

Review

Non-pharmacological therapies for depressive symptoms in breast cancer patients: Systematic review and meta-analysis of randomized clinical trials

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ABSTRACT

Objective: Depressive symptoms are common comorbidities among breast cancer (BC) patients. Non-pharmacological therapies (NPTs) such as exercise and psychotherapy may reduce depressive symptoms; however, the evidence is inconclusive. The objective of this study is to evaluate if NPTs reduce depressive symptoms among BC patients.

Methods: A systematic review and meta-analysis of randomized clinical trials (RCTs) of NPTs for BC patients were performed. A literature search was conducted from eight databases in English, Portuguese and Spanish from 2006 to 2017. Inclusion criteria were: RCTs that evaluated depressive symptoms as a primary or secondary outcome that did not include pharmacological interventions and did include a non-intervened control group, with at least 30 participants in non-terminal BC stage with no current psychiatric illness. A meta-analysis for each NPT was performed with DerSimonian and Laird's method for the random effects model. Sensitivity analyses were conducted. Heterogeneity and publication bias were assessed.

Results: A total of 41 eligible RCTs were identified. Overall, NPTs significantly reduced depressive symptoms (Summary standardized mean difference (SMD) = -0.516; 95%CI: -0.814, -0.218; $I^2 = 96.2$). Of the types of NPTs, psychotherapy significantly reduced depressive symptoms (Summary SMD = -0.819; 95% CI: -1.608, -0.030; $I^2 = 91.53$). A significant difference emerged for Mindfulness (Summary SMD = -0.241; 95% CI: -0.412, -0.070; $I^2 = 28.6\%$) and yoga (Summary SMD = -0.305; 95% CI: -0.602, -0.007; $I^2 = 41.0\%$) when the heterogeneity was reduced. No evidence of publication bias was observed.

Conclusions: Psychotherapy and mind-body therapies may reduce depressive symptoms in women with BC. Laughter and couples therapy warrant attention in future studies.

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1. Introduction

Breast cancer (BC) is the most prevalent female cancer worldwide [1]. It is estimated that 9.4–66.1% of women with BC suffer from depressive symptoms [2] which decrease the patient's quality of life [3], increase BC treatment costs [4], hinder return to work [5], and accelerates the retirement of working women [6].

Non-pharmacological therapies (NPTs) by definition are those treatments that are not registered as drugs (psychostimulants, hormonal steroids or antidepressants) [7]. They improve patients' health, acting on the hypothalamic-hypophyseal-adrenal axis [8,9]. An example of these is talking therapies, which may include meeting with a counselor, a health educator and/or survivors [7]. Another example of NPTs is interventions based on physical activity (e.g. dancing, exercise, etc.), or exposing the body to a particular contact or stimulus (e.g. massage, music, etc.), or combinations of strategies including recreational and artistic tasks [10,11]. NPTs have been used as adjuvants in BC patients, showing significant effects in the reduction of important comorbidities such as fatigue [12,13], deterioration of quality of life [14] and cognitive functions [15]. In comparison with pharmacological antidepressants, NPTs do not interfere with cancer primary treatment or generate adverse reactions [16] and are more frequently preferred by patients [17].

NPTs may also reduce depressive symptoms in BC patients, however, the information about their efficacy is not yet conclusive, probably due to lack of comparability of interventions among studies. Previously, an aggregation of NPTs was proposed by our research group, with the aim of increasing the homogeneity within groups of NPTs. The purpose of this manuscript was to evaluate if those NPT groups are related to a reduction of depressive symptoms among BC patients.

2. Material and methods

The *Cochrane handbook for systematic reviews of interventions* [18] was followed.

2.1. Literature search

Searches were conducted in Cochrane Central Register of Controlled Trials (CENTRAL), via the Cochrane Library, MedLINE, Scientific Electronic Library On Line (SCIELO), APA PsycNET, Trip Medical Database, Literatura Latinoamericana y del Caribe en Ciencias de la Salud (LILACS), Evidence-Informed Policy (EVIPNet of WHO), and EMBASE; from 2006 January 1st to 2017 December 31st; with English, Spanish and Portuguese as language restrictions.

A combined search strategy was used. The keyword "psychotherapy" was replaced consecutively by: "psychotherapeutic process", "physical activity", "exercise", "mind body therapy" and "yoga". An example of the strategy used in MedLINE was: (((breast neoplasm [MeSH Terms]) AND breast cancer [Title/Abstract])) AND ((depressive symptoms [Title/Abstract]) OR depression [Title/Abstract])) AND psychotherapy [MeSH Terms].

2.2. Study selection

The inclusion criteria were: Randomized clinical trial (RCT) studies of NPTs to reduce depressive symptoms in patients with BC who were not in terminal stage or had psychiatric illnesses; with a minimum sample size of 30 participants; with a control group that did not have any intervention; that evaluated depressive symptoms as a primary or secondary outcome and reported them, before and after the intervention, on a continuous scale.

Initially, titles and abstracts were reviewed; and if the information was not enough to conclude if the studies were eligible, full-texts were read by two reviewers. When differences existed, a consensus was reached through discussion.

2.3. Data extraction

Characteristics of selected studies were recorded in Excel[®] format. When the study had more than one NPT, each of the arms was included separately. Treatment duration was recorded in weeks. Only post-treatment evaluation of depressive symptoms was recorded. NPTs were grouped according to a classification made by Coutiño et al., into non-combined therapies (psychotherapy, social support, art, laughter, and exercise) and combined therapies (couples therapy, Mindfulness Based Stress Reduction or imagery + relaxation, and yoga or spiritual growth + physical activity).

2.4. Statistical analysis

Standardized mean differences (SMD) and deviations were estimated for each clinical trial using Hedges' *g*. Signs were set so that negative effect sizes for depressive symptoms indicated improvements in favor of treatment.

Summary SMD and 95% confidence intervals (CI) for each NPT group were estimated using DerSimonian and Laird's method for the random effects model [19].

Heterogeneity was tested with Cochran's chi-square test (*Q*) by stratifying studies according to region, treatment duration, and test used to measure depressive symptoms. To quantify the extent of heterogeneity the *I*² statistic was used.

A sensitivity analysis was performed excluding one study at a time, followed by the exclusion of two studies at the same time to identify those most contributing to heterogeneity.

The potential for publication bias was assessed using a funnel plot in conjunction with Egger's test [20]. All analyses were performed with the Stata 14 statistical software[®] [21].

3. Results

A total of 3027 studies were identified, from which 753 were eliminated because they were duplicated. After applying the eligibility criteria, 41 clinical trials were obtained; seven were included twice because they had more than two arms, yielding 48 comparisons (Fig. 1).

The characteristics of the eligible studies are presented in Table 1 [22–62]. In total, there were 4869 patients with BC, from

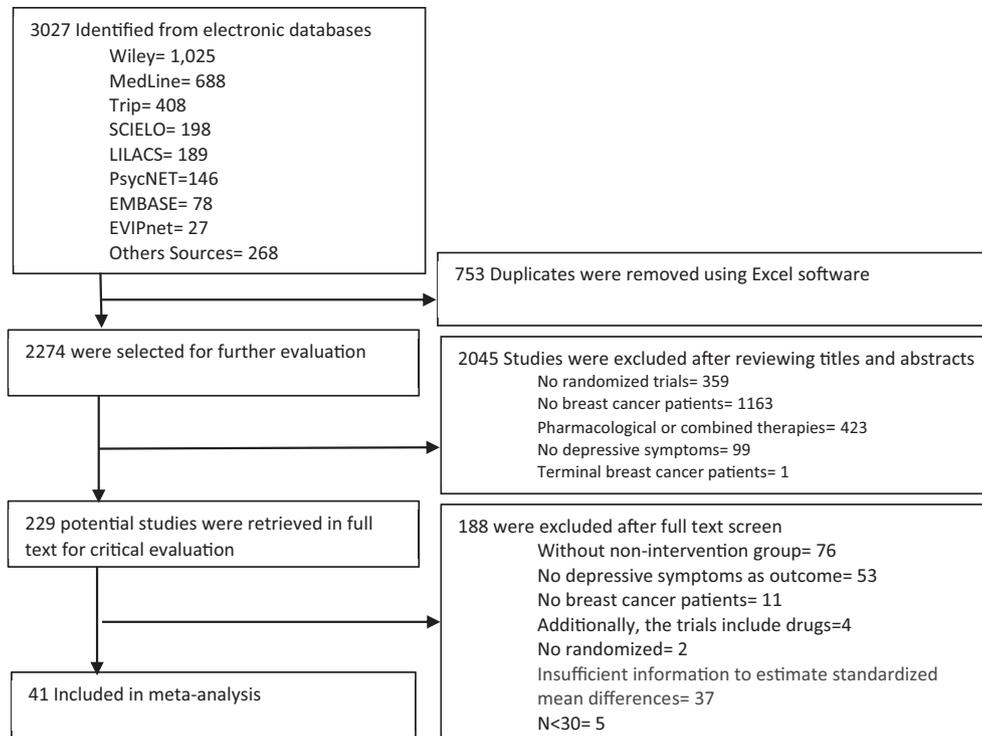


Fig. 1. Flowchart of studies selection process.

whom 2450 were allocated in the treatment arm. The majority of the studies were conducted in North America. No studies were found in Africa, Oceania, or Latin America, with the exception of Brazil. The most reported NPTs were social support, followed by exercise. The duration of NPTs varied from two to 24 weeks. The most commonly used test to measure depressive symptoms was CES-D, followed by HADS, POMS, and BDI.

Based on the total number of comparisons ($N = 48$), a significant summary reduction of depressive symptoms was found among treated patients, compared with the untreated patients (Summary SMD = -0.516 ; 95% CI: $-0.814, -0.218$; $I^2 = 96.2$).

The reduction of depressive symptoms remained significant according to the region where the studies were conducted, for treatments lasting seven to eight weeks, and for those that used POMS and HADS tests, with I^2 ranging from 33.5 to 98.6% (Table 2).

After stratifying for NPT type, the reduction of depressive symptoms only remained significant for patients treated with psychotherapy (Summary SMD = -0.819 ; 95% CI: $-1.608, -0.030$; $Z = 2.03$; $P = 0.042$; $I^2 = 91.5$) and yoga (Summary SMD = -0.385 ; 95% CI: $-0.633, -0.136$; $Z = 3.03$; $P = 0.002$; $I^2 = 53.6$). Laughter had marginally significant summary effects, with heterogeneity of 41.3%. For the other NPTs, non-significant summary effects were obtained, with heterogeneities ranging from zero to 98.0% (Fig. 2).

No evidence of publication bias was observed (Egger's test $P = 0.918$) (Fig. 3).

4. Discussion

The results of this meta-analysis show that psychotherapy and yoga significantly reduce depressive symptoms in patients with active or recently completed BC treatment. Laughter showed a marginally significant reduction, while treatments based on exercise, social support, couple therapy, writing and mindfulness or imagery plus relaxation did not significantly reduce depressive

symptoms.

Psychotherapy has consistently shown to benefit the treatment of depressive symptoms. In three meta-analyses, it has been estimated summary SMDs in favor of treatment, ranging from -0.336 to -1.01 [63–65]. The results of this study confirmed the previous findings and place the magnitude of the reduction at an intermediate point of -0.819 (95% CI: $-1.608, -0.030$; $I^2 = 91.5\%$). In the sensitivity analysis, this reduction remained significant (Summary SMD = -0.768 ; 95% CI: $-1.062, -0.473$), without heterogeneity, by eliminating Qiu et al. and Savard et al. studies. It might be possible that differences in the inclusion criteria of patients among studies explain the observed heterogeneity, since Qiu et al. [26] included metastatic patients from six to 36 months after surgery; in Savard et al. [23] participants had also chronic insomnia syndrome derived from BC diagnosis or treatment, while the rest of the patients were non-metastatic and in active or recently completed treatment.

In the present meta-analysis, a significant reduction was found with yoga. However, a high heterogeneity was present. By eliminating two studies in which the treatment included physical activation and spiritual activities, a significant reduction of depressive symptoms remained (Summary SMD = -0.305 ; 95% CI: $-0.602, -0.007$; $Z = 2.01$; $P = 0.045$; $I^2 = 41.0\%$). This reduction in heterogeneity may be explained by differences in the duration and treatments' content: in five studies only yoga was given for six to 12 weeks, while in Zhou et al. [61] and Kóvacs et al. [59] no yoga was considered, and the duration of NPTs were shorter than six and longer than 12 weeks, respectively.

Information on the reduction of depressive symptoms with laughter therapy is scarce for patients with BC [40,41]. Further studies are needed to demonstrate if laughter therapy reduces depressive symptoms in cancer patients.

The results of this meta-analysis do not show a significant benefit of exercise alone on depressive symptoms and confirmed the findings of Furmaniak et al. [66]. Other studies, where exercise

Table 1
Randomized clinical trials of non-pharmacological interventions for depressive symptoms in breast cancer patients.

ID	First author, year ^[Ref]	Country	Type of NPT	Name of Intervention	Frequency	Duration in weeks	Test	N Treatment (As analyzed)	N Control (As analyzed)
1	Marchioro, 1996 [22]	Italy	Psychotherapy	Psychological	Weekly 50-min individual sessions	NR ^a	BDI ^a	18	18
2	Savard, 2005 [23]	Canada	Psychotherapy	Cognitive Behavioral	Weekly group sessions	8	HADS ^b	27	30
3	Yoo, 2009 [24]	Korea	Psychotherapy	Cognitive Behavior Nursing	Weekly 2-hr sessions	6	CES-D ^c	35	36
4	Garssen, 2012 [25]	The Netherlands	Psychotherapy	Stress Management	5 days and 1-day pre-surgery and on 2 days and 1-month post-surgery	5	POMS ^d	34	36
5	Qiu, 2013 [26]	China	Psychotherapy	Cognitive-Behavioral	Weekly 2-hr group sessions	10	HAMD ^e	31	31
6	Fukui, 2000 [27]	Japan	Social Support	Psychosocial group	Weekly 1.5-hr sessions	6	POMS ^d	25	25
7	Fukui, 2000 [27]	Japan	Social Support	Psychosocial group	Weekly 1.5-hr sessions	6	HADS ^b	25	25
8	Sandgren, 2003 [28]	USA	Social Support	Health education by telephone	Individual 30-min phone sessions	6	POMS ^d	78	55
9	Sandgren, 2003 [28]	USA	Social Support	Emotional expression by telephone	Individual 30-min phone sessions	6	POMS ^d	89	55
10	Winzelberg, 2003 [29]	USA	Social Support	Internet support group (Bosom Buddies)	Different frequency for each participant	12	CES-D ^c	36	36
11	Dolbeault, 2009 [30]	France	Social Support	Psycho-educational group	Weekly 2-hr sessions	8	POMS ^d	81	87
12	David, 2011 [31]	Germany	Social Support	Counseling via e-mail	Different frequency for each participant	8	BSI ^f	31	34
13	Lee, 2013 [32]	Korea	Social Support	Dyadic peer support	20-min face-to-face or by phone sessions	6	HADS ^b	49	46
14	Ashing, 2014 [33]	USA	Social Support	Telephonic in English language	Biweekly 40–50-min telephone sessions	16	CES-D ^c	45	39
15	Ashing, 2014 [33]	USA	Social Support	Telephonic in Spanish language	Biweekly 40–50-min telephone sessions	16	CES-D ^c	54	61
16	Heiney, 2015 [34]	USA	Social Support	Tele-conferencing intervention (STORY)	Different frequency for each participant	10	POMS ^d	82	86
17	Lewis, 2015 [35]	USA	Social Support	Educational parenting	5 Biweekly 1-hr sessions	10	CES-D ^c	90	86
18	Nápoles, 2015 [36]	USA	Social Support	Community-based, translational stress management (Nuevo Amanecer)	8 Weekly 1.5-hr sessions	8	BSI ^f	76	75
19	Kim, 2017 [37]	Korea	Social Support	Nurse-led psychological intervention	Weekly sessions	7	HADS ^b	29	24
20	Park, 2012 [38]	Korea	Art-Therapy	Writing	Weekly 1.5-hr sessions	6	HADS ^b	29	29
21	Jensen-Johansen, 2013 [39]	Denmark	Art-Therapy	Expressive writing	Weekly 20-min sessions	3	BDI-SF ^g	251	251
22	Kim, 2009 [40]	Korea	Laughter-Therapy	Laughter Therapy	4 Weekly 60-min sessions	2	HADS ^b	31	29
23	Cho, 2011 [41]	Korea	Laughter-Therapy	Laughter Therapy	2 Weekly 60-min sessions	4	BDI-II ^h	16	21
24	Mutrie, 2007 [42]	United Kingdom	Exercise	Supervised group exercise	2 Weekly 45-min sessions	12	BDI ^a	82	92
25	Cadmus, 2009 [43]	USA	Exercise	Maintaining Physical Activity during Cancer Treatment (IMPACT)	5 Weekly 30-min session	24	CES-D ^c	25	25
26	Cadmus, 2009 [43]	USA	Exercise	Yale Exercise and Survivorship (YES)	5 Weekly 30-min session	24	CES-D ^c	37	37
27	Sprod, 2010 [44]	USA	Exercise	Exercise training	2-3 Weekly 60-min sessions	12	BDI ^a	29	17
28	Sprod, 2010 [44]	USA	Exercise	Exercise training	2-3 Weekly 60-min sessions	24	BDI ^a	68	17
29	Eyigor, 2010 [45]	Turkey	Exercise	Pilates Exercises	3 Weekly sessions	8	BDI ^a	27	15
30	Mehnert, 2011 [46]	Germany	Exercise	Physical exercise rehabilitation group	Twice weekly 90-min sessions	10	HADS ^b	30	28
31	Chen, 2013 [47]	Canada	Exercise	Qigong	5 Weekly 40-min sessions	6	CES-D ^c	49	46
32	Ratcliff, 2016 [48]	USA	Exercise	Stretch	3 Weekly 60-min sessions	6	CES-D ^c	56	54
33	Bultz, 2000 [49]	Canada	Couples Therapy	Educational and support group for partners	One evening a week for 1.5–2 h	6	POMS ^d	15	19
34		Greece			5 Biweekly sessions	10	CES-D ^c	20	20

Table 1 (continued)

ID	First author, year [Ref]	Country	Type of NPT	Name of Intervention	Frequency	Duration in weeks	Test	N Treatment (As analyzed)	N Control (As analyzed)
35	Kalaitzi, 2007 [50] Nunes, 2007 [51]	Brazil	Couples Therapy Combined	Brief Psycho-sexual Intervention Relaxation and guided imagery	Daily 30-min structured group sessions	4	BDI ^a	20	14
36	Hoffman, 2012 [52]	United Kingdom	Combined	Mindfulness-Based Stress Reduction	Weekly 2-hr group session + 45-min for 6–7 d/wk at home	8	POMS ^d	103	111
37	Chen, 2015 [53]	Taiwan	Combined	Relaxation with guided imagery	Daily 20-min at home sessions for 7 days after chemotherapy	2	HADS ^b	32	33
38	Bower, 2015 [54]	USA	Combined	Mindfulness meditation	Weekly 2-hr group session	6	CES-D ^c	39	32
39	Kenne, 2017 [55]	Sweden	Combined	Mindfulness-Based Stress Reduction	Weekly 2-hr session + 20-min 6 d/wk as homework	8	HADS ^b	62	52
40	Kenne, 2017 [55]	Sweden	Combined	Self-instructing Mindfulness-Based Stress Reduction	20-min 6 d/wk at home	8	HADS ^b	52	52
41	Reich, 2017 [56]	USA	Combined	Mindfulness-Based Stress Reduction	Weekly 2-hr session + 15–45 min daily	6	CES-D ^c	154	146
42	Culos-Reed, 2006 [57]	Canada	Combined	Yoga	Weekly 75-min session	7	POMS ^d	20	18
43	Danhauer, 2009 [58]	USA	Combined	Restorative yoga	Weekly 75-min session	10	CES-D ^c	22	22
44	Kovács, 2012 [59]	Hungary	Combined	Physical, psychological and spiritual growth	5-day residential lifestyle camp (once) + Daily 1.5-hr at home sessions + Weekly 5-hr group psychotherapy	14	BDI ^a	36	87
45	Cramer, 2015 [60]	Germany	Combined	Yoga	Weekly 90-min session	12	HADS ^b	19	21
46	Zhou, 2015 [61]	China	Combined	Music therapy and progressive muscle relaxation after mastectomy	Twice a day in early morning and once in the evening for until discharged from hospital	NR*	ZSDS ⁱ	85	85
47	Ratcliff, 2016 [48]	USA	Combined	Yoga	3 Weekly 60-min sessions	6	CES-D ^c	53	54
48	Lancot, 2016 [62]	Canada	Combined	Bali Yoga Program (BYP-BC)	Weekly 90-min group sessions	8	BDI ^a	54	38

*NR= Not reported.

^a BDI= Beck Depression Inventory.

^b HADS= Hospital Anxiety and Depression.

^c CES-D = Center for Epidemiologic Studies-Depression Scale.

^d POMS= Profile of Mood States.

^e HAMD= Hamilton Depression Rating Scale.

^f BSI= Brief Symptom Inventory.

^g BDI-SF= Beck Depression Inventory- Short Form.

^h BDI-II= Beck Depression Inventory-II.

ⁱ ZSDS = Zung Self-Rating Depression Scale.

Table 2

Summary standardized mean difference after stratifying non-pharmacological treatments for selected characteristics.

Characteristics	Number of studies	Standard Mean Difference (95% CI)	I ²	Z	P
Region					
North America	22 [*]	-0.659 (-1.278, -0.040)	98.1	2.09	0.037
Europe	13	-0.313 (-0.441, -0.184)	34.8	4.75	0.000
Asia	11	-0.549 (-0.935, -0.164)	86.0	2.80	0.005
Treatment duration					
≤5 weeks	6 ^{**}	-0.334 (-0.645, -0.022)	65.4	2.10	0.036
6 weeks	13	-0.769 (-1.475, -0.063)	97.5	2.14	0.033
7–9 weeks	11	-0.274 (-0.441, -0.107)	44.7	3.22	0.001
10–13 weeks	10	-0.902 (-1.952, 0.149)	98.3	1.68	0.092
≥14 weeks	6	0.072 (-0.210, 0.354)	58.3	0.50	0.618
Test					
CES-D ¹	16 ^{***}	-0.853 (-1.762, 0.056)	98.6	1.84	0.066
HADS ²	12	-0.378 (-0.749, -0.007)	86.0	2.00	0.046
POMS ³	9	-0.713 (-1.168, -0.258)	92.1	3.07	0.002
BDI ⁴	8	-0.135 (-0.348, 0.076)	33.5	1.26	0.209
OVERALL	N = 48	-0.516 (-0.814, -0.218)	96.2	3.39	0.001

* Brazil and Turkey were not grouped into any region.

** 2 studies did not report duration.

*** 5 studies with a single test: 1.CES-D = Center for Epidemiologic Studies-Depression Scale; 2. HADS = Hospital Anxiety and Depression; 3. POMS = Profile of Mood States; 4.BDI= Beck Depression Inventory.

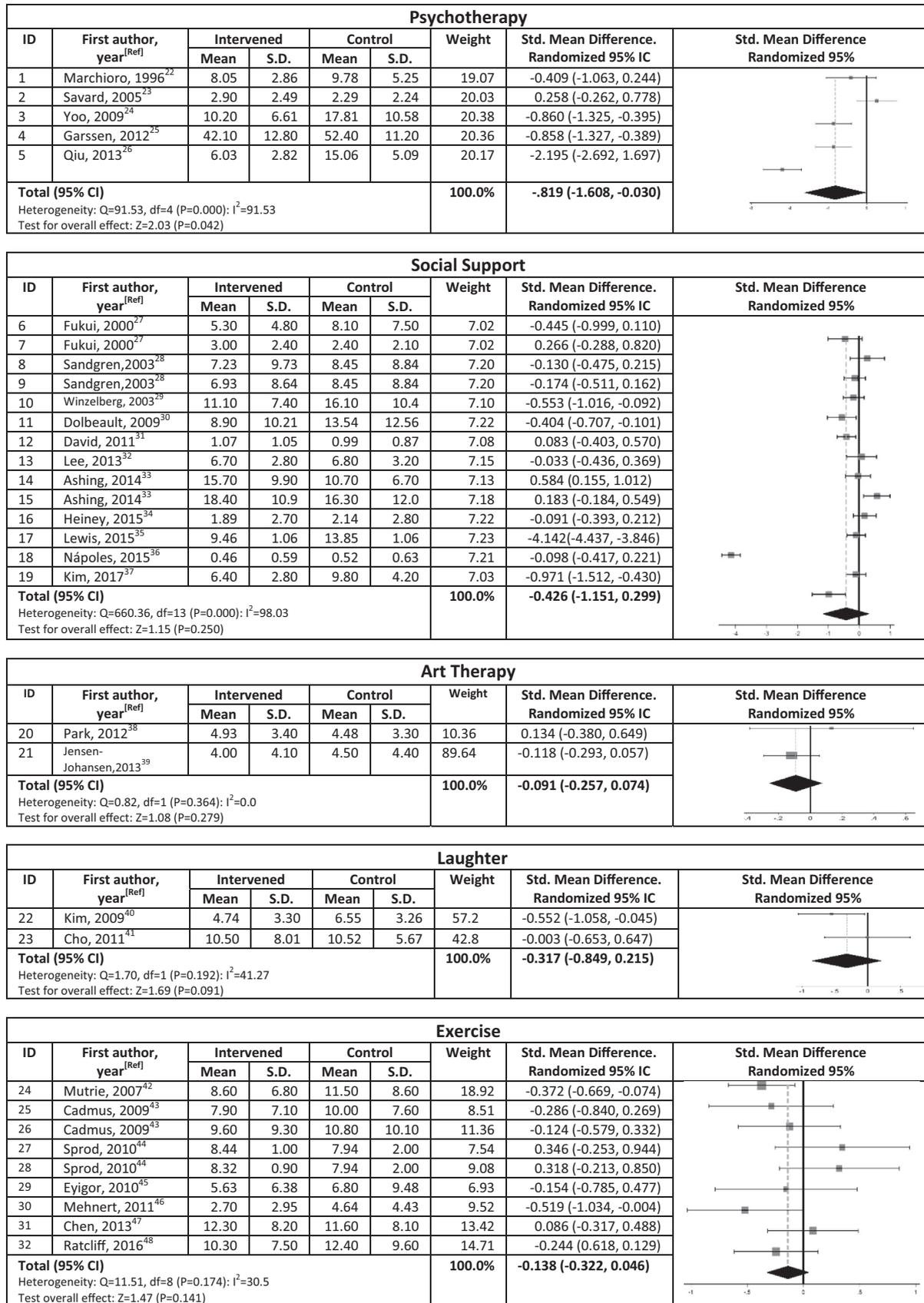


Fig. 2. Forest plot of non-pharmacological treatments for depressive symptoms among breast cancer patients.

has been combined with yoga and contemplative activities, suggest a significant reduction in depressive symptoms, but with high heterogeneity [67], possibly determined by the inclusion of yoga.

Treatments based on imagery or MBSR, did not significantly reduce depressive symptoms. The heterogeneity, however, was reduced and the summary effect emerged significant (Summary SMD = -0.241; 95% CI: -0.412, -0.070; Z = 2.76; P = 0.006; I² = 28.6%) when a study [54] that included premenopausal BC survivors, was eliminated. Huang et al. [68] also reported a significant reduction in depressive symptoms due to MBSR.

Social support treatments did not reduce depressive symptoms. The summary SMD had high heterogeneity even when two studies, that contributed the most to the heterogeneity were excluded (Lewis et al. [35] and Kim et al. [37]). The heterogeneity of social support treatments reduced the comparability among studies and does not allow a conclusion to be reached about their effectiveness on depressive symptoms reduction [69,70].

This is the first time that a summary measure for couple's therapy for depressive symptoms in patients with BC has been reported. The results suggest a reduction in depressive symptoms; however, they did not reach statistical significance probably because they were based on only two studies. Further studies are needed to elucidate the effectiveness of couple's therapy.

To interpret these results, it should be considered that only RCTs with a non-intervention control group were included, which may have increased the power to detect differences between intervened and not intervened groups. However, it was not possible to evaluate if the reduction of depressive symptoms is reversible since most of the studies did not include a follow-up to the patients after the

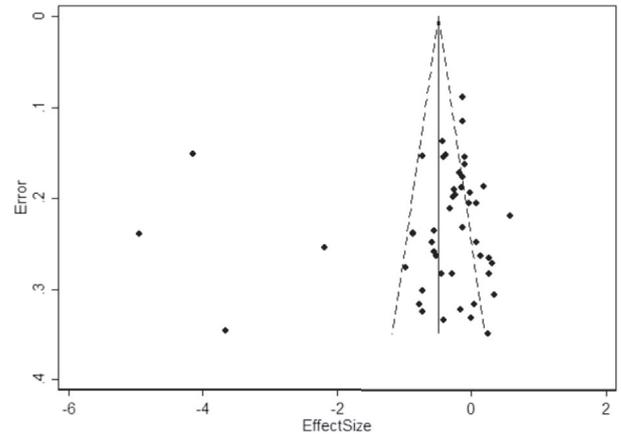


Fig. 3. Funnel plot of non-pharmacological treatments for depressive symptoms among breast cancer patients.

intervention. In addition, time at BC diagnosis was not considered as an eligibility criterion and may have produced heterogeneity.

In summary, this meta-analysis suggests that psychotherapy and yoga or spiritual growth techniques combined with physical activity treatments are useful to reduce depressive symptoms in women with non-metastatic BC. The use of laughter and couple's therapy to reduce depressive symptoms in BC patients is inconclusive and warrants attention in future studies.

Couples								
ID	First author, year ^[Ref]	Intervened		Control		Weight	Std. Mean Difference. Randomized 95% IC	Std. Mean Difference Randomized 95%
		Mean	S.D.	Mean	S.D.			
33	Bultz, 2000 ⁴⁹	3.7	1.25	10.2	2.1	49.9	-3.654 (-4.331, -2.977)	
34	Kalaitzi, 2007 ⁵⁰	20.45	2.31	22.65	3.33	50.1	-0.768 (-1.387, -0.148)	
Total (95% CI)						100.0%	-2.208 (-5.036, 0.621)	
Heterogeneity: Q=37.99 df=1 (P=0.000); I ² =97.37 Test for overall effect: Z=1.53 (P=0.126)								
Based on Mindfulness Based Stress Reduction or Imagery + Relaxation								
ID	First author, year ^[Ref]	Intervened		Control		Weight	Std. Mean Difference. Randomized 95% IC	Std. Mean Difference Randomized 95%
		Mean	S.D.	Mean	S.D.			
35	Nunes, 2007 ⁵¹	12.26	6.38	10.64	6.67	13.80	0.249 (-0.434, 0.932)	
36	Hoffman, 2012 ⁵²	10.00	9.95	14.96	13.23	14.50	-0.422 (-0.690, -0.153)	
37	Chen, 2015 ⁵³	2.19	1.49	3.27	2.13	14.20	-0.585 (-1.072, -0.100)	
38	Bower, 2015 ⁵⁴	9.9	1.64	18.47	1.8	14.23	-4.948 (-5.416, -4.481)	
39	Kenne, 2017 ⁵⁵	3.30	3.30	3.80	3.80	14.38	-0.141 (-0.510, 0.227)	
40	Kenne, 2017 ⁵⁵	3.00	2.90	3.80	3.80	14.36	-0.237 (-0.621, 0.148)	
41	Reich, 2017 ⁵⁶	8.12	5.45	8.82	6.05	14.53	-0.122 (-0.348, 0.105)	
Total (95% CI)						100.0%	-0.886 (-1.954, 0.182)	
Heterogeneity: Q=366, df=6 (P=0.000); I ² =98.36 Test for overall effect: Z=1.63 (P=0.104)								
Based on Yoga or spiritual growth + physical activity								
ID	First author, year ^[Ref]	Intervened		Control		Weight	Std. Mean Difference. Randomized 95% IC	Std. Mean Difference Randomized 95%
		Mean	S.D.	Mean	S.D.			
42	Culos-Reed, 2006 ⁵⁷	2.22	2.65	5.50	6.03	9.86	-0.718 (-1.355, -0.081)	
43	Danhauer, 2009 ⁵⁸	8.10	8.90	17.80	16.90	10.83	-0.718 (-1.309, -0.127)	
44	Kovács, 2012 ⁵⁹	11.44	2.27	12.63	4.96	16.62	-0.273 (-0.662, 0.115)	
45	Cramer, 2015 ⁶⁰	8.50	1.50	8.40	2.40	10.19	0.049 (-0.571, 0.670)	
46	Zhou, 2015 ⁶¹	30.21	3.31	33.40	5.30	19.85	-0.722 (-1.023, -0.421)	
47	Ratcliff, 2016 ⁶²	12.2	9.70	12.40	9.60	16.95	-0.021 (-0.400, 0.358)	
48	Lanctot, 2016 ⁶²	11.15	0.83	11.43	0.99	15.71	-0.311 (-0.726, 0.104)	
Total (95% CI)						100.0%	-0.385 (-0.633, -0.136)	
Heterogeneity: Q=12.92, df= 6 (P=0.044); I ² =53.57 Test overall effect: Z=3.03 (P=0.002)								

Fig. 2. (continued).

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Conflicts of interest

The authors have no conflicts of interest.

Ethical approval

This investigation was conducted with secondary data, so that approval of an Ethical Committee was not required.

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