $p = 0.03$)	71%
				Coping, CECS	- "Emotional suppression" and the CECS unhappiness subscale was diminished after intervention - Women who practiced daily or more had lower levels for CECS unhappiness and CECS total than control patients	

(Continued)

Table 4. (Continued)

Citation, author, year, and country	Study design, assessment timepoints Comparison	Sample	Mean age, ±standard deviation, (range)	Variable of interest; Measuring instruments	Main fundings	QualSyst score
Fjell et al. (2020)[59]; Sweden	- RCT - Intervention using mobile health application to manage symptoms	*n* = 149 - *n* = 74 for Interventional group - *n* = 75 for Control group	- Interventional group = 48 (10.6) - Control group = 50 (11.6)	EF, EORTC-QLQ-C30 Psychological symptoms; MSAS	- At *t* − 2, the IG rated statistically significant ($p = 0.008$) higher EF than CG - At *t* − 1, the Interventional group rated higher prevalence of difficulty sleeping - At *t* − 2, the Interventional group reported higher prevalence of feeling sad compared to Control group	75%
Basen-Engquist et al. (2020)[60]; USA	- RCT - Intervention to prevent wight gain.	*n* = 37 - *n* = 19 for Interventional group - *n* = 18 for Control group).	- Interventional group = 49.6 (13.3) - Control group = 49.2 (9.2)	Role emotional and mental health; MOS SF-36	- Interventions to prevent weight gain did not result in changes in Role Emotional and Mental Health	86%
De Groot et al. (2020)[61]; Netherlands	- RCT - FMD or RD 3 days before and the day of NACT	*n* = 131	- FMD = 49.0 (31–71) - Regular diet = 51.0 (27–71)	Psychological distress; Distress Thermometer	- Patients receiving the FMD program developed a 90%–100% response to NACT, but psychological distress levels did not significantly decrease	89%
Lugtenberg et al. (2021)[62]; Netherland	RCT, FMD or RD 3 days before and the day of NACT	*n* = 131	- FMD = 49.0 (31–71) - RD = 51.0 (27–71)	EF; EORTC-QLQ-C30	- Significant improvement in EF in both arms (patient with RD and who adheres to FMD) during NACT - Patients receiving the FMD have better scores than those with RD during NACT	89%
Fasching et al. (2023)[44]; Germany	- Prospective, multicenter, single-arm Phase II trial	*n* = 50	52.2 (11.5)	EF; EORTC-QLQ-C30	- At *t* − 1, the mean score of motional functioning was 64.1 (23.2) - At *t* − 2, the mean score of motional functioning was 64.1 (23.2) - The lowest EF score was marked at baseline, 60.4 (20.8), then improved in the middle of NACT to 69.1 (19.6) and decreased slightly to 64.1 (23.2) recorded just before surgery; however, the author did not present the statistical significance of the variation in these EF values	86%
Barakat et al. (2022)[64]; Egypt	- RCT - Metformin group arm - Control group arm	*n* = 80 - Metformin group, *n* = 36 - Control group, *n* = 38	- Metformin group, 49.14 ± 11.22 - Control group, 47.13 ± 10.53	EF; EORTC-QLQ-C30	- Improvement in EF in both arms was not significant	93%
de Moor et al. (2008)[48]; USA	- RCT - Expressive writing groups versus normal writing group		- *n* Expressive writing = 56.89/10.79 - *n* Normal writing = 50.31/10.08	-Distress; BSI -Quality of sleep; PSQI -Coping; The EACS	- The Expressive Writing and Normal Writing groups did not differ in terms of overall distress, perceived stress, sleep disturbances, or pain after the intervention	75%

EACS, Emotional Approach Coping Scale; EF, emotional functioning; NACT, neoadjuvant chemotherapy; RCT, randomized controlled trial; STAI, State-Trait Anxiety Inventory; FCRI-SF, Fear of Cancer Recurrence Inventory—Short Form; FoP-Q-SF, Fear of Cancer Progression Questionnaire—Short Form; HADS, Hospital Anxiety and Depression Scale; HADS-D, HADS-Depression; HADS-A, HADS-Anxiety; CECS, Courtauld Emotional Control Scale; MSAS, Memorial Symptom Assessment Scale; FEC 100, 5Fluorouracile-Epirubicine-Cyclophosphamide; MOS SF-36, Medical Outcomes Study Short Form-36; FMD, fasting mimicking diet; RD, regular diet; EORTC-QLQ-C30, Cognitive Function Scale of the European Organization for Research and Treatment of Cancer (EORTC) Quality-of-life Questionnaire C30; NR, not reported; BSI, Brief Symptom Inventory; PSQI, Pittsburgh Sleep Quality Index.

Table 5. Characteristics of included qualitative studies.

Citation, Autor, year and country	Study design, Assessment timepoints Comparison	Sample	Mean of age, ±SD (range)	Themes	Main results	Quality assessment
Beaver et al. (2016)[67]; UK	Interviews audio-recorded	*n* = 20	48 (30–67)	Coping with the rapid transition from "well" to "ill"	- Undergoing NACT can be a challenging and traumatic experience for women - It involves coping with the knowledge that cancer remains in the body and experiencing immediate and often severe side effects - The transition from being fit and healthy to being "ill" while still managing work and family responsibilities can make the experience particularly difficult	85%
				Information needs and decision making	- Patients would have difficulty retaining information received at the time of diagnosis - The full information was not desired by all participants because they viewed it as potentially frightening - Women searched for information on the net, but it was generally seen as terrifying and anxious. However, online blogs and forums can be comforting for some participants	
				Needing empathy and support	- Participants stated a need for empathy and support with the physical and psychological effect of diagnosis and therapy - Few women said they had benefited from psychological support - Participants preferred to receive support from other patients who had undergone neoadjuvant chemotherapy	
				Impact on family	- It was important to participants that their families were protected from emotional pain, bad news, and perceived frightening information - There was no assistance provided to participants in learning the best behavior and communication strategies for playing their family role	
				Creating a new "normal"	- Despite the long term emotional and physical symptoms, participants wanted to return to their "normal" lives while returning to work and assuming their family role	
Herrmann et al. (2018)[69]; Australia	Interviews audio-recorded	*n* = 24	51 ± 7.3	Patients' perceptions of being provided with a treatment choice	- It was perceived by some women that they had no other treatment options - They stated that their doctors strongly influenced their decision, stating that this is the "best" treatment - Some women struggled to accept the nature of the NACT decision - Women viewed the decision-making process as a burden	85%
				Taking decisions in an emergency situation	- The need for important action to avoid a deteriorating of their cancer led many women to feel that a quick decision on NACT was necessary - A number of women reported that they appreciated their doctor's suggestions regarding a therapy plan and her offer to adjust the protocol of treatment at any moment	
				Decision-making strategies	- Reducing deciding factors: The majority of women consider a key reason for admitting NACT, such as breast conserving therapy, a NACT that would affect the whole body. moreover, personal circumstances or on what they considered psychological acceptable are also involved in their decision of the NACT - "Claiming" the decision: most of women did not take an active role in choosing NACT, as demonstrated by the use of the passive voice when describing the decision-making process - Using additional information: NACT decisions were confirmed by using additional information, such as the Decision Aid program. Additional information helped some women understand their treatment choices and complete their doctors' explanations	

(Continued)

Table 5. (Continued)

Citation, Autor, year and country	Study design, Assessment timepoints Comparison	Sample	Mean of age, ±SD (range)	Themes	Main results	Quality assessment
Fjell et al. (2022)[65]; Sweden	- Semi structured interview guide	*n* = 40 - *n* Interventional group = 21 - *n* Control group = 19	Interventional group: 51.7 (12.5; 30–73) Control group: 54.2 (13.5; 35–77)	The health care context (Interventional group and Control Group reported both positive and negative experiences)	- Patients who experienced access to nurses found it satisfactory and beneficial. But, those with accessibility issues frustrated by their inability to find answers - Lack of continuity in care, confusion, and a lack of security were reported as a result of meeting too many nurses and physicians in each appointment	80%
				Being a recipient of care (Interventional group and Control group reported both positive and negative experiences)	- Oncology clinics had a warm atmosphere and the nurse had a caring and reassuring relationship with patients. However, some patients reported a cold relational situation with the nurses and were unable to express their needs - Patient satisfaction with written and verbal information was generally high. In some cases, patients felt that information regarding the reasons for NACT was withhold	
				Taking an active role as a patient (Interventional group and Control group reported both positive and negative experiences)	- Some patients expressed their need to obtain more information using other resources - Patients declare their satisfaction and acceptation with the care provided to them - The possibility of discussing topics related to their care was important for their sense of involvement - Having a treatment plan simplified their daily organization	
				The value of the application (This section concerns the Interventional group)	- The patients described using a mobile health application as an easy and accessible source of information especially how to manage their symptoms - In the event of severe symptoms or concerns, patients were able to reach the contact nurse directly using the mobile health application - The app allowed patients to report symptoms to their nurse about their health condition. The patients felt seen and listened to, as they felt they were being monitored positively	
Saita et al. (2023)[45]; Italy	Audio-recording of the interview Participants' coping styles as measured by the Mini-Mental Adjustment to Cancer	*n* = 14	77.21 ± 12.14; (54–91)	Relationship	- It may be difficult for the participants to access treatments, prioritize their personal health, and position themselves as care receivers due to the roles assumed within the family members - Women fear they are no longer able to be a resource for their families, or that they will be burdened with caregiving - Family relationships can motivate patient to pursue treatment after diagnosis - "Relationships" cluster was associated significantly to high rates of Fighting Spirit	85%
				Ineluctability	- Cancer diagnosis and intensive treatment led to a sense of fear and panic, and hope for the future served as a coping mechanism	
				Disease	- Upon confirmation of the diagnosis of LABC, the women experienced high levels of distress and anxiety, which impaired their ability to cope with the disease	
				Surgery	- Decision surgery was considered being a necessary step, adding to concerns about prognosis, attractiveness, and body image - Surgery was associated significantly to "anxious preoccupation" as coping strategy	
				Diagnosis	- It is impossible for patients to understand when they encounter the first symptoms and they do not even attempt to perform a self-exam or engage in any form of care	

Several designs were considered for the articles included in this systematic review. Hence, there were 20 prospective studies,[29–33,35,36,39,40–42,46,47,49-51,57,58,63,68] 5 cross-sectional studies,[34,37,52–54] 11 randomized controlled trial (RCT) studies,[38,43,44,48,55,56,59–62,64] a retrospective and longitudinal study,[66] and 4 qualitative studies.[65,45,67,69]

Notably, China was the country with the maximum number (six) of publications,[34,47,49,50,51,63] followed by Korea with five publications.[32,36,40–42]

Study quality assessment

The quality assessment scores for the studies included in the quantitative synthesis ranged from 64% to 95%. For quantitative studies, two cross sectional studies[52,53] and two longitudinal studies[30,31] had a rate of less than 80%, whereas other studies with the same design had a rate of more than 80%. For the randomized trials, a total of 12 articles had a rate of 71%–93%, and only 3 articles[61,62,64] reported blinding of patients (Tables 3–5).

Quality assessment scores for the qualitative studies ranged from 80% to 85%. All the studies had clearly defined objectives with an appropriate design involving the use of clear and systematic methods. Nevertheless, qualitative studies had some limitations related to sampling and procedures for establishing the credibility of data, such as triangulation or member checking.

Sample characteristics

LABC filled most of the articles,[29–32,34,36–43,45,47,49,51–53,55–60,63–69] but some particular types were included, such as non-metastatic HER2-negative BC in[46,54,61,62] and triple negative breast cancer (TNBC).[44] Additionally, postmenopausal BC patients with HR-positivity and their clinical stage, including T1c-T2, N0, and M0, were included in the study by Taira et al.[33] in patients with LABC, whereas LeVasseur et al.[35] included patients at stage I and stage IIa.

Commonly used NACT protocols were based on a combination of anthracycline and taxane[29,32,36,40,51,54] or, alternatively, Cyclophosphamide, Adriamycin, and Fluorouracil regimens.[30,31] Additionally, one study[41] focused exclusively on the AC regimen, whereas another study[42] was based on two protocols: doxorubicin/cyclophosphamide (AC) or docetaxel/doxorubicin (TA). Furthermore, in the study by LeVasseur et al.,[35] some patients received NACT, whereas others received neoadjuvant endocrine therapy, without specifying their protocols. However, one study[33] was limited to neoadjuvant endocrine therapy based on letrozole. Regarding the comparison of subgroups, Chellappan et al.[53] presented protocols based on paclitaxel and doxorubicin administered every 3 days or every week. Barakat et al.[64] investigated the safety and tolerability of adding Metformin to NACT, and a study conducted by Rezapour et al.[57] assessed QoL in BC patients receiving AC-based therapy compared with those receiving Paclitaxel and Gemcitabine based regimens. Furthermore, some articles[34,47,49,59,61,62,63] described the utilization of various therapy regimens, whereas other studies[37,39,52,55,56,66,67] failed to specify the administered protocol.

Quantitative studies

In this section, we present the results related to PD and its different forms, namely, depression, anxiety, emotional, and/or psychological domains of QoL, and psychological symptoms. We then present the results related to coping strategies.

PD forms

Psychological distress. Six studies introduced PD through psychometric scales such as the Distress Thermometer,[55,56,61,66] total Hospital Anxiety and Depression Scale (HADS) score,[33] and Brief Symptom Inventory.[29,48] In terms of the prevalence of PD, one study[33] showed that it was significantly reduced after the initiation of NET, with a rate of 42% at baseline and 31% after NET, whereas two studies showed changes in PD. Indeed, a recent retrospective and longitudinal study[66] found that the level of distress peaked a month before treatment onset and fell steadily during NACT, and that the distress level of individuals receiving NACT was lower than that of individuals who received other treatment.[66] In the second study,[29] results showed that patients had significantly elevated levels of PD at baseline compared to the end of NACT.

Depression. Six instruments were featured in the included studies to measure depression. Fourteen studies employed the HADS,[29,30,32,33,36–39,40–43,58,63] three utilized[34,47,51] the Self-Rating Depression Scale, two used[31,54] the Beck Depression Inventory, and two[50,53] involved the Hamilton Depression Rating Scale (HAMD). Additionally, one study used the Profile of Mood State-Depression and another[63] applied the Patient Health Questionnaire-9.

Ten studies[30–32,36–38,40–42,51], evaluated the prevalence of depression at baseline, ranging from 0% to 46%. After NACT, four studies[30,31,40,63] reported the prevalence of depression, with estimates ranging from 40% to 78.5%. Regarding the change in depression during NACT, only one study[29] reported that depression scores decreased significantly.

Regarding depression correlates, patients living in joint families[30] and those with children[54] tended to experience lower rates of depression. By contrast, patients with low perceived social support (PSS) expressed a high level of depression.[32] Moreover, increased depression levels have been linked to delays in diagnosis and initiation of neoadjuvant treatment.[54]

Clinically, women who report higher levels of depression also demonstrate greater cognitive difficulties.[37]

However, in a study conducted by Hermelink et al.,[58] there was no significant correlation between cognitive test results and depression before NACT, whereas at the end of NACT, depression was associated with self-reported cognitive complaints.[58] Furthermore, certain side effects such as sadness, worry, nausea, and vertigo had a significant impact on the development of depression.[63] Additionally, an increase in the pain symptoms by one point resulted in a 1.123 times higher risk of depressive mood.[63] It should also be noted that patients with depression at baseline, compared to non-depressed patients, had a significantly high nutritional risk[51] and low BMI and potassium, total cholesterol, sodium, total protein, and fasting glucose levels during NACT.[51]

Anxiety. Seven instruments were used to measure anxiety in the 19 included articles. HADS was used in 11 articles.[29,32,33,36,38,39,40–43,70] The self-rating anxiety scale was used in three articles.[34,47,48] Two studies used the Spielberger State-Trait Anxiety Inventory,[55,56] and the Beck Anxiety Inventory was used in only one study.[54] LeVasseur et al.[35] identified patients with anxiety using three instruments: the Edmonton Symptom Assessment Scale-Anxiety, the Canadian Problem Checklist, and the Psychosocial Screen for Cancer Revised.

At baseline, anxiety ranged from 5.5% to 54%.[32,35–38,41–42] However, after NACT and before surgery, only one prospective study[40] revealed an anxiety rate of 27%. When comparing anxiety means, four studies found that anxiety significantly decreased between the beginning and end of NACT[29,47,49,50] and declined during neoadjuvant letrozole (LET) (NET).[33]

Regarding sociodemographic correlates of anxiety, there was no significant association,[54] whereas the study of Kemer et al.[54] found that increased anxiety levels were associated with delays in diagnosis or the beginning of neoadjuvant treatment.

Clinically, anxiety remained significantly related to persistent chemotherapy-induced peripheral neuropathy[36] and the late chronotype[41] during NACT. Women who experienced a high level of anxiety also reported more difficulties with cognitive function. In contrast, one study[40] found that anxiety was moderately correlated with QoL during NACT.

PD as a domain of QoL. The study of PD can also be extracted from the dimensions encompassing the QoL scales used in patients with BC. Our results found the use of domains of the following QoL scales: EWB of the Functional Assessment of Cancer Therapy-Breast (FACT-B),[33,52,54] EF of the European Organization for Research and Treatment of Cancer-Quality-of-life Questionnaire-C30 (EORTC-QLQ-C30),[57,59,62,64] and mental health and role emotional (MH and RE) of the Medical Outcomes Study Short Form-36 (MOS SF-36).[60] Below, we present the correlations between these psychological dimensions. Thus, the EWB can improve or deteriorate depending on the nature of the NAT. Thus, EWB showed a significant improvement from baseline and during treatment based on NET,[33] whereas, in another study,[53] patients receiving weekly NACT had significantly better EWB than those receiving NACT every 3 weeks. Moreover, women who received social support from family or friends reported an improvement in EWB.[54] Regarding the coronavirus pandemic, patients who underwent NACT and acquired COVID-19 infection had a lower EWB ($p = 0.03$). In terms of the EF sub-scale of EORTC-QLQ-C30, the patients who received Paclitaxel and Gemcitabine at the end of NACT had a significantly higher mean EF than those who received Doxorubicin and Cyclophosphamide.[57]

Psychological symptoms. The results in this section are based on multi-symptom patient-reported outcome questionnaires that involve psychological symptoms. The M.D. Anderson Symptom Inventory (MDASI) was used in two studies,[32,63] whereas Fjell et al.[59] employed the Memorial Symptom Assessment Scale (MSAS) and Endocrine Symptom subscales added to the FACT-B.[33] Quality of sleep was also assessed with the Pittsburgh Sleep Quality Index (PSQI).

In a prospective study[32] using the MDASI, certain psychological symptoms, such as sadness, distress, memory loss, and insomnia, showed a significant decrease during NAT. Moreover, patients who experienced moderate-to-high levels of PSS presented significantly lower scores for distress, insomnia, and memory loss during NACT,[32] whereas another study[63] found that after NACT, 90.4% of patients suffered from sadness. Further, PSS from the friends group stated a significant decrease in distress, insomnia, sadness, and memory loss; and PSS from the significant others group reported a decrease in sadness and insomnia.[63] Taira et al.[33] presented the prevalence of psychological symptoms at baseline. It was noted that 42% of the patients had problems with interest in sex, 5.7% had irritability, and 5.5% presented with mood swings.

Sleep quality was assessed using the PSQI before NACT in three Korean studies.[36,41,42] In fact, two studies found that 16.2%[36] and 16.4%[42] of the patients experienced poor sleep quality. Furthermore, 18.2% of patients had poor sleep quality in the third study.[41] In another study,[46] a significant increase in sleep duration was reported from baseline to the end of FEC 100 and from baseline to the end of all sessions of NACT.

Coping strategies. This section outlines the various scales used to assess coping strategies. We discuss the key findings of each study in relation to the coping strategies.

Our results showed that five articles[29,38,40,52,68] involved coping strategies during the NACT. The instruments used in these studies included the Ulm Coping Manual,[29]

Connor–Davidson Resilience Scale,[40] Courtauld Emotional Control Scale (CECS) in Walker's RCT study,[38] the subscale "satisfaction with treatment and coping with disease management" in the QOL-Questionnaire for Cancer Patients Treated with Anti-Cancer Drugs-the Breast (QOL-ACD-B),[68] and the Rosenberg Self Esteem Scale.[52]

Regarding the key findings of coping strategies, a longitudinal study by Tschuschke et al.[29] reported that before NACT, "fighting spirit coping" as an effective strategy was positively correlated with "social support coping," and higher levels of "cognitive restructuring" were associated with lower psychological stress. During NACT, "resigned coping" decreased, whereas "social support coping" increased significantly. After the NACT, "active coping strategies" ("complying" with treatment," "cognitive restructuring, "social support coping," and "fighting spirit") were correlated with better psychological adaptation, whereas "resigned coping" was associated with poorer psychological adjustment.[29] Overall, a higher score of "fighting spirit" was associated with better adaptation to treatment.[29]

Resilience as an adaptive strategy, was mentioned in the study by Lee et al.,[40] which found that before NACT, resilience was negatively correlated with depression and anxiety at each time point during NACT. In a study by Aprilianto et al.,[52] self-esteem, an essential resource for coping with and adapting to cancer, reached a high level in 28.6% of patients, a moderate level in 48.2%, and a low level in 23.2% during NACT. Moreover, patients with a higher level of self-esteem reported better social support from their families. As a domain of the QOL-ACD-B scale, "satisfaction with treatment and coping with disease" did not change significantly between the two groups, those with high or low QoL, either before or after NACT.[68]

Interventional studies. De Groot et al.[61] showed that patients receiving the fasting mimicking diet (FMD) program developed a 90%–100% response to the NACT, but PD levels did not significantly decrease under this intervention. In the study of Lugtenberg et al.[62] that included HER2-negative BC patients receiving NACT showed that those receiving the FMD had better scores of EF than those with a regular diet during NACT. In another RCT based on a decision aid program,[55] the authors showed that the mean baseline PD scores in patients undergoing NACT were not different from those in patients undergoing adjuvant chemotherapy. However, the same authors in another article[56] showed that PD, anxiety, and fear gradually decreased significantly after the dispensation of the Decision Aid program in patients undergoing NACT. In the RCT study by Walker et al.[38] based on a relaxation training and guided imaging program, depression in patients under the NACT increased significantly until cycle 5 and then declined until the end of NACT. The intervention decreased emotional suppression as a coping strategy, as measured by the CECS. Furthermore, women who practiced daily or more had lower levels of CECS unhappiness and the total score of CECS than control women. for CECS unhappiness and total score of CECS.[38] It should be remembered that the CECS is a questionnaire segregated into three subscales for the suppression or expression of anger, anxiety, and unhappiness mood.

One study found that an intervention group using a mobile health app experienced lower EF than the control group after completing the NACT.[59] Additionally, the intervention group had a lower prevalence of feeling sad and a better score on the MSAS-Psych subscale than the control group.[59] However, Barakat et al. found that the addition of Metformin to NACT did not improve EF scores from baseline to the last cycle of the NACT.[64]

In summary, we can infer those programs such as the fasting-mimicking diet, the decision aid program, relaxation training and guided imagery, or the mobile health app can have a positive effect on the indicators of PD in patients with BC undergoing NACT.

Qualitative studies

The synthesis of the four qualitative articles included in this systematic review allowed us to design three themes related to patients' experiences during NACT: (a) patient challenges and needs during the NACT; (b) information and decision-making regarding the NACT; and (c) interventions and strategies reassuring patients during the NACT.

PD during NACT. During diagnosis, it was difficult for patients to assimilate what happened when the first symptoms of BC were discovered, and they did not attempt to perform a self-examination or engage in any form of care.[45] They experienced a high level of distress and anxiety,[45] and had a sense of fear and panic.[45] Receiving the NACT regimen was expected to be a challenging and traumatic experience.[67] It was difficult for them to know that cancer remained in the body during NACT and that severe side effects may occur.[67] Thus, they transitioned from fit and healthy to ill.[67] Additionally, the patients expressed concerns about their families. In particular, they worried about their children and husbands' reactions to the worrisome information they received about the disease.[67] Regarding care, patients noted that the lack of continuity in care was reported as a result of meeting too many nurses and physicians in each appointment,[65] and that accessibility issues were caused by lack of time, and nurses were frustrated. The findings also indicated that few women said that they had benefited from psychological support,[67] and others preferred to receive support from patients who had undergone the NACT.[67] Furthermore, surgical decision-making raised prognostic concerns among participants who mobilized anxious preoccupation as a coping strategy.[45]

Information and decision-making about NACT. Receiving information can be considered a source of frustration and anxiety.[67] Indeed, patients would have difficulty retaining the information received at the time of diagnosis, and receiving all the information was perceived as stressful.[67] They also reported experiencing anxiety when searching for information on the Internet.[67] Patients participating in the study of Fjell et al.[65] reported insufficient information in certain areas of care, whether others felt there was too much information. In some cases, the patients felt that information regarding the reasons for NACT was withheld.[65] Therefore, they expressed the need to obtain more information using other resources.[65] Women viewed the decision-making process as a burden rather than an opportunity.[69] They struggled to accept the preferential nature of NACT, particularly because the survival benefits were comparable to those of the initial surgery.[69] Additionally, some women perceived that they had no other treatment options[69] and that their doctors influenced their decisions, stating that it was the best option.[69] Thus, they did not play an active role in choosing NACT.[69]

Among the reasons involved in decision-making was the need for urgent action to avoid deterioration in their health condition, which led women to feel that a quick decision was necessary.[69] For most women, decision-making occurred either during or shortly after their first oncology consultation.[69] They considered key reasons for admitting NACT, such as breast-conserving therapy rather than mastectomy, personal circumstances, or what they considered psychological acceptable.[69]

Interventions and coping strategies reassuring patients during NACT. Patients considered family relationships as a motivating factor to pursue treatment after diagnosis, and it was associated with high rates of fighting spirit.[45] Regarding informational coping, patients sought to use additional information about NACT decisions by receiving written information or a decision-aid program,[69] which helped them understand their doctors.[69] Furthermore, the patients expressed their satisfaction with written and verbal information[65] and viewed that online forums could be reassuring.[67]

Regarding NACT and care, several women reported that they appreciated their doctor's suggestions regarding a treatment plan and their offer to adjust the treatment protocol at any moment.[69] Patients also reported that discussing topics related to the NACT was important for their sense of involvement[65] and that receiving the treatment plan simplified their daily organization.[65] Furthermore,[65] access to nurses was viewed as a beneficial and warm atmosphere in oncology clinics that allowed patients to have reassuring relationships.

For using health mobile applications in the study by Fjell et al.,[65] the patients described them as an easy and accessible source of information, especially on how to manage their symptoms.[65] They confirmed that in the event of severe concern, they were able to reach the contact nurse directly.[65] This application allowed patients to report their health conditions to nurses. Patients felt seen, listened to, and monitored positively.[65] The main elements of the results section are illustrated in Figure 2.

Discussion

This systematic review analyzed 41 articles about PD and coping strategies in patients with BC during the receipt of NAT to examine their prevalence and changes, the different associated determinants, and different interventions reducing the level of PD.

Through our review, we identified 13 forms of PD: depression, anxiety, emotional domains related to QoL, stress, fear, sleep disturbances, self-esteem, problems with interest in sex, irritability, mood swings, insomnia, memory loss, and sadness. The included articles reported multiple coping strategies such as fighting spirit, social support, cognitive restructuring, compliance with treatment, resilience, emotional suppression, CECS unhappiness, satisfaction with treatment, coping with disease, and informational coping.

Prevalence and change of PD

Before the start of the NACT, only one study[29] estimated PD using the DT scale, with a prevalence of 42%, whereas the results showed that the prevalence of depression ranged from 0% to 46% and anxiety ranged from 5.5% to 54%. Regarding other psychological symptoms in patients receiving NET,[33] 42% of patients had problems with interest in sex, 5.7% had irritability, and 5.5% presented mood swings. An analysis of the qualitative studies included in this review concluded that during the diagnosis phase, distress, anxiety, fear, and panic were the main disturbances reported by patients.[45]

We considered these prevalence (PR) rates to be heterogeneous and difficult to compare with the results of similar studies. However, the use of different measurement scales, especially to assess depression and anxiety, as well as the sensitivity of the answers to the questionnaires, contributed to producing different PR rates, while we cannot underestimate the psychological shock of diagnosis and treatment for patients.[11]

Conversely our findings before and after NAT showed that depression rates ranged from 40% to 78.5%, although only one prospective study reported an anxiety rate of 27% after NACT.[58] In addition, one study[63] found that 90.4% of patients experienced sadness. The articles that presented the PR of different forms of PD after NAT and before surgery were relatively limited. This could have led to an underestimation of the magnitude of PD during this phase. Indeed, this period is marked by the management of adverse effects of NACT as well as preparation

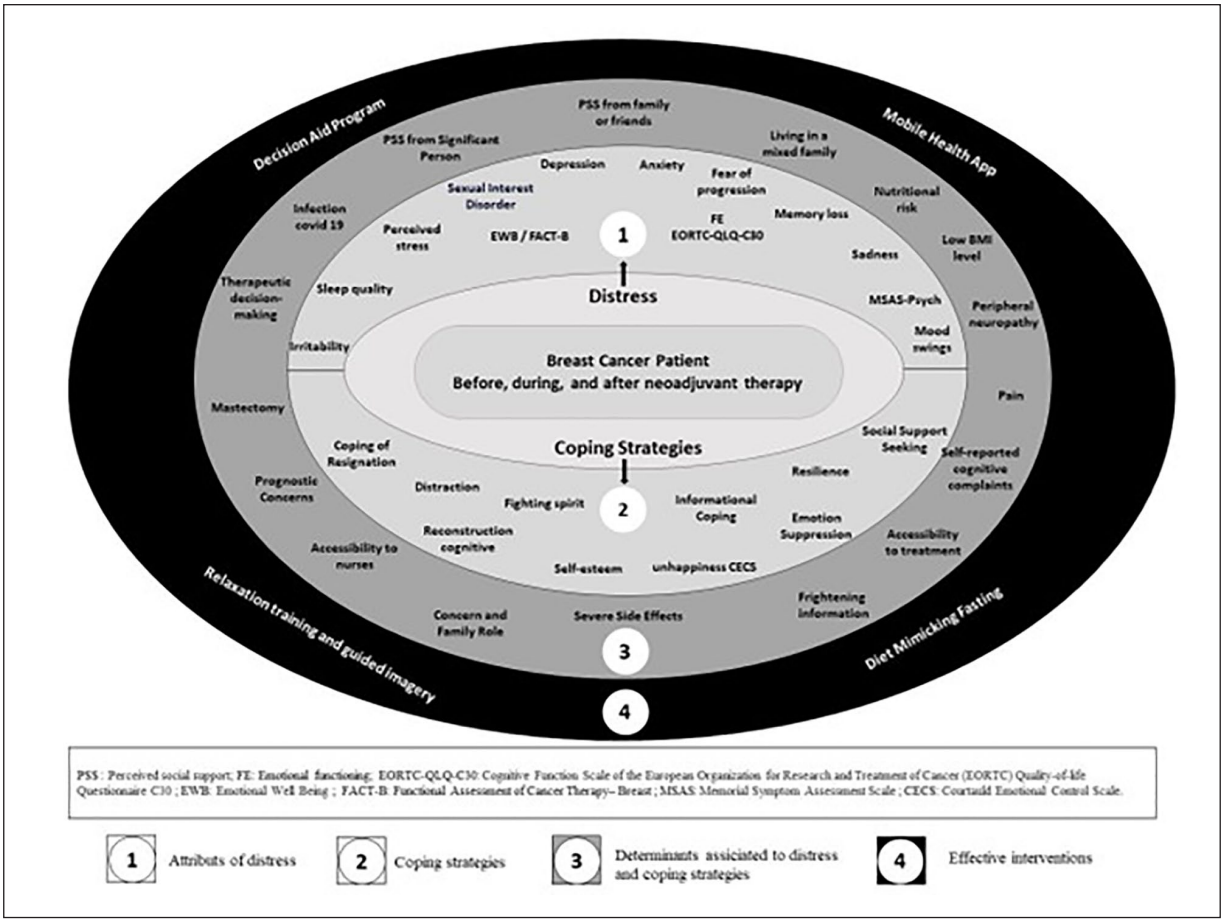

Figure 2. Conceptual map of psychological distress and coping strategies attributes, determinants, and effective intervention approaches.

for surgery. However, the included articles did not cover the PR of PD for each NACT cycle. Consequently, it is difficult to follow its evolution correctly. However, some of these articles examined variations in the mean scores of psychological variables, comparing them before and after receiving NACT, and only one article explored these changes in each NACT cycle.[66] Two studies measured it at mid-treatment and at the end.[33,46]

Our results showed that at the start of NACT, the levels of PD, depression, anxiety, sadness, insomnia, and memory loss were high but gradually decreased until the end of treatment; hence, the level of EWB showed improvement. In comparison with the findings of a recent prospective study related to adjuvant chemotherapy in early-stage BC, the percentage of patients presenting with anxiety decreased from the beginning to the end of complete treatment. Similarly, the mean anxiety scale scores reduced and EWB improved during this journey.[71]

Despite this variability, the findings highlighted a problem that must be considered.[72] It is essential to assess PD in patients with cancer as soon as the diagnosis is announced, until the start of chemotherapy, at each NAT cycle, and in the period from the end of NAT to the time of surgery. Therefore, providing adequate attention and appropriate interventions for these psychological problems during these periods is crucial.[72,73]

Determinants associated with distress

The results of this systematic review highlighted the various determinants of PD. Thus, high PSS was correlated with lower levels of insomnia, distress, and memory loss during NAT[32] and when PSS arose from family and friends, EWB (FACT-B)[54] and self-esteem[52] improved. Additionally, lower levels of depression were associated with patients who had sons and daughters,[54] lived in joint families,[30] and had low PSS.[32] Moreover, insomnia and sadness decreased when the level of "PSS stems from the significant person" was high.[32]

Regarding clinical determinants, adverse symptoms of NACT such as worry, sadness, vertigo, nausea, and pain had an impact on developing depression.[63] Patients with higher levels of depression or anxiety reported experiencing more cognitive difficulties before NACT and self-reported more cognitive complaints after NACT.[37,58] Compared to non-depressed patients, patients with depression at baseline had

a significantly higher nutritional risk and lower BMI, potassium, total cholesterol, sodium, total protein, and fasting glucose levels during NACT.[51] This review led us to propose further research exploring psychological clusters in patients with LABC from diagnosis to the time of surgery. In addition, Kemer et al.[54] found that delays in the diagnosis or commencement of NAT were related to higher levels of depression and anxiety. In this context, researchers have concluded that any delay of more than 3 months between the first medical consultation, and the start of cancer treatment is associated with a more advanced stage of the disease and reduced survival.[74–78] We suggest strengthening "patient navigation" programs for patients with BC, to overcome the obstacles that mainly cause delays in therapeutic management. Such projects would also help reduce PD in these patients.[79] Regarding COVID-19 infection, there was poor EWB (FACT-B) in patients undergoing NACT who were diagnosed with COVID-19. These results are consistent with those of previous studies on COVID-19 and cancer.[80] Therefore, they emphasize the need to offer support to patients during difficult periods, including future pandemics.[81–83] Qualitative studies identified several determinants that contribute to PD. These included the side effects of NAT, living with the perception of being "sick," as well as concerns about family members, the nature and sources of information received, and the decision-making process.[45,67] Other determinants were also revealed,[65] such as the lack of continuity of care, meeting different nurses and doctors, and the consequences of the surgery that they had to undergo after NACT.

Coping strategies

Regarding coping strategies, two articles[29,40] included in this review found that before NACT, higher levels of "cognitive restructuring" were associated with lower psychological stress[29] and that resilience was negatively correlated with depression, anxiety, and QoL during NACT.[40] Cognitive restructuring, considered an adaptive coping strategy, involves identifying unhelpful thoughts that lead to feelings such as anxiety and depression and analyzing them for their truth, accuracy, and validity while developing more helpful ones.[84] Given the significance of this strategy, the development of clinical interventions that rely on cognitive restructuring is of utmost importance in patient care. Our results also showed that during NACT, "resigned coping" decreased, whereas "social support coping" increased significantly.[29] After NACT,[29] "active coping strategies" were correlated with better psychological adjustment, whereas "resigned coping" was associated with poorer psychological adaptation.[29] Resignation occurs when an individual struggles to achieve unattainable goals, resulting in PD and reduced well-being.[85] Concerning informational coping, qualitative studies reported that patients searched for information on the Internet, but it was seen as terrifying and anxious[67] and they expressed their need for empathy, support, and advice to cope with the effects of the diagnosis.[65,67] They sought additional information on NACT decisions by receiving written information or a decision-support program.[69] Our results are consistent with those of several studies, demonstrating that adopting active positive coping strategies during diagnosis and seeking social support are associated with better psychological adjustment.[86–90] Moreover, negative strategies such as anxious preoccupation, feelings of lack of control, avoidance, and denial are associated with deteriorating MH in patients with cancer.[81,83,91,92]

Intervention to reduce psychological distress

Among the interventions that demonstrated efficacy in this systematic review, the AD program,[55,56], mobile health application,[59] FMD program,[62] and relaxation training and guided imaging program[38] were found to be beneficial in reducing the extent of PD during NACT.

Per the present systematic review, the DA program[55,56] was characterized by a decrease in fear of progression, anxiety, and distress from baseline until the end of the NAT. The results also indicated that using a mobile health application showed an improvement in EF (EORTC-QLQ-C30), a lower prevalence of feeling sad, and better MSAS-Psych scores after NAT.[59] Regarding the qualitative study results, the patients described the use of this mobile application as an easy and accessible source of information, particularly on how to manage their symptoms, and as a safe space for interaction with nurses.[65] Self-management programs based on mobile technology are increasingly providing various types of care, including psychological interventions.[93] These studies support the feasibility and efficacy of digital psychosocial interventions,[94,95] which may decrease anxiety, depression,[96,97] and distress.[94]

Furthermore, in this review, patients receiving an FMD program showed an improvement in EF (EORTC-QLQ-C30) during NACT.[62] In another RCT study[38] based on a relaxation training and guided imaging program, depression increased until sequence 5, and then increased until the end of NACT. Moreover, the intervention reduced emotional suppression and unhappiness.[38]

By referring to recent guidelines on the management of distress, depression, and anxiety,[17,98,99] we identified other interventions for patients with BC. These include psychoeducation, cognitive-behavioral therapy, supportive therapy or counseling, relaxation training or mindfulness-based therapy, supportive expressive therapy, problem-solving therapy, and other interventions.

Limitations

The findings of this systematic review cannot be generalized owing to several limitations. Although most publications were limited to depression and anxiety, we attempted to introduce other concepts attributed to PD by referring to

the definitions mentioned in the NCCN guideline.[17] This approach did not, however, provide sufficient clarity on PD, since a total of 13 attributes were involved. Consequently, our ability to draw a definitive conclusion remains limited, and we were unable to accurately compare the different levels and attributes of PD because of the varied measurement tools used in the included articles. However, owing to the limited number of articles involved in the study, we were unable to obtain a clear picture of coping strategies before and at each cycle of NET; specifically, we were unable to identify the most mobilized strategies. Furthermore, most of the included quantitative studies presented only prevalence values without other statistics, such as confidence intervals. Therefore, the conclusions of this analysis are not suitable for a meta-analysis and should be interpreted with caution.

Conclusion

This systematic review identified the main conclusions drawn from an analysis of the included articles. Thus, the rates of PD and its attributes in patients who were followed up sometimes exceeded 50%. Additionally, various factors associated with PD were identified, and their identification remains crucial for predicting distress and guiding future research. However, results concerning coping strategies are limited, highlighting the need for further research on these strategies. These findings highlight the importance of addressing PD and assessing coping strategies in patients with LABC at crucial points from diagnosis to the end of NAT, and immediately before surgery.

This systematic review, alongside an examination of key psycho-oncology guidelines, highlights the main interventions that can help reduce PD and facilitate the adoption of effective coping strategies. Implementing these strategies would improve the preparation and support for patients throughout their care pathway, not only during NAC, but also at later stages, such as radiotherapy, hormone therapy, and plastic surgery.

Declarations

Ethics approval and consent to participate

This systematic review was based on the analysis of articles rather than the direct collection of patient data, making it inapplicable for ethical approval.

Author contribution(s)

Majid Omari: Data curation; Formal analysis; Investigation; Resources; Visualization; Writing—original draft.
Lamiae Amaadour: Data curation; Formal analysis; Investigation; Resources; Writing—original draft.
Achraf El Asri: Methodology; Resources; Validation.
Zineb Benbrahim: Methodology; Validation.
Nawfel Mellas: Supervision; Validation.
Karima El Rhazi: Conceptualization; Methodology; Supervision.
Mohammed El Amine Ragala: Conceptualization; Methodology; Supervision.
Jaouad El Hilaly: Conceptualization; Methodology; Visualization.
Karima Halim: Conceptualization; Methodology; Visualization.
Btissame Zarrouq: Conceptualization; Methodology; Project administration; Supervision; Validation; Writing—review & editing.

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Competing interests

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Registration

The protocol has been registered at PROSPERO under number: CRD42021230300.

Availability of data and materials

Data sharing did not apply to this article because no datasets were generated or analyzed in the current study.

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Supplemental material

Supplemental material for this article is available online.

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