Effectiveness of physical exercise combined with psychological intervention on anxiety and depression of breast cancer patient: A meta-analysis.

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BACKGROUND: *Anxiety and depression are common psychological health problems in breast cancer patients, which not only increase the risk of cancer recurrence but also affect the quality of life of patients. Exercise combined with psychological intervention, as an important intervention method, has an improvement effect on anxiety and depression in breast cancer patients. However, there is currently a lack of evidence-based research to explore its clinical value and significance.*

OBJECTIVES: *to explore the effects of exercise combined with psychological intervention on anxiety and depression in breast cancer patients using the method of meta-analysis.*

METHODS: *PUBMED, Web of Science, The Cochrane Library, Ovid, China National Knowledge Infrastructure (CNKI), Wanfang Data Knowledge Service Platform, and VIP Chinese Scientific Journals Database were searched from the database's inception to September 2022. Randomized controlled trials (RCTs) of exercise combined with psychological intervention for breast cancer anxiety and/or depression were collected independently by five researchers for literature screening, quality evaluation, and data extraction. The quality of the literature*

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was evaluated according to the "Risk of Bias Assessment Method" recommended by the Cochrane Handbook, and meta-analysis was performed using RevMan5.3.

Results: *A total of 15 articles including 1338 breast cancer patients were included in this study. The meta-analysis results showed that the experimental group had lower anxiety scores [SMD = -1.25, 95% CI (-1.56, -0.95), P< 0.0001] and depression scores [SMD= -1.65, 95% CI (-2.49, -0.81), P = 0.0001] than the control group after exercise combined with psychological intervention.*

Conclusions: *Exercise combined with psychological intervention can effectively alleviate anxiety and depression in breast cancer patients compared with the control group. However, further high-quality large-sample studies are needed to verify these conclusions due to the limitations of the included studies.*

Introduction

Breast cancer is one of the most common cancers worldwide (Loibl, Poortmans, Morrow, Denkert, & Curigliano, 2021) as reported by global cancer registry data in 2020. It has surpassed lung cancer to become the most common malignant tumor, accounting for 11.7% of all cancers (Sung et al., 2021). In 2020, more than 2.26 million new cases of breast cancer were diagnosed globally, with approximately 685,000 deaths. Breast cancer patients in China accounted for 12.2% of all newly diagnosed cases worldwide and 9.6% of all breast cancer deaths (Fan et al., 2014). While the prognosis for breast cancer patients is generally good, their psychological health is often negatively affected during the long-term diagnosis, treatment, and rehabilitation process. Anxiety and depression are the main psychological health disturbances experienced by breast cancer patients, which increase the risk of cancer recurrence and all-cause mortality (Wang et al., 2020). Currently, medications or non-drug therapies can be used to treat anxiety and depression in breast cancer patients (Olsson Möller, Beck, Rydén, & Malmström, 2019); however, the use of drugs may unavoidably result in side effects (Do & Schnittker, 2022). Clinical trials have shown that exercise intervention and psychological intervention can both alleviate anxiety and depression in breast cancer patients (Do & Schnittker, 2022; Lin, Clark, Tu, Bosworth, & Zullig, 2017). Furthermore, aerobic exercise combined with cognitive-behavioral therapy has been found to have a better effect on alleviating negative emotions in breast cancer patients compared to aerobic exercise alone (Cohen, Rogers, Petruzzello, Trinh, & Mullen, 2021). In recent years, scholars have applied exercise combined with psychological intervention to the intervention and treatment of anxiety and depression in breast cancer patients, but

studies have had small sample sizes and varying results. There is currently a lack of evidence-based research to systematically evaluate the effects of exercise combined with psychological intervention for anxiety and depression in breast cancer patients. Therefore, this study aims to use meta-analysis to systematically search for studies that utilize exercise combined with psychological intervention to treat anxiety and depression in breast cancer patients, evaluate its intervention effect, and provide theoretical reference for improving negative emotions in breast cancer patients in the future.

Materials and Methods

This study strictly follows the requirements of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Liberati et al., 2009) guidelines in conducting a meta-analysis and systematic review.

INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria:

(1) randomized controlled trials (RCTs),
(2) breast cancer patients as participants,
(3) exercise combined with psychological intervention as the experimental group's intervention, which includes aerobic and resistance exercise (Ammitzbøll et al., 2019), mindfulness(Würtzen et al., 2015), support, and other psychological interventions (Weis, Gschwendtner, Giesler, Adams, & Wirtz, 2020); routine treatment or care for the control group is necessary.
(4) Outcome measures include anxiety and depression scores gathered from measurement scales such as Self-rating Anxiety Scale (SAS), State Anxiety Inventory (SAI), Hamilton Anxiety Scale (HAMA), Self-rating Depression Scale (SDS), Back Depression Inventory (BDI-II), and Hamilton Depression Scale (HAMD).
(5) Literature must be written in either Chinese or English.

Exclusion criteria:

(1) non-randomized controlled trials,
(2) studies that include patients with other types of tumors,
(3) literature that consists of case reports, reviews, meta-analyses, etc,
(4) literature that cannot provide full-text data or has irrelevant information.

Development of search strategy

The study formulates appropriate search strategies for Chinese and English databases to retrieve relevant RCTs on the impact of exercise combined with psychological intervention

on anxiety and depression in breast cancer patients. The study also traces the reference lists of articles to maximize the comprehensive search of eligible literature. As an example, the PubMed database search strategy is presented as follows:

#1: Breast Neoplasms"[MeSH Terms]

#2: Breast cancer OR breast carcinoma OR breast tumor OR Breast neoplasm OR Mammary Cancer

#3: (exercise OR exercise therapy) AND (psychology OR psychotherapy)

#4: anxiety OR depression

#5: #1 OR #2

#6: #5 AND #3 AND #4

Literature screening and data extraction

The retrieved literature was imported into EndNote X9, and duplicate articles were excluded. Then, five researchers independently screened and extracted data from the literature according to the inclusion and exclusion criteria. In case of disagreements, a third party was involved to discuss and make a decision. During the screening process, the titles and abstracts were read first, and the literature was preliminarily screened. Afterwards, a secondary screening was carried out based on the full text to obtain literature that met the inclusion and exclusion criteria for analysis in this study. Data were extracted from all included articles according to a pre-designed form, which mainly included the first author's name, publication year, age of the research objects, sample size, intervention measures, and outcome indicators.

QUALITY ASSESSMENT OF INCLUDED LITERATURE

Five researchers independently evaluated the quality of the literature, and when there were differences of opinion, a third party was involved in discussion to reach a decision. According to the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al., 2011), quality assessment was performed on six aspects, including sequence generation, allocation concealment, blinding, integrity of data, selective reporting, and other biases. The literature was classified into three levels: low risk, high risk, and unclear risk, corresponding to grades A, B, and C, respectively. level indicates that all criteria are met, and the possibility of bias is low; B-level means partial compliance, indicating a moderate possibility of bias; and C-level indicates complete non-compliance, indicating a higher possibility of bias.

STATISTICALL ANALYSIS

The results of the included studies were analyzed using the RevMan 5.4. Standardized mean difference (SMD) and its 95% confidence interval (CI) were used as the effect size for continuous variables. The heterogeneity among the literature was assessed by I^2 test (Huedo-Medina, Sánchez-Meca, Marín-Martínez, & Botella, 2006). If there was no significant statistical heterogeneity among the literature ($I^2 \leq 50\%$, $P \geq 0.10$), a fixed-effect model was used for meta-analysis. If there was statistical heterogeneity ($I^2 > 50\%$, $P < 0.10$), a random-effect model was used. If outcome indicators data were obtained from different scales, standardized

mean difference (SMD) was used for meta-analysis; if scale type and scale levels were the same, mean difference (MD) was used for analysis. Subgroup analysis or sensitivity analysis was performed if necessary to explore the source of heterogeneity and evaluate the stability of the results. Publication bias was evaluated using the funnel plot method, with $P < 0.05$ indicating statistical significance of the difference.

Results

LITERATURE SEARCH RESULTS

A total of 3,314 articles were initially retrieved through computerized searches. After removing 331 duplicate articles using EndNote X9, 2,927 articles were obtained. After reviewing the titles and abstracts, 110 articles were further screened for full-text review, resulting in the inclusion of 15 articles. The specific process and results of literature screening are shown in Figure 1.
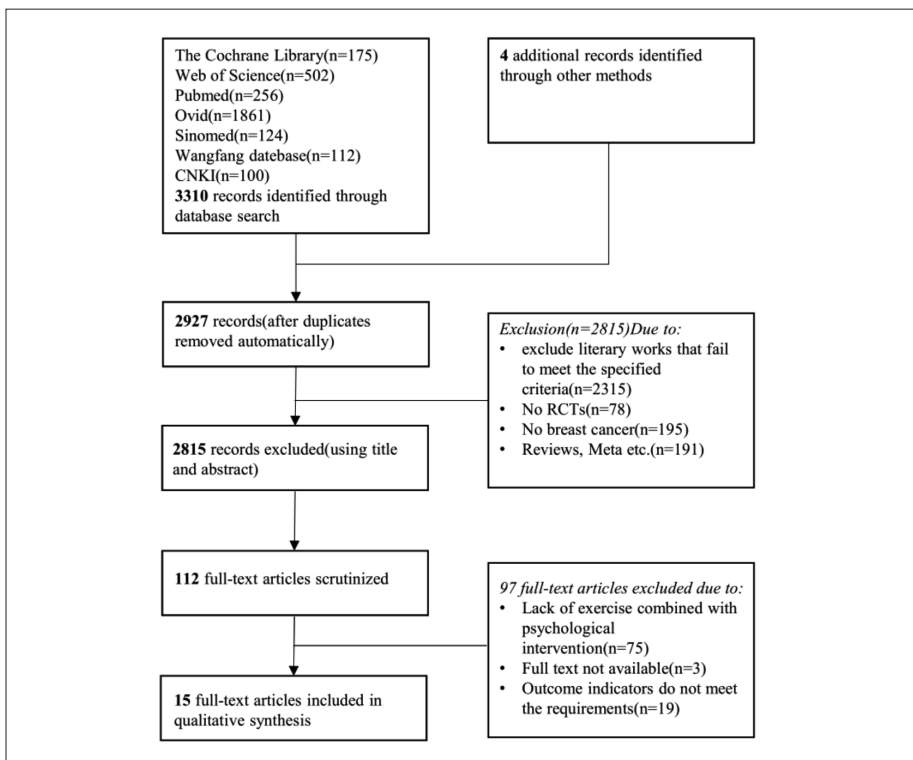

Fig. 1 - Flow chart and results of RCT screening.

Basic characteristics of included studies: Fifteen articles (Cailan, 2013; Fudi, Huan, & Huiyan, 2018; Huifang, 2018; Lijun, Yi, & Hui, 2020; Lintao, 2017; Liqun, 2020; Liu et al., 2008; Rongli, Xiuqing, & Yuzhen, 2018; Taohua, Weiwei, & Guangling, 2020; Xialing, 2018; Xiaojuan, Jing, Yanli, & Hongying, 2021; Xiaoning, 2018; Xiuling, 2018; Y. yang, 2022; J. Y. Zhang, Li, Meng, & Zhou, 2022) were included (Table I), including 1,338 breast cancer patients (667 in the intervention group and 671 in the control group). Among the 15 studies, 15 studies evaluated anxiety levels using the SAS scale, and 13 studies evaluated depression using the SDS scale. The interventions mainly included supportive psychological care combined with rehabilitation nursing and aerobic exercise combined with psychological care.

QUALITY ASSESSMENT OF INCLUDED STUDIES

The quality of the literature was evaluated in each section according to bias risk assessment methods recommended in the Cochrane Handbook for Systematic Reviews of Interventions. Two studies (Liu et al., 2008; Xiaojuan et al., 2021) were rated as A-level quality, and the remaining 13 articles were rated B-level. Overall, research quality was moderate. Nine studies (Huifang, 2018; Lintao, 2017; Rongli et al., 2018; Taohua et al., 2020; Xialing, 2018; Xiaojuan et al., 2021; Xiuling, 2018) used coin toss or random number table to allocate participants randomly; the allocation method in other studies was not explicitly stated. All studies reported complete results without other sources of bias (Figure 2).

META-ANALYSIS RESULTS:

The effect of exercise combined with psychological intervention on anxiety in breast cancer patients

The 15 studies included in this research all reported on the improvement of anxiety in breast cancer patients through exercise combined with psychological intervention. However, the study by Guan Xiaoning (Xiaoning, 2018) did not report on anxiety separately, and data on anxiety could not be extracted. Therefore, Meta-analysis of 14 studies showed that exercise combined with psychological intervention had a statistically significant improvement in the anxiety scores of breast cancer patients compared with conventional care (SMD=-1.25, 95% CI: -1.56 to -0.95, *P*<0.0001), as shown in Figure 3. To further explore the source of heterogeneity, subgroup analysis of anxiety in breast

TABLE I
Basic Characteristics Of The Included Rcts

Study (Publication Time)	Age		Sample Size		Interventions		Interventions Duration	Assessment Measures	Outcomes
	Experimental group	Control group	Experimental group	Control group	Experimental group	Control group			
(Liu et al., 2008)	52.0±8.30	46.10±7.81	12	16	Qigong + Body and mind group therapy	Usual care	2 months	BDI-II-SAI-BMSWBI	Anxiety, depression, physical and mental health
(J. Y. Zhang et al., 2022)	47.79±5.14	47.20±7.65	29	29	Tai Chi + Mindfulness	Usual care	8 weeks	PGTI-PSS-SAS	Anxiety, perceived stress, post-traumatic growth
(Xiaojuan et al., 2021)	41.73±7.85	40.56±8.26	46	46	Aerobics + continuous psychological care	Usual care	8 weeks	SAS-SDS	Anxiety and depression
(Xiaoning, 2018)	38.88±14.09	36.36±16.01	70	70	Aerobic rehabilitation exercise (Qigong, dance) + psychological rehabilitation therapy	Routine nursing + exercise training	2 weeks	SDS-HAMD-HADS	Anxiety and depression
(Lintao, 2017)	50±1.39	51±2.36	31	31	Rehabilitation nursing + supportive psychological nursing	Usual care	>16 days	SAS-SDS-SF-36	Anxiety, depression, quality of life
(Xiuling, 2018)	52.0±9.8	51.8±9.6	50	50	Rehabilitation nursing + supportive psychological nursing	Usual care	/	SAS-SDS-SF-36	Anxiety, depression, quality of life
(Cailan, 2013)	35–62	34–63	66	66	Rehabilitation nursing + supportive psychological nursing	Usual care	90 days	SAS-SDS-SF-36	Anxiety, depression, quality of life
(Liqun, 2020)	38.58±6.72	38.57±6.82	44	44	Rehabilitation nursing + supportive psychological nursing	Usual care	/	SAS-SDS-KPS	Anxiety, depression, quality of life

(Continue) - TABLE I

Study (Publication Time)	Age		Sample Size		Interventions		Interventions Duration	Assessment Measures	Outcomes
	Experimental group	Control group	Experimental group	Control group	Experimental group	Control group			
(Y, yang, 2022)	49.1±2.2	48.5±2.3	37	37	Aerobic exercise + relaxation training	Usual care	/	HAMA-HAMD-PSQI-SF-36-QLQ-C30	Anxiety, depression, sleep quality
(Taohua et al., 2020)	45.13±10.77	47.87±11.94	47	47	Aerobic exercise + psychological care	Routine care + relaxation training	3 months	HAMA-HAMD-SF-36-QLQ-C30	Anxiety, depression, quality of life
(Rongli et al., 2018)	47.82±5.47	47.30±5.72	45	45	Aerobic exercise + Mindfulness-based stress reduction therapy	Usual care	6 weesk	SAS-SDS-SF-36	Anxiety, depression, quality of life
(Hui-fang, 2018)	49.12±7.35	48.36±8.48	40	40	Comprehensive nursing intervention model	Usual care	1 months	SAS-SDS-FACT-B	Anxiety, depression, quality of life
(Lijun et al., 2020)	58.61±3.13	57.32±2.78	75	75	Rehabilitation nursing + emotional nursing	Routine nursing + rehabilitation training	6 months	SAS-SDS-PI-GI-CD-RISC	Anxiety, depression, mental state
(Fudi et al., 2018)	49.67±4.76	49.72±4.81	35	35	Rehabilitation nursing + supportive psychological nursing	Usual care	3 months	SAS-SDS	Anxiety and depression
(Xi-aling, 2018)	50.4±8.5	51.2±8.3	40	40	Yoga aerobics + psychological care	Usual care	6 months	SAS-SF-36	Anxiety, quality of life

Notes: BDI-II = Beck Depression Inventory II, BMSWBI = Body-Mind-Spirit Wellbeing Inventory, PGTI = Pittsburgh Sleep Quality Index, SAS = Zung Self-rating Anxiety Scale, SDS = Zung Self-rating Depression Scale, HADS = Hospital Anxiety and Depression Scale, SF-36 = Short Form-36 Health Survey, KPS = Karnofsky Performance Status, HAMA = Hamilton Anxiety Rating Scale, HAMD = Hamilton Depression Rating Scale, QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30, FACT-B = Functional Assessment of Cancer Therapy - Breast, PIGI=Posttraumatic Growth Inventory, CD-RISC = Connor-Davidson Resilience Scale.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Cailan, 2013	?	?	?	?	+	+	+
Fudi et al., 2018	?	?	?	?	+	+	+
Huifang, 2018	+	+	?	?	+	+	+
J. Y. Zhang et al., 2022	+	+	+	+	+	+	+
Lijun et al., 2020	?	?	?	?	+	+	+
Lintao, 2017	+	+	?	?	+	+	+
Liqun, 2020	?	?	+	?	+	+	+
Liu et al., 2008	+	+	+	?	+	+	+
Rongli et al., 2018	+	+	?	?	?	+	+
Taohua et al., 2020	+	+	?	?	+	+	+
Xialing, 2018	+	+	?	?	+	+	+
Xiaojuan et al., 2021	?	?	?	?	+	+	+
Xiaoning, 2018	+	+	?	?	+	+	+
Xiuling, 2018	?	?	?	?	+	+	+
Y. yang, 2022	+	+	?	?	+	+	+

Fig. 2 - Risk of bias assessment for each included RCT about depression treated using attention bias modification.

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Cailan, 2013	35.9	7.6	66	48.7	7.2	66	9.8%	-1.72 [-2.12, -1.32]
Fudi et al., 2018	41.25	4.53	35	46.51	4.38	35	6.1%	-1.17 [-1.68, -0.66]
Huifang, 2018	38.56	9.71	40	47.39	12.14	40	7.6%	-0.80 [-1.25, -0.34]
J. Y. Zhang et al., 2022	48.66	3.99	29	51.53	4.49	29	5.6%	-0.67 [-1.20, -0.14]
Lijun et al., 2020	41.8	6.4	75	46.71	3.12	75	13.7%	-0.97 [-1.31, -0.63]
Lintao, 2017	23.69	1.05	31	31.26	4.69	31	3.9%	-2.20 [-2.84, -1.56]
Liqun, 2020	34.06	5.25	44	55.93	10.26	44	4.7%	-2.66 [-3.24, -2.08]
Liu et al., 2008	36.92	8.15	12	44.19	12.65	16	2.7%	-0.64 [-1.41, 0.13]
Rongli et al., 2018	43.78	3.34	45	48.21	4.16	45	7.8%	-1.16 [-1.61, -0.72]
Taohua et al., 2020	14.25	3.01	47	16.61	3.12	47	9.0%	-0.76 [-1.18, -0.34]
Xialing, 2018	32.26	6.78	40	41.35	8.13	40	6.9%	-1.20 [-1.68, -0.72]
Xiaojuan et al., 2021	45.64	7.76	46	51.83	9.52	46	8.9%	-0.71 [-1.13, -0.28]
Xiuling, 2018	44.2	5.6	50	57.3	6.7	50	6.5%	-2.11 [-2.60, -1.61]
Y. yang, 2022	12.72	2.05	37	14.58	2.01	37	6.9%	-0.91 [-1.39, -0.43]
Total (95% CI)			**597**			**601**	**100.0%**	**-1.20 [-1.33, -1.08]**

Heterogeneity: Chi² = 74.77, df = 13 (P < 0.00001); I² = 83%
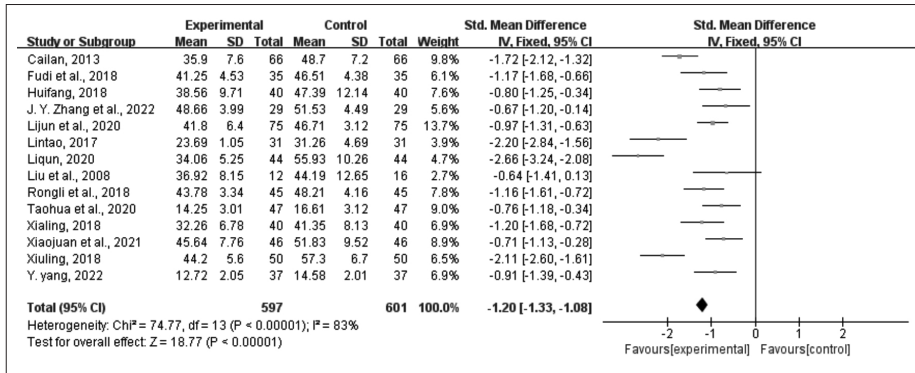Test for overall effect: Z = 18.77 (P < 0.00001)

Fig. 3 - Forest plot of effects on anxiety status after intervention in experimental and control groups.

cancer patients was performed based on different intervention measures, evaluation tools, and intervention times of the included studies, which were divided into three subgroups (Table II). Based on different intervention measures, the studies were divided into two groups. Four studies used rehabilitation nursing combined with supportive psychological care as the intervention measures,

TABLE II
Subgroup Analysis Of Exercise Combined With Psychological Intervention on anxiety in breast cancer patients

Subgroup		Studies SMD/MD	Effect size			Heterogeneity test	
			95%CI	P	I² (%)	P	
Interventions	Rehabilitation nursing + supportive psychological nursing	4	-2.07	[-2.32, -1.82]	<0.001	58	0.07
	Aerobic exercise +Psychological nursing	5	-0.93	[-1.13, -0.73]	<0.001	0	0.41
Assessment	SAS	11	-7.23	[-7.90, -6.56]	<0.001	93	<0.001
	HAMA	2	-2.04	[-2.78, -1.30]	<0.001	0	0.53
	SAI	1	-7.27	[-15.00, 0.46]	0.07	Not evaluated	Not evaluated
Time	≥10weeks	5	-1.15	[-1.34, -0.97]	<0.001	64	0.02
	<10weeks	6	-1.19	[-1.39, -0.99]	<0.001	92	<0.001

and five studies used aerobic exercise combined with psychological intervention. The anxiety scores of the experimental group were lower than those of the control group in both groups [rehabilitation nursing combined with supportive psychological care: SMD=-2.07, 95% CI (-2.32,-1.82), *P*<0.001; aerobic exercise combined with psychological intervention: SMD=-0.93, 95% CI (-1.13,-0.73), *P*<0.001], and the differences were statistically significant. The studies were divided into three groups based on different evaluation tools; 11 studies used SAS, 2 studies used HAMA, and 1 study used SAI. The anxiety scores of the experimental group using SAS or HAMA were lower than those of the control group [SAS: MD=-7.23, 95% CI (-7.90,-6.56),*P*<0.001; HAMA: MD=-2.04, 95% CI (-2.78,-1.03), *P*<0.001], and the differences were statistically significant. The score of using SAI has no statistical significance (MD = - 7.27, 95%CI (-15.00, 0.46), *P*= 0.07). According to whether the intervention time is greater than 10 weeks, the 5 studies with intervention time greater than or equal to 10 weeks and the 6 studies with intervention time less than 10 weeks were divided into two groups. Regardless of whether the intervention time was greater than 10 weeks or less than 10 weeks, the anxiety scores of the experimental group were lower than those of the control group (≥10 weeks: SMD = -1.15, 95% CI (-1.34, -0.97), *P*<0.001; <10 weeks: SMD = -1.19, 95% CI (-1.39, -0.99), *P*<0.001).

The results demonstrate that there was no statistical heterogeneity (I^2=0%, *P*=0.41; I^2=0%, *P*=0.53) in the two subgroups which used aerobic exercise combined with psychological care and assessment tools for HAMA. The heterogeneity was derived from other literature. After conducting sensitivity analysis and excluding four studies by Sun, Lin-tao, et al., a meta-analysis using a fixed effect model showed no statistical heterogeneity among all

Study or Subgroup	Experimental			Control			Weight	Std. Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Fudi et al., 2018	41.25	4.53	35	46.51	4.38	35	8.1%	-1.17 [-1.68, -0.66]
Huifang, 2018	38.56	9.71	40	47.39	12.14	40	10.1%	-0.80 [-1.25, -0.34]
J. Y. Zhang et al., 2022	48.66	3.99	29	51.53	4.49	29	7.5%	-0.67 [-1.20, -0.14]
Lijun et al., 2020	41.8	6.04	75	46.71	3.12	75	18.1%	-1.02 [-1.36, -0.68]
Liu et al., 2008	36.92	8.15	12	44.19	12.65	16	3.5%	-0.64 [-1.41, 0.13]
Rongli et al., 2018	43.78	3.34	45	48.21	4.16	45	10.5%	-1.16 [-1.61, -0.72]
Taohua et al., 2020	14.25	3.01	47	16.61	3.12	47	12.0%	-0.76 [-1.18, -0.34]
Xialing, 2018	32.26	6.78	40	41.35	8.13	40	9.2%	-1.20 [-1.68, -0.72]
Xiaojuan et al., 2021	45.64	7.76	46	51.83	9.52	46	11.8%	-0.71 [-1.13, -0.28]
Y. yang, 2022	12.72	2.05	37	14.58	2.01	37	9.1%	-0.91 [-1.39, -0.43]
Total (95% CI)			406			410	100.0%	**-0.92 [-1.07, -0.78]**

Heterogeneity: Tau² = 0.00; Chi² = 6.88, df = 9 (P = 0.65); I² = 0%
Test for overall effect: Z = 12.47 (P < 0.00001)

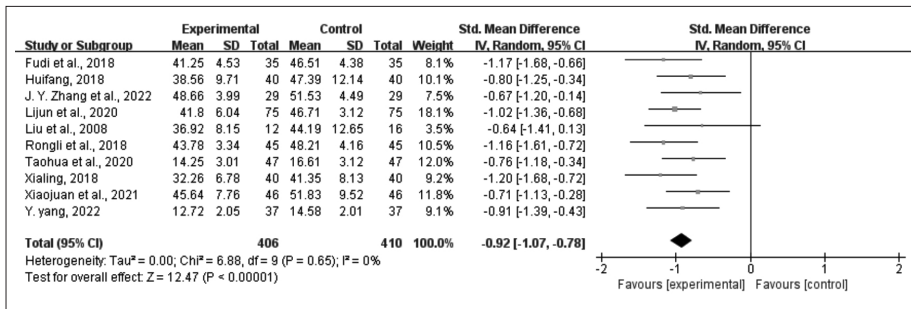Favours [experimental]   Favours [control]

Fig. 4 - Forest plot of effects on anxiety status after intervention in experimental and control groups (after the desensitization).

the studies (I^2=0%, P=0.65). The anxiety scores of the intervention group were 1.25 points lower than those of the control group (P<0.0001), indicating that exercise combined with psychological intervention is beneficial to improving anxiety status in breast cancer patients (see Figure 4).

The Effect of Exercise Combined With Psychological Intervention On Depression In Breast Cancer Patients

Our study included 13 reports that reported the improvement of depression in breast cancer patients after exercise combined with psychological intervention. Due to the inconsistency of scales used in each study, SMD was used to combine the results. The results of heterogeneity test showed that there was significant heterogeneity among the studies (I^2 = 97%, P<0.0001), so a random-effect model was used for Meta-analysis. The results showed that the difference in depression scores of breast cancer patients who received exercise combined with psychological intervention was statistically significant compared to those who received routine care [SMD= -1.56, 95% CI (-2.34, -0.78), P<0.0001], as shown in Figure 5. To further explore the source of heterogeneity, the included studies were divided into three subgroups according to intervention measures, assessment tools, and intervention time (Table III). According to different intervention measures, the studies were divided into two groups: four studies used rehabilitation nursing combined with supportive psychological care, and four studies used aerobic exercise combined with psychological intervention. The depression scores of
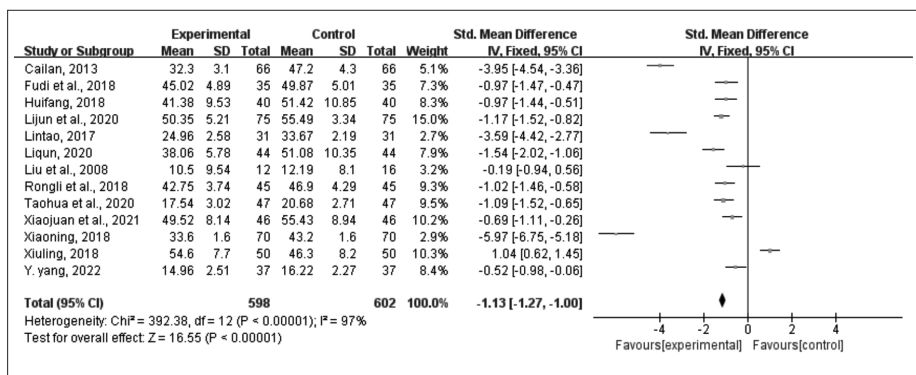
Fig. 5 - Forest plot of effects on depression status after intervention in experimental and control groups.

TABLE III
Subgroup analysis of exercise combined with psychological Intervention On Depression In Breast Cancer patients

Subgroup		Studies SMD/ MD	Effect size			Heterogeneity test	
			95%CI	P	I²(%)	P	
Interventions	Rehabilitation nursing + supportive psychological nursing	4	-1.21	[-1.47,-0.94]	<0.001	99.00	<0.001
	Aerobic exercise +Psychological nursing	4	-0.83	[-1.05, -0.61]	<0.001	29.00	0.24
Assessment	SDS	10	-8.90	[-9.30, -8.50]	<0.001	97	<0.001
	HAMD	2	-2.14	[-2.94, -1.35]	<0.001	81	0.02
	BDI-II	1	-1.69	[-8.39,5.01]	0.62	Not evaluated	Not evaluated
Time	≥10weeks	4	-1.75	[-2.07, -1.43]	<0.001	97	<0.001
	<10weeks	6	-1.52	[-1.72, -1.32]	<0.001	97	<0.001

Note: Xiaoning Guan's study(Xiaoning, 2018) did not report anxiety symptoms separately, and the measurement scales for depressive symptoms included SDS and HAMD. Zhang JY and Xiaoling Zou's study(Xialing, 2018; J. Y. Zhang et al., 2022) did not report depressive emotions.

the experiment group were lower than those of the control group [rehabilitation nursing combined with supportive psychological care: SMD = -1.21, 95% CI (-1.47, -0.49), *P*<0.001; aerobic exercise combined with psychological intervention: SMD= -0.83, 95% CI (-1.05, -0.61), *P*<0.001], and the differences were statistically significant. According to different assessment tools, the studies were divided into three groups: ten studies used SAS, one study used HAMA, and one study used SAI. The anxiety scores of the experiment groups using SAS or HAMA were lower than those of the control groups [SDS: MD = -8.90, 95% CI (-9.30, -8.50), *P*<0.001; HAMA: MD=-2.14, 95% CI (-2.94, -1.35), *P*<0.001], and the differences were statistically significant. However, using BDI-II scores did not have statistical significance [MD=-1.69, 95% CI (-8.39, 5.01), *P*=0.62]. According to the intervention time greater than or equal to 10 weeks being divided into two groups, four studies had an intervention time greater than or equal to 10 weeks, and six studies had an intervention time less than 10 weeks. Regardless of whether the intervention time was greater than or less than 10 weeks, the depression

scores of the experimental group were lower than those of the control group (≥10 weeks: SMD = -1.75, 95% CI (-2.07,-1.43), *P*<0.001; <10 weeks: SMD = -1.52, 95% CI (-1.72,-1.32), *P*<0.001).

The results showed that there was significant heterogeneity among subgroups, as shown in Table III. Sensitivity analysis was conducted by excluding four studies with high heterogeneity, including Xiaoning Guan et al. Afterward, a fixed-effects model was used for the Meta-analysis and still showed moderate heterogeneity (P=0.04, I^2=52%), as observed in Figure 6. According to the Wang Dan et al. method (Dan et al., 2009), heterogeneity processing analysis was performed, which may be related to the imbalance of baseline levels after grouping. The results indicated that the anxiety scores of the experimental group were 1.01 points lower than those of the control group (P<0.0001), suggesting that exercise combined with psychological intervention is beneficial for improving the depressive status of breast cancer patients.

PUBLICATION BIAS

Publication bias is an important factor affecting the quality of Meta-analyses, and a funnel plot with symmetrical distribution is commonly used to evaluate publication bias. In this study, a funnel plot was used to assess the risk of publication bias, evaluating anxiety (Figure 7) and depression levels (Figure 8) of breast cancer patients as outcome indicators, using the SE(SMD) values of included studies' anxiety and depression scores as the y-axis and SMD as the x-axis. The results were presented as funnel plots. The results showed that the funnel plot for anxiety

Study or Subgroup	Experimental			Control			Weight	Std. Mean Difference IV, Fixed, 95% CI	Std. Mean Difference IV, Fixed, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Fudi et al., 2018	45.02	4.89	35	49.87	5.01	35	10.6%	-0.97 [-1.47, -0.47]	
Huifang, 2018	41.38	9.53	40	51.42	10.85	40	12.1%	-0.97 [-1.44, -0.51]	
Lijun et al., 2020	50.35	5.21	75	55.49	3.34	75	21.7%	-1.17 [-1.52, -0.82]	
Liqun, 2020	38.06	5.78	44	51.08	10.35	44	11.4%	-1.54 [-2.02, -1.06]	
Liu et al., 2008	10.5	9.54	12	12.19	8.1	16	4.6%	-0.19 [-0.94, 0.56]	
Rongli et al., 2018	42.75	3.74	45	46.9	4.29	45	13.5%	-1.02 [-1.46, -0.58]	
Taohua et al., 2020	17.54	3.02	47	20.68	2.71	47	13.9%	-1.09 [-1.52, -0.65]	
Y. yang, 2022	14.96	2.51	37	16.22	2.27	37	12.2%	-0.52 [-0.98, -0.06]	
Total (95% CI)			**335**			**339**	**100.0%**	**-1.01 [-1.17, -0.85]**	

Heterogeneity: Chi² = 14.56, df = 7 (P = 0.04); I² = 52%
Test for overall effect: Z = 12.25 (P < 0.00001)

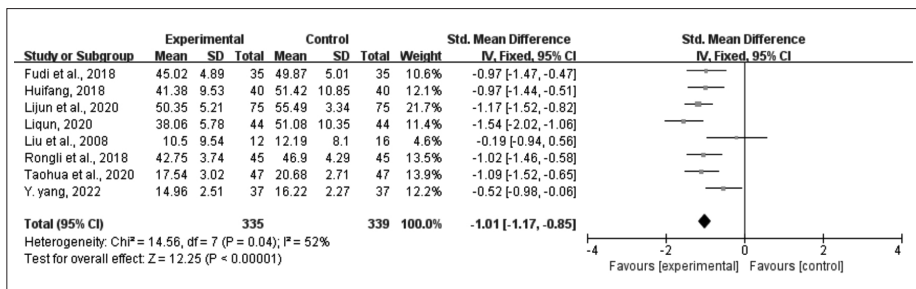Favours [experimental]   Favours [control]

Fig. 6 - Forest plot of effects on depression status after intervention in experimental and control groups (after the desensitization).
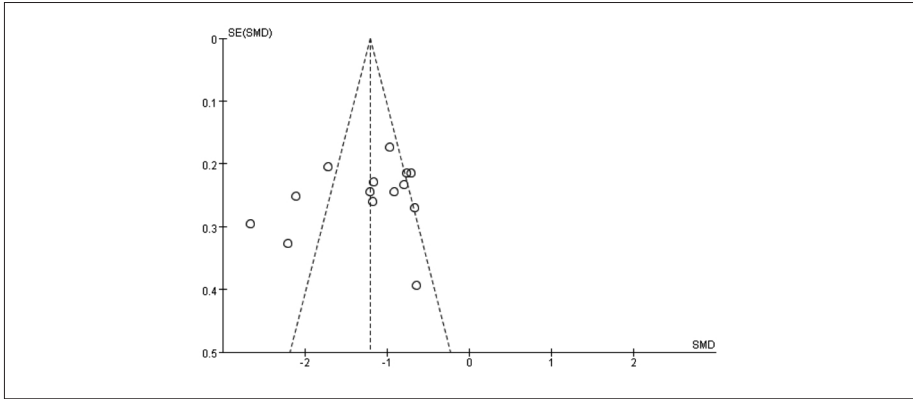
Fig. 7 - Funnel plot of the effect of exercise combined with psychological intervention on anxiety of breast cancer patients.
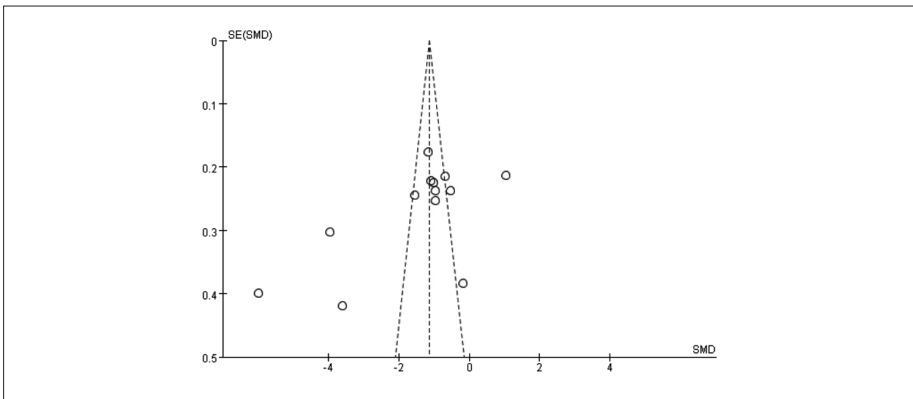

Fig. 8 - Funnel plot of the effect of exercise combined with psychological intervention on depression in breast cancer patients.

was roughly inverted funnel-shaped, with a relatively even distribution of included studies and few scattered studies, which might be related to heterogeneity among studies, indicating mild publication bias in the included studies. However, the funnel plot for depression was asymmetric, possibly due to a greater risk of publication bias in the included studies. (See Figures 7 and 8).

Discussion

Methodological Quality Assessment Of Included Studies

Among the 15 RCT studies included, two had a quality assessment rating of A, and the remaining 13 were rated B. The reasons for this include nine studies using random number tables or coin tossing for allocation concealment, while the remaining studies only reported "random allocation", and three studies implemented concealed grouping and used blinding for implementers and participants. Some studies did not report blinding for implementers, participants, and outcome evaluators, which may have led to certain measurement and selection biases. Overall, the quality of the literature was medium.

Analysis of the Impact of Exercise Combined with Psychological Intervention On anxiety and depression in patients with breast cancer

Breast cancer patients undergo a long treatment process that includes surgery, chemotherapy, and radiation therapy. They are under pressure from the disease and death, which can lead to negative emotions such as anxiety and depression. This hampers their recovery and decreases their quality of life (Courneya et al., 2012; Nho, Reul Kim, & Nam, 2017). Additionally, negative emotions such as anxiety and depression can affect patients' physical and mental well-being, resulting in a decrease in the number of immune cells, subsequent immune suppression, and an adverse effect on recovery (Hu et al., 2018; Nho et al., 2017). This study used Meta-analysis to explore the effects of exercise combined with psychological intervention for anxiety and depression among breast cancer patients. The included studies were rigorously assessed through a systematic review to analyze the effectiveness of this intervention. The results showed that after exercise combined with psychological intervention, anxiety and depression scores in the intervention group were lower than those in the control group, indicating that this intervention is effective in alleviating anxiety and depression in breast cancer patients. Psychological intervention supports patients' understanding of their illness, gives emotional support, reduces stress levels, helps them cope better with their disease, and builds confidence in overcoming the disease (Feiyan & Lihua, 2017). Exercise interventions can improve the cardiopulmonary function of cancer patients, improve muscle metabolism, stimulate the secretion of endorphins in the pituitary gland, excite the central nervous system, and enhance tolerance to stimulation (Wu et al., 2023). In the research

by Chen Meigui et al (Meigui et al., 2021), a combined mindfulness-based therapy and physical intervention had a stronger intervention effect on cancer patients' psychological status due to its dual effects of psychosomatic intervention. The electrical stimulation generated by the human body during exercise can relieve muscle tension and anxiety and depression, relax the brain cortex, and reduce psychological stress levels (Taohua et al., 2020). By providing psychological intervention and appropriate exercise training, personalized nursing plans can be developed, which help patients relieve physical discomfort, promote functional recovery, and allow nursing staff to better understand the patient's psychological state. This builds bridges of communication between breast cancer patients and others, helps them alleviate negative emotions such as anxiety and depression, and improves confidence in treatment and recovery. Subgroup analysis results showed that there was no statistical difference in depressive scores between the experimental and control groups with aerobic exercise combined with psychological intervention, which is not consistent with previous research results (P. Yang, Yang, Cao, Yang, & He, 2022). This may be related to differences in the exercise mode and intervention time and requires further experimental verification. After analyzing the subgroups according to the assessment tool, it was found that there was no statistical difference in anxiety and depression scores for breast cancer patients in Liu CJ's study, which may be related to the inclusion of too few studies and different emphasis on evaluation content by the included subgroup, thus, future studies should select appropriate assessment tools according to specific research objectives. After analyzing subgroups based on intervention time, it was found that there was no significant difference in outcomes produced by interventions of varying durations, and both ≥10 weeks of intervention time and <10 weeks of intervention time led to a certain degree of alleviation of anxiety and depression in breast cancer patients. Once the expected improvement was achieved, the outcome of further intervention showed no significant difference, which is similar to previous research results (J. Zhang, Xu, Wang, & Wang, 2016). This may be due to the lack of knowledge, fatigue, and medical expenses among patients. In the early stages of cancer, patients are often shocked and terrified due to a lack of knowledge of breast cancer. This leads to anxiety and depression during the early stages of the disease. As patients learn more about the prognosis of breast cancer, their psychological burden decreases. Additionally, with prolonged treatment time and control of clinical symptoms, some patients experience fatigue, which hampers the effectiveness of intervention. Over time, as the initial control of cancer reduces medical costs, patients 'psychological burdens decrease, and their response to intervention stabilizes. Therefore,

timely and active intervention is necessary to help breast cancer patients understand their illness better, improve clinical outcomes, and further research into long-term effects is required.

COMPARISON OF COMBINED EXERCISE AND PSYCHOLOGICAL INTERVENTION WITH SINGLE INTERVENTION FOR REDUCING ANXIETY AND DEPRESSION IN BREAST CANCER PATIENTS

Three studies have reported on combined intervention and single intervention. In studies by Guan Xiaoning and Zhou Lijun, the control group received exercise training or rehabilitation training, while the experimental group received exercise combined with psychological intervention. The experimental group showed better outcomes than the control group in all outcome indicators. Psychological interventions included cognitive-behavioral therapy, music therapy, and relaxation therapy. In Guan Xiaoning's study, patients were provided with correct disease knowledge to timely change their negative emotions, while in Zhou Lijun's study, patients were guided to maintain a relaxed and happy mindset through emotional diversion to activate positive mechanisms within the body and reduce subconscious tension and anxiety. These findings are consistent with previous studies that suggest positively affecting the endocrine and immune system of the body can improve negative emotions (Fu, Sun, Wang, Cui, & Zhang, 2022). In Yuan Taohua's study, the control group received psychological care and the experimental group received exercise combined with psychological intervention. After the intervention, the anxiety and depression scores of both groups increased compared to before intervention, but the increase was greater in the control group. The effect of exercise combined with psychological intervention was significantly better than that of single intervention. There are various forms of exercise intervention, such as aerobic exercise, resistance training, and multimodal exercise. Different exercise methods and mechanisms have differences in effectiveness (Xiaolin, Ruzhen, & Caiqin, 2021). At the same time, the arrangement of exercise intensity and volume is an important factor to consider when selecting an exercise program as it affects the health benefits for breast cancer patients (Figueira et al., 2018). In Yuan Taohua's study, patients were given aerobic exercise to stimulate the pituitary gland to secrete endorphins, increase the body's tolerance to stimulation, and relieve muscle tension, depression, and cortical relaxation of the brain during exercise. However, during high-intensity exercise, tumor necrosis factor and interleukin-1 levels increase in muscle tissue and the circulato-

ry system, leading to muscle cell atrophy, energy consumption, discomfort, and fatigue (Khalilimeybodi, Daneshmehr, & Sharif Kashani, 2018; Nam et al., 2023). Therefore, to enhance the effects of exercise combined with psychological intervention, it is important to consider factors such as exercise method and intensity. Currently, domestic and foreign research on anxiety and depression in breast cancer mainly focuses on single interventions, and there is limited research on the combined interventions for both. The results of this Meta-analysis suggest that exercise combined with psychological intervention can effectively improve anxiety and depression in breast cancer patients. In the future, these combined interventions could be a research focus for improving the mental states of breast cancer patients, as they have important implications for enhancing patients' quality of life and improving their prognosis.

LIMITATIONS

(1) Language limitations excluded literature that was not written in Chinese or English, which may result in incomplete literature inclusion.

(2) The generation of RCT randomization schemes, allocation concealment, and blinding methods may have some heterogeneity, which may result in bias risks.

(3) There is little literature on intervention types and it is difficult to perform more accurate subgroup analysis to assess the effect of different intervention types due to the difficulties in implementing combined exercise and psychological interventions in clinical work and follow-up difficulties.

(4) The quality of interventions varied. This study did not report whether psychological intervention providers had received strict professional training, which may have led to bias in the intervention results.

Conclusion

This study evaluated the impact of exercise combined with psychological intervention on anxiety and depression in breast cancer patients through Meta-analysis. Thirteen studies were analyzed, and it was found that after using exercise combined with psychological intervention, the levels of anxiety and depression were significantly improved in patients. However, there is a need to clarify the duration of intervention time. In the future, studies of this type should standardize and improve the intervention programs as much as possible to reduce the impact of methodological weaknesses on the research.

The sample size in this study was limited, and more large-sample studies are needed to provide higher-level evidence for the impact of exercise combined with psychological intervention on anxiety and depression in breast cancer patients.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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