Effects of physical activity on depressive symptoms during breast cancer survivorship: a meta-analysis of randomised control trials

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ABSTRACT

Background Breast cancer is one of the most common cancers affecting women worldwide, and depressive symptoms are disturbing side effects of cancer diagnosis and treatment. Physical activity and exercise have emerged as an alternative treatment in handling psychological distress throughout breast cancer survivorship.

Aim The aim of this review was to present the results of (1) physical activity and (2) exercise interventions in terms of type and duration regarding depressive symptoms among breast cancer survivors during and after treatment. The hypothesis was that cancer survivors who are engaged with physical activity will demonstrate statistically significant lower levels of depressive symptoms when compared with non-exercising control groups.

Methods We searched PubMed, Elsevier and Google Scholar for recent articles published between January 2011 and November 2016. Fourteen randomised control trials with 1701 patients in total were assessed.

Results Significant differences in levels were found between exercise intervention groups and control groups, while moderate aerobic exercise interventions with an optimal duration of ≥135 min for up to 12 weeks are significantly more beneficial in depressive symptoms than resistance, aerobic endurance, resistance training and yoga interventions.

Conclusions It is concluded that when progressive exercise programmes are prescribed according to the individual needs, capabilities and preferences of breast cancer survivors, they offer a valid alternative to depression mood management throughout the course of survivorship.

INTRODUCTION

Breast cancer remains by far the most common cancer affecting women worldwide, with an estimated 25% incidence rate among all female cancers.1 This disturbing figure is somehow mitigated by the increasing survival rates of patients with breast cancer, which are attributed mostly to improvements in diagnosis (eg, early detection) and treatment.12 In fact, the 5-year, 10-year and 15-year relative survival rates for breast cancer of 80%–95%, 83% and 78%, respectively, are of the highest 5-year survival rates among female malignancies.13 Thus, breast cancer is nowadays considered a treatable chronic disease, rather than a fatal one. This new perspective has led to a new era in oncology treatment, namely, survivorship, which refers to those who are cancer free for at least 5 years after diagnosis.24 Specifically, a breast cancer survivor is anyone who has been diagnosed with the disease from the point of diagnosis to the end of life.3 Survivorship encompasses all phases during cancer,
from active treatment to recovery, in which the transition from being a ‘patient’ with breast cancer to ‘survivor’ takes place through living after recovery, including those who are symptom free or stable and finally up to the phase where advanced cancer, recurrence and death may occur.16

Inevitably, at some point right after diagnosis or throughout their survivorship, most breast cancer survivors will encounter different physical and psychological side effects related to cancer and its treatments.7 With the well-documented extended longevity of breast cancer survivors, the challenge for the medical community has shifted from merely treating the disease to acknowledging and successfully managing these symptoms and side effects in a way that will improve patients’ overall quality of life and provide them with emotional care and support during survivorship.8

Depressive mood is a negative psychological outcome usually reported by breast cancer survivors both during and after treatment, with prevalence ranging between 1.5% and 46%.9 Symptoms are more intense during diagnosis and active treatment, and prevalence is twice as high compared with that found in the general population.10 Despite a gradual reduction in depressive rates throughout survivorship, some women remain chronically with depressive symptoms or become depressed after treatment, especially women with disease recurrence for whom levels of depression mood increase sharply.11 12 Moreover, depression mood may cause poor adherence to treatment plans and even reduce the chance of survival in women with breast cancer;7 8 which, if left untreated, can increase the risk for physiological comorbidities.13 These associations underline the paramount importance of applying effective treatments to reduce depressive symptoms in breast cancer survivors.

Previous evidence suggests that physical activity is a non-pharmacological, safe, feasible and relatively low-cost alternative to depression mood management among women with breast cancer.7 14 15 Performing any form of regular exercise and maintaining an active lifestyle in general plays an important role for breast cancers survivors. It helps them to reduce specific side effects of treatment, for example, weakness and depressive symptoms, and it has been shown to increase survival rates and decrease the risk of cancer reappearance.14 In fact, major health organisations recommend that cancer survivors should have at least 150 min of moderate-intensity or 75 min of high-intensity exercise combined with a minimum of two strengthening exercise sessions on a weekly basis.6

Most of the available research findings suggest that physical activity is an effective way for depression management in breast cancer survivors, despite the fact that several limitations and methodological weaknesses of relevant studies have been consistently reported. These include, but are not limited to, small sample sizes, studies mostly involving white participants, poor reporting of adherence and differences in socioeconomic status, failure to follow intent-to-treat analysis and, most importantly, low baseline depression levels as well as depression not being the primary study outcome. Most of the included studies in the aforementioned reviews and meta-analyses have been published before 2012, and in some cases, review articles involving breast cancer survivors are overlapping. Yet to our knowledge, the effect of exercise in depressive symptoms among breast cancer survivors has not been critically evaluated due to non-uniform reporting of modes, intensity, frequency and duration of exercise interventions. Because of this, many systematic reviews have suggested that the optimal exercise programme and programme components need to be further explored.7 15 16

Therefore, the purpose of this literature review paper is to present the most recent studies dealing with the effects of physical activity and exercise on depression mood experienced by breast cancer survivors. Moreover, we aim to clarify if scientists have reached a consensus about the most beneficial physical activity and exercise intervention in terms of type and duration for breast cancer survivors during and after treatment. It is hoped that the information provided will be valuable for doctors, psychologists, physiologists and also for the survivors themselves.

METHODS

Literature search

We searched PubMed, Elsevier and Google Scholar up to November 2016. The reference list of the retrieved articles was examined for cross references. The search included the use of terms such as breast cancer, depression, depressed mood, physical activity, exercise, treatment, psychological effects or a combination of these terms. For the purposes of this study, we used the term ‘depressed mood’, which is a symptom of depression,9 as a synonym to depressive symptoms in order to avoid the parallelism with the clinical disorder. Moreover, authors have used the terms ‘exercise’ and ‘physical activity’ alternatively. While some studies have used exercise interventions where the main goal was fitness improvement and required access to facilities or equipment, other studies referred to different forms of physical exertion of moderate physical activity, such as home-based walking regimes or even occupational and household activities.14 17

Inclusion criteria

Studies included in this review met the following criteria: (a) were written in English; (b) were published in 2011 and beyond (for secondary studies from the same research team, an original article had to be published in 2008 and afterwards; the year 2011 was chosen because there was a gap in literature findings in meta-analysis for the effect of exercise in depression in breast cancer survivors); (c) participants were adult women diagnosed with breast cancer based on mammography and biopsies; (d) included an intervention programme involving physical activity; (e) used a randomised controlled trial (experimental) design; and (f) results for depression outcomes.
Exclusion criteria
Studies were excluded mainly due to: (a) inclusion of other types of cancer survivors; (b) inability to have access to the entire article; and (c) publication date before 2011 or before 2008 for primary or secondary studies.

Data extraction
Relevant data were extracted by an excel template including: (1) characteristics of the study and participants (first author, year of publication, mean age, sample size; (2) characteristics of exercise intervention (type, total duration, intensity, frequency, session duration); and (3) outcomes of intervention on depressive symptoms.

Methodological quality assessment
The methodological quality of the studies was assessed according to PEDro criteria list, which is a set of 10 criteria for quality assessment of randomised controlled trials. Each item was scored as yes (√) or no (–).

Outcomes
The primary outcome was the standardised mean difference in depressed mood measured by total scores on the Hospital Anxiety and Depression Scale (HADS) or by the Center for Epidemiologic Studies-Depression (CES-D) questionnaire by the Beck Depression Inventory (BDI-II) or scores of Profile of Mood State (POMS) (table 1). Secondary outcome measures included type and duration of exercise and depressed mood. Additionally, outcomes from the effect of exercise interventions in depressive symptoms in patients during treatment and post-treatment were measured.

Statistical analysis
Data were pooled for all studies examined: (1) the effect of exercise in general, (2) the effect of the different types of intervention on depressive symptoms, (3) the effect of the duration of intervention and (4) the effect of the exercise intervention during and after treatment. More specifically, we performed effect size analysis in the studies that used high exercise duration within a week period and the exercise duration of the overall exercise programme (≥12 weeks). The separation of the studies regarding both the exercise duration within a week period and the exercise duration of the overall exercise programme was made with the help of 50th percentile. For studies that included more than one follow-up comments, the last follow-up was used in order to conclude the effect of exercise on depression. For the intervention group, studies were classified according to the exercise moderators in four types: aerobic (e.g., cardiovascular exercise, treadmill running and walking), resistance (muscle strength training), aerobic and resistance and yoga.

Effect sizes were computing using the Comprehensive Meta Analysis V.2.0. Hedges’ g was used as a measure of the effect size. The standardised mean difference between the exercise and the control groups divided by the pooled SD was used to compute the effect size in each study. An effect size ≤0.2 reflects a negligible difference, between 0.2 and ≤0.5 a small difference, between ≥0.5 and ≤0.8 a moderate difference and ≥0.8 a large difference.

Prior to analysis, data were assessed for publication bias using the methods of Begg and Egger Statistical heterogeneity among studies was measured by Q-statistic together with I² test.

RESULTS
Study selection
A total of 432 were retrieved from the database. A total number of 15 relevant systematic reviews and meta-analyses were also examined from the reference list in order to identify additional studies. Using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines, 14 randomised controlled trials were finally included, while 107 articles were excluded in which the design of the study failed to meet the inclusion criteria (figure 1).

Methodological quality of included studies
We assessed 14 randomised control trials according to the PEDro criteria list. In all 14 studies, 2 studies met eight criteria, 9 studies met seven criteria, 2 studies met six criteria and 1 of the them met five criteria. The mean PEDro score of the studies was 6.1±2, indicating high quality (table 2).

Reviewed studies and breast cancer survivor characteristics
In total, 14 studies met all inclusion criteria and are presented in this review. All studies were published between 2011 and 2016, and the actual year of trial completion for more than half of them was after 2011. Six of them were conducted in North America (USA n=4 and Canada n=2) and eight in Europe (Germany and Spain n=2 each, United Kingdom n=2, Turkey and the Netherlands n=1 each). Sample sizes ranged from 1034 to 30031 participants, with a mean of 60.7, while nine studies recruited less than 100 breast cancer survivors. Control groups included participants assigned to usual care, health education, wait list, relaxation and stretching comparable with the interventions applied to exercise groups. Ten and 8 out of the 14 studies reported on adherence and adverse events related to exercise intervention, respectively. Five studies reported on participant’s ethnicity, 10 on marital status and 7 on menopausal state. Data on income (n=3), education (n=9) and occupation (n=7) were also reported, with two studies providing data on all three variables of women’s socioeconomic status.

For assessment of participants’ depression levels, studies used the CES-D questionnaire (n=5), the BDI...
| Study | Primary outcome | Measure tool and scoring | Baseline depression score, mean (SD) Intervention(s)/control | Post-treatment and follow-up depression scores and differences from baseline, mean (SD) Intervention(s)/control |
|-------|----------------|--------------------------|------------------------------------------------|----------------------------------------------------------------------------------------------------|
| Bower et al 29 | Fatigue | BDI-II (0–63; higher is worse) | 15.5 (7.5)/14.3 (7.5) | PT: 12 weeks: 7.5 (5.8)/11.6 (7.1); groups differed significantly 50.3%/18.8% reduction in symptoms
FU: 3 months: 9.9 (8.0)/10.5 (7.9); groups did not significantly differ 36.1%/32.2% reduction in symptoms |
| Cantarero-Villanueva et al 38 | Fatigue | POMS (0–60; higher is worse) | 52.39 (12.14)/52.42 (11.01) | PT: 8 weeks: 47.15 (9.34)/52.40 (10.91); groups differed significantly 10%/0.04% reduction in symptoms
FU: 6 months: 48.17 (8.94)/55.30 (12.12); groups differed significantly 8% reduction/5.5% increase in symptoms |
| Naumann et al 34 | Physiological function, QoL, depression, fatigue | BDI (0–63; higher is worse) | Ex: 11.7 (2.7)/ExC: 15.0 (3.03)/C: 15.3 (3.10)/8.9/1 (2.89)† | PT: 8 weeks†: Ex: 8.1 (1.31)/ExC: 11.0 (1.48)/C: 15.0 (1.51)/10.91 (1.44); Ex and ExC intervention groups differed significantly with control group 30.7%/26.6%/2%/22.5% reduction in symptoms |
| Cantarero-Villanueva et al 33 | Fatigue | POMS (0–60; higher is worse) | 48.55 (9.31)/52.25 (11.55) | PT: 8 weeks: 45.58 (9.68)/53.71 (11.60); groups differed significantly 6.1% reduction/2.8% increase in symptoms
FU: 6 months: 46.03 (8.94)/55.30 (12.12); groups differed significantly 5.2% reduction/0.8% increase in symptoms |
| Ergun et al 42 | Cytokine levels | BDI (0–63; higher is worse) | Supervised: 7.75 (6.69)/home based: 9.05 (8.18)/educational: 7.5 (7.95)† | PT: 12 weeks: supervised: 4.70 (4.10)/home based: 8.88 (10.48)/educational: 5.15 (5.18); groups did not significantly differ 39.4%/1.9%/31.3% reduction in symptoms |
| Spahn et al 35 | Fatigue | HADS (0–21; higher is worse) | 5.3 (3.6)/6.4 (3.4) | PT: 10 weeks: 3.8 (3.7)/5.7 (3.4); groups did not significantly differ 28.3%/10.9% reduction in symptoms
FU: 3 months: 5.3 (4.3)/6.0 (4.3); groups did not significantly differ 0%/6.3% reduction in symptoms |
| Chandwani et al 26 | Physical and mental components of QoL | CES-D (0–60; cut-off score ≥16) Yoga: 15.4 (1.5)/stretching: 11.7 (0.8)/wait list: 15.1 (1.4) | Groups did not significantly differ at any of the four time points PT: 6 weeks: 17.3 (1.4)/17.8 (1.1)/15.8 (1.4) 12.3%/52.1%/4.6% increase in symptoms
FU: 1 month: 13.1 (1.7)/11.6 (1.4)/12.3 (1.3) 14.9%/0.6%/18.5% reduction in symptoms
FU: 3 months: 13.9 (1.7)/9.6 (1.4)/12.9 (1.6) 9.7%/17.9%/14.6% reduction in symptoms
FU: 6 months: 13.9 (1.8)/10.4 (1.4)/11.5 (1.3) 9.7%/11.1%/23.8% reduction in symptoms |
| Courneya et al 39 | Depression | CES-D short form (0–30; cut-off score ≥8) | High: 6.3 (5.1)/combined: 5.8 (5.0)/standard: 5.6 (5.9) | Groups did not significantly differ at any of three time points (1/3 and 2/3 through chemotherapy, postchemotherapy) FU: high: 5.9 (0.33)/combined: 6.4 (0.32)/standard: 6.8 (0.33)‡ 6.3% reduction/10.3%/21.4% increase in symptoms |
| Saxon et al 32 | NS indices of psychological health status (depression/ perceived stress, HPA axis regulation and immune function) | BDI-II (0–63; higher is worse) | 11.3 (7.6)/10.2 (5.5) | FU: 6 months: 5.1 (4.9)/6.1 point reduction clinically meaningful)/7.9 (6.0); groups differed significantly 54.9%/22.5% reduction in symptoms |
| Steindorf et al 30 | Fatigue | CES-D (linearly rescaled to 0–100, cut-off score ≥8) | 26(17)/28(17) | PT: 12 weeks: 25 (18)/25 (17); groups did not significantly differ 3.8% reduction/10.7% increase in symptoms |
| Rock et al 8 | QoL (vitality and functioning) | CES-D (0–60; cut-off score ≥16) | 9.9 (0.50)/9.7 (0.50) | FU: 6 months: 11.4 (0.44)/10.6 (0.44); groups did not significantly differ 15.1%/9.3% increase in symptoms
12 months: 11.9 (0.45)/10.9 (0.47); groups did not significantly differ 20.2%/12.4% increase in symptoms
24 months: 11.8 (0.47)/9.9 (0.47); groups differed significantly in favour of control group 19.2%/2% increase in symptoms |

Continued
(n=4), the HADS (n=3) and the POMS (n=2). Depression was the sole primary outcome measure in only one study,\(^39\) while in three more studies,\(^32\) \(^34\) \(^40\) depression was included either as primary or not as psychosocial/psychological outcome. In eight studies, primary outcomes included fatigue,\(^29\) \(^30\) \(^33\) \(^35\) \(^37\) \(^38\) \(^41\) and in three quality of life,\(^31\) \(^34\) \(^36\) and behaviour change, leisure time physical activity and cytokine levels (n=1 each).

The median age of the included breast cancer survivors was 52 years. In all studies, women had been diagnosed with 0–IIIc stage breast cancer. When reported, the majority of participants were postmenopausal (75.2%), white (73.5%), married (68.9%), employed (67.9%) and well educated (59.1%). Participants had completed cancer treatment prior to physical activity intervention in eight studies,\(^29\) \(^31\)–\(^35\) \(^37\) \(^38\) \(^41\) while in six studies\(^30\) \(^36\) \(^37\) \(^39\)–\(^41\) participants were undergoing adjuvant therapy, that is, chemotherapy and/or radiation therapy during exercise intervention (table 3).

### Exercise intervention characteristics

In 11 studies, the length of the interventions ranged from 6 (shortest\(^36\)) to 12 weeks and from 16 to 52 weeks (longest)\(^32\) \(^37\) \(^39\) in the remaining 3 studies. The reported exercise frequency was 2–3 sessions per week for the majority of the studies, while duration varied from 30 to 90 min per session. Consequently, weekly exercise duration ranged from 90 to 270 min. Exercise intensity also varied widely, from low to vigorous (high), with moderate intensity being most frequently reported. Many studies reported that intensity was determined and adjusted/prescribed following the American Cancer Society (ACS), the American Heart Association (AHA) and the American College of Sports Medicine (ACSM) recommendations and guidelines.

Types of exercise used in interventions solely or in combination included aerobic, resistance, aerobic and yoga exercises. More specifically, two studies involved a yoga intervention,\(^29\) \(^36\) three\(^35\) \(^39\) \(^40\) only aerobic, two studies applied resistance intervention programmes and six a combination of aerobic and resistance training programme.\(^32\)–\(^34\) \(^37\) \(^38\) \(^42\) When reported, activities for aerobic exercises included walking and/or the use of treadmill, elliptical, cross-trainer, cycling/rowing ergometer, various movements in water, fast arm movements and whole-body aerobic and step exercises. For resistance exercise, whole-body activities with or without the use of equipment (elastic/resistance/Thera bands, machines, dumbbells, stability balls, etc) were used. Of the 14 interventions, 12 involved supervised exercise sessions, while 2 included only home-based sessions. All studies had over 80% up to as high as 99% retention rates, while adherence rates, when reported, varied from 70% to 92.7%, and the majority of the studies observed no adverse events related to exercise (data not shown).

Table 4 summarises exercise intervention characteristics of the reviewed studies.

### Table 1

| Study | Measure tool and scoring | Primary outcome | Baseline depression score, mean (SD) | Intervention(s)/control | Post-treatment and follow-up depression scores and differences from baseline, mean (SD) |
|-------|--------------------------|-----------------|-------------------------------------|------------------------|---------------------------------------------------------------------------------|
| Schmidt et al\(^41\) | CES-D (linearly rescaled to 0–100, cut-off score >38) | Fatigue | 20.3 (10.7)/20.3 (9.9) | PT: 12 weeks | 20.4 (12.8)/21.1 (13.2); groups did not significantly differ 0.5% reduction/3.9% increase in symptoms |
| Travier et al\(^37\) | Fatigue | HADS (20-item Dutch version) | 2.5 (3.1)/2.4 (2.7) | PT (18 weeks) | NR. Groups did not significantly differ at PT (18 weeks) and FU (36 months) |
| Gokal et al\(^40\) | Physical social measures (depression included) | Psychosocial measures (depression included) | HADS: 5.52 (3.79)/6.68 (4.00) | POMS-SF: 4.92 (5.31)/6.68 (5.72) | PT: HADS: 4.44 (3.37)/6.16 (2.21); groups did not significantly differ 19.6%/7.8% reduction in symptoms POMS-SF: 1.68 (2.01)/6.44 (4.99); groups differed significantly 65.8%/3.6% reduction in symptoms |

*Significant reduction in depression score from baseline (P<0.05). †Adjusted mean (SE). ‡Average adjusted mean score (SE). §Adjusted mean (SE). ¶Significant difference from baseline. **Significant difference from baseline (P<0.05). ***Significant difference from baseline (P<0.01). ****Significant difference from baseline (P<0.001). **Significant difference from baseline (P<0.0001). \[Significant difference from baseline (P<0.00001). \]
Effects of exercise interventions on depressive symptoms

Based on the fourteen reviewed randomised control trials, which included 1701 participants in total, we found that reduction in depressive symptoms showed a small to moderate effect in depressive symptoms in favour of the exercise (figure 2), $g = -0.38$ (95% CI $-0.89$ to $0.13$, $P=0.14$). The heterogeneity between studies was moderate ($\chi^2=57.24$, df=13, $P<0.00001$; $I^2=77\%$) (figure 3).

Effects from the type of exercise interventions on depressive symptoms

Aerobic exercise interventions

With regard to the type of the exercise intervention, aerobic interventions yielded a large and significant effect on depression at the last follow-up measurement compared with the control groups (figure 4), $g = -1.23$ (95% CI $-1.97$ to $-0.49$, $P=0.001$). There was no substantial heterogeneity ($\chi^2=1.43$, df=2, $P=0.49$; $I^2=0\%$). The mean length of these interventions was 12.66±3 weeks, 120 min of moderate aerobic exercise per week.

Resistance exercise interventions

In addition, the resistance exercise interventions yielded a small and less significant effect in favour of the exercise group, $g = -0.37$ (95% CI $-4.15$ to $3.41$, $P=0.85$). There was no substantial heterogeneity ($\chi^2=0.03$, df=1, $P=0.86$; $I^2=0\%$). The mean length of these interventions was 12 weeks, 120 min of moderate resistance exercise per week.

Aerobic and resistance exercise interventions

The six aerobic and resistance exercise interventions yielded a moderate effect in favour of exercise, $g = -0.79$ (95% CI $-1.64$ to $0.07$, $P=0.07$). The heterogeneity was moderate ($\chi^2=17.82$, df=5, $P=0.003$; $I^2=72\%$) (figure 5). The mean length of these interventions was 13±6 weeks, 165 min of moderate aerobic and resistance exercise per week.

Yoga exercise interventions

The two yoga supervised interventions showed no statistically significant differences in depression compared with the control group, $g = 1.31$ (95% CI $-1.85$ to $4.47$, $P=0.42$). There was no substantial heterogeneity ($\chi^2=0.66$, df=1, $P=0.42$; $I^2=0\%$). The mean length of these interventions was 9±3 weeks, 180 min of low yoga exercise per week.

Effects from the duration of exercise interventions on depressive symptoms

Exercise duration: up to 12 weeks

Exercise duration up to 12 weeks yielded a moderate to large effect, $g = -1.69$ (95% CI $-2.66$ to $-0.73$, $P=0.0006$). The heterogeneity was low ($\chi^2=13.32$, df=9, $P=0.15$; $I^2=32\%$) (figure 6).

Exercise duration: over 12 weeks

Exercise duration over 12 weeks yielded a small and less significant effect, $g = -0.13$ (95% CI $-0.47$ to $0.73$, $P=0.68$).
### Table 2 Methodological quality assessment

| Study                      | Random allocation | Concealed allocation | Baseline similarity | Blinding of participants | Blinding of therapists | Blinding of assessors | Measures of key outcomes more than 85% of participants | Intention-to-treat analysis | Between-group statistical comparisons | Point measures and measures of variability | Total |
|----------------------------|-------------------|----------------------|---------------------|--------------------------|------------------------|-----------------------|--------------------------------------------------------|-------------------------------|------------------------------------------|-------------------------------------------|--------|
| Bower et al                | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 8      |
| Cantarero-Villanueva et al | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 6      |
| Naumann et al              | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 7      |
| Cantarero-Villanueva et al | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 7      |
| Ergun et al                | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 6      |
| Spahn et al                | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 7      |
| Chandwani et al            | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 7      |
| Courneya et al             | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 7      |
| Saxton et al               | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 7      |
| Steindorf et al            | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 8      |
| Rock et al                 | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 7      |
| Schmidt et al              | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 6      |
| Traver et al               | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 7      |
| Gokal et al                | ×                  | ×                    | ×                   | ×                        | ×                      | ×                     | ×                                                      | ×                             | ×                                        | ×                                          | 5      |

**Discussion**

In this literature review, we used studies published in the last years in order to assess the effects of physical activity and exercise interventions on depressive symptoms in breast cancer survivors. The main analysis indicates that exercise has a small to moderate effect (g=−0.38) on depression mood compared with the control groups. The heterogeneity was high (I²=77%), and the results from the methods of Begg and Egger et al yielded no evidence of publication bias. This indicates that exercise is beneficial to breast cancer survivors compared with inactivity.

The heterogeneity was high (I²=91%) for the effect of exercise interventions on depressive symptoms in breast cancer survivors. Exercise interventions in patients under treatment yielded a moderate effect (g=−0.54; 95% CI −1.16 to 0.08; P=0.09). The heterogeneity was high (I²=86%). Exercise interventions in patients post-treatment yielded a small and less significant effect (g=−0.05; 95% CI −0.95 to 0.85; P=0.91). The heterogeneity was high (I²=86%).
### Table 3: Sample and breast cancer characteristics

| Study, first author, year, country | Actual years of trial | Age of participants (years), mean (SD) | Sample size (N) | Race/ethnicity % | Body mass index (kg/m²), mean (SD) | Marital status (married %) | Employment status (%) | Income status (high %) | Education (>high school %) | Cancer stage | Time of measurement (since diagnosis or treatment) at baseline or timing | Menopausal status (postmenopausal %) |
|------------------------------------|-----------------------|----------------------------------------|-----------------|-----------------|-------------------------------------|--------------------------|---------------------|------------------|--------------------------|--------------|-------------------------------------------------------------------|-------------------------------------|
| Schmidt (2015) Germany            | 2010–2013             | 52.2 (9.9)/ 53.3 (10.2)                | 52/49           | NR              | 25.7 (4.6)/ 26.3 (4.9)              | NR                       | NR                  | NR               | NR                       | 0–III       | During adjuvant chemotherapy                                        | NR                                  |
| Courneya (2014) Canada            | 2008–2011             | 50.1 (8.8)/50.5 (9.4)/ 49.2 (8.4)     | 101/104/96      | White 84.7      | 25.2 (4.5)/ 28.2 (6.5)/ 26.0 (4.9) | 64.5                     | 41.9                | 54.3             | 64.8                     | 0–III C     | Initiating adjuvant chemotherapy                                   | NR                                  |
| Steindorf (2014), Germany         | 2011–2013             | 55.2 (9.5)/56.4 (8.7)                 | 80/80           | NR              | 26.9 (5.4)/ 27.6 (4.8)              | NR                       | NR                  | NR               | NR                       | 0–III       | During radiotherapy                                                 | NR                                  |
| Chandwani (2014) USA              | 2006–2009             | 52.38 (1.35)/ 51.14 (1.32)/ 52.11 (1.34) | 53/56/54       | White 64.7      | 26.5 (4.6)/ 26.3 (4.9)              | NR                       | 67.5                | 57               | 55.7                     | 74.3         | Undergoing radiotherapy                                             | NR                                  |
| Traver (2015), Netherlands        | 2010–2013             | 49.7 (8.2)/ 49.5 (7.9)                | 102/102         | NR              | 25.8 (4.4)/ 26.8 (5.2)              | 76                       | NR                  | NR               | 40.7                     | 0–III       | Within 6 weeks of diagnosis during chemotherapy                    | 38.2                                |
| Gokai (2016) UK                   | 2012–2013             | 52.08 (11.7)/ 52.36 (8.9)             | 25/25           | NR              | 27.20 (4.82)/ 28.25 (5.83)          | 76                       | 86                  | NR               | 22                       | 0–III       | During chemotherapy                                                  | 62                                  |
| Cantarelo-Villanueva (2012), Spain| 2009–2010             | 49(9)/48(9)                           | 38/40           | NR              | 61                                  | 58.2                     | NR                  | 43.2             | 0–III A                  | Finished coadjuvant treatment except hormone therapy               | 65.6                                |
| Naumann (2012) USA                |                       | 49.0 (10.0)/ 49.0 (8.2)/ 51.8 (11.5)  | 11/12/10        | NR              | 27.3 (1.50)/ 27.5 (1.49)/ 27.4 (1.49) | NR                       | NR                  | NR               | NR                       | 0–III       | Within 12 months of treatment completion except hormone therapy    | NR                                  |
| Bower (2012) USA                  | 2007–2010             | 54.4 (5.7)/53.3 (4.9)                 | 16/15           | White 87        | 24.2 (5)/25.3 (3.4)                 | 74                       | NR                  | 83.8             | 58                       | 0–II        | At least 6 months post-treatment                                    | 100                                 |
| Cantarelo-Villanueva (2013), Spain| 2009–2010             | 49 (7)/47 (8)                         | 34/34           | NR              | 63                                  | 57.4                     | NR                  | 44.2             | 0–III A                  | Finished oncology treatment except hormone therapy in the previous 18 months | 72.1                                |
| Spahn (2013) Germany              |                       | 58.1 (8.5)/ 55.3 (11.4)               | 32/32           | NR              | 26.6 (4.1)/ 26.9 (4.3)              | NR                       | NR                  | NR               | NR                       | I–III       | Completed treatment except hormone therapy at least 3 months before | NR (menopausal transition)          |
| Ergun (2013) Turkey                |                       | 49.65 (8.25)/55.05 (6.85)/ 50.30 (10.37) | 20/20/20       | NR              | 26.55 (4.40)/ 28.64 (6.15)/ 50.30 (10.37) | 77                       | 47                  | NR               | 38                       | 0–III       | Completed treatment                                                 | 100                                 |

Continued
Table 3 Continued

| Study, first author, year, country | Actual years of trial | Age of participants (years), mean (SD) Intervention(s)/control | Sample size (N) Intervention(s)/control | Race/ethnicity % | Body mass index (kg/m²), mean (SD) Intervention(s)/control | Marital status (married %) | Employment status* (%), Education (>high school) % | Income status (high %) | Cancer stage | Time of measurement (since diagnosis or treatment at baseline or timing) | Menopausal status (postmenopausal %) |
|-----------------------------------|-----------------------|---------------------------------------------------------------|----------------------------------------|-----------------|-----------------------------------------------------------|---------------------------|-------------------------------------------------|------------------------|-------------|------------------------------------------------------|--------------------------|
| Saxton et al (2014), UK NR         | 55.8 (10.5) / 55.3 (8.6) | 44/41 White 99                                                | 29.7 (3.5) / 31.1 (8.7)                | 68.2            | NR                                                        | NR                       | NR                                             | NR                     | 0–III       | Completed treatment 3–18 months previously            | NR                       |
| Rock et al (2015), USA 2010–2012  | 56.4 (9.5) / 56.0 (9.47) | 344/348 White 79                                               | >25 for both groups                    | 66.9            | 91.6                                                      | NR                       | 85.7                                           | I–III                  | Completed treatment                                    | 87.4                     |

*Employed and retired and on sick leave. †Indicates original articles describing details about participant characteristics and/or intervention design. ‡Adjusted mean (SE).

Although the majority of participants in the reviewed studies scored at baseline, it is important to be referred that exercise interventions had significant positive effects on depressive symptoms at baseline and those women under treatment. This finding may help physicians and care practices for the future research. Other studies have examined the role of exercise in breast cancer survivors under cancer treatment but, due to their moderate methodological quality, no safe conclusions can be drawn. 

According to the ACS guidelines, adults should be engaged in at least 150 minutes of moderate aerobic exercise programmes. Continuous aerobic exercise training increases the levels of nor-adrenaline, epinephrine, serotonine and β-endorphine hormones, which are responsible for depressive symptoms.

Resistance exercise interventions yielded no significant effect on depressive symptoms, g=−0.37, but due to the small number of studies included in this analysis, these findings should be interpreted with caution.


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## Table 4  Intervention characteristics

| Study                          | Intervention group(s) components | Control group(s) treatment | Intervention group(s) | Exercise activity | Length (weeks) | Frequency (sessions/week) | Duration/session (minutes) | Intensity |
|-------------------------------|----------------------------------|-----------------------------|------------------------|-------------------|----------------|---------------------------|---------------------------|-----------|
| Bower et al                  | Lyengar yoga                      | Health education classes    | Yoga, supervised       | Yoga              | 12            | 2                         | 90                        | Low       |
| Cantarero-Villanueva et al   | Multimodal physical training and recovery procedures | UC                          | AE, RE, stretching, massage, supervised | AE: unspecified work progressing to fast working with arms movement RE: Core stability exercises: soft-ball, fit-ball, elastic band | 8              | 3                         | 90                        | AE: moderate (ACSM/AHA rec) RE: 75% of maximum load, whole-body progressive 2–3 sets of 10–15 reps |
| Naumann et al                | Multimodal exercise training/exercise and counselling/counselling programme | UC                          | AE, RE, patient-specific rehab core training, flexibility, supervised | NR                | 8              | 3                         | 45–60                     | Moderate (ACSM rec) |
| Cantarero-Villanueva et al   | Deep-water aquatic exercise programme | UC                          | AE, RE, mobility, stretching, supervised | AE: different horizontal movements RE: exercises progressively with equipment (pool noodles, pull buoy, swimming board) | 8              | 3                         | 60:10 warm up, 40 (5–15 AE+RE), 10 cool down | AE: moderate (ACSM/AHA rec) RE: whole-body progressive 2–3 sets of 10–15 reps BPRES (ACSM/AHA rec) |
| Ergun et al                   | Supervised exercise/home-based exercise | Education programme | AE, RE, stretching, relaxation, supervised/AE, home based | AE: brisk walking, RE: Thera band whole-body, semisquats | 12             | 3                         | 75: 45: AE+RE (10 warm up), 30 Walking/30 | RE: moderate, AE: moderate |
| Spahn et al                   | Multimodal mind-body programme (nutrition counselling, relaxation, physical exercise, stress reduction, cognitive restructuring, hydrotherapy) | Home-based walking intervention | AE, supervised (weeks 1, 3, 10) and home based | Walking | 10             | 3                         | 30                        | HR: 180– (chronological age:10) bpm |
| Chandwani et al              | Yoga                      | Stretching/wait list | Yoga, supervised | Yoga: treadmill, elliptical, cycling/rowing ergometer or combination | 16.4          | 3                         | 60                        | Low       |
| Courneya et al               | High AE programme/combined AE+RE programme | Standard AE programme (25–30min vigorous ACSM and ACS rec) | AE, RE, supervised | AE: four leg exercises, five upper-body exercises | 24             | 3                         | 49:30AE+10–15 RE | AE: vigorous average high: 65.2%, combined: 67.4% of VO2 peak RE: 60%–75% of estimated 1 RM, 2 sets of 10–12 reps |
| Saxton et al                 | Multimodal exercise and dietary advice programme | UC                          | AE, RE, supervised | AE: treadmill, cross-trainer, cycling/rowing ergometer RE: resistance bands, hand weights, stability balls | 24             | 3                         | 60                        | Low       |
| Steindorf et al              | Progressive resistance training | Muscle relaxation | RE, supervised, group | Machine-based resistance exercises, three leg exercises, five upper body exercises | 12             | 2                         | 60                        | 60%–80% of 1 RM 1–3 sets of 8–12 repetitions (ACSM rec) |
| Rock et al                   | Intensive exercise and weight loss programme | Written material on exercise and diet | Unsupervised and home based | Machine-based resistance exercises, three leg exercises, five upper body exercises | 12             | 2                         | 60                        | 60%–80% of 1 RM 1–3 sets of 8–12 repetitions (ACSM rec) |
| Schmidt et al                | Progressive resistance training | Muscle relaxation | RE, supervised | Machine-based resistance exercises, three leg exercises, five upper body exercises | 12             | 2                         | 60                        | Low       |

Continued
Table 4  Continued

| Study                  | Intervention group(s) components | Control group(s) treatment | Exercise mode, supervised versus home based in intervention group(s) | Exercise activity | Length (weeks) | Frequency (sessions/week) | Duration/session (minutes) | Intensity |
|-----------------------|---------------------------------|---------------------------|---------------------------------------------------------------------|------------------|----------------|--------------------------|---------------------------|-----------|
| Travier et al94       | Individualised exercise programme | UC                        | AE, RE, supervised                                                  | AE: interval training, mode NR                                     | 18             | 2                        | 60:5 warm up, 25 AE+RE, 5 cool down | AE: Alternating at (3×2 min to 2×7 min) or below (3×4 min decreasing to 1×7 min) ventilatory threshold HR RE: 45%–75% of 1 RM, 1–2 sets of 10–20 repetitions |
| Gokal et al86         | Self-managed progressive programme | AE, home based            | Walking                                                             | 12               | 3             | 30                       | Moderate (Department of Health, Physical Activity, Health Improvement and Prevention rec, 2004) |

ACS, American Cancer Society; ACSM, American College of Sports Medicine; AE, Aerobic; AHA, American Heart Association; BRPES, Borg Rating Perceived Exertion Scale; RE, Resistance; RM, Repetition Maximum; UC, Usual Care.

Limitations and future research

The primary study included the primary outcomes of interest and the secondary outcomes that were identified as the secondary outcome in the majority of the studies. Furthermore, the small sample sizes (less than 100 participants) have led to the comparison of different definitions of depression symptoms among women. The findings from the current study showed that exercise is a significant alternative way to decrease depressive symptoms among breast cancer survivors, even those under treatment, with moderate aerobic exercise interventions being most effective than other interventions with duration up to 135 min per week for up to 12 weeks. The high retention and adherence rates reported in most studies in conjunction with the recording of minimum adverse events related to exercise encourage in adverse events and safety of exercise interventions.

From clinical practice, it might be worth offering exercise interventions starting as early as possible after diagnosis to help survivors.

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From clinical practice, it might be worth offering exercise interventions starting as early as possible after diagnosis to help survivors.
Figure 3 Forest plot of effect sizes gauging impact of exercise on depression.

Figure 4 Forest plot of effect sizes gauging impact of the aerobic exercise on depression.

Figure 5 Forest plot of effect sizes gauging impact of the aerobic and resistance exercise on depression.

exercise intensity was not possible given that the 11 out of 14 included studies used moderate intensity in their exercise protocols.

Despite those limitations, we provide concrete evidence that exercise is associated with beneficial outcomes in breast cancer survivors. Future studies should seek to recruit depressed cancer survivors regardless of their willingness to participate in exercise interventions at first, by screening all potential participants and subsequently offering advice through physicians and oncology healthcare professionals about the biological and psychological positive effects of exercise during and after breast cancer treatment. Accordingly, large randomised controlled trials should include diverse ethnic and minority groups as well as other subgroups of breast cancer survivors, such as younger women and women who are of a lower level of education or unemployed, in order to identify those who will mostly benefit regarding depressive symptoms from exercise intervention.

CONCLUSIONS

Depressive symptoms and depressive mood are a major psychosocial side effect of breast cancer diagnosis and treatment and are associated with poor adherence to treatment plan and reduced survival rates. Thus, effective treatments are of utmost importance. Engaging in regular physical activity is known to improve physical fitness and psychological well-being of breast cancer survivors. Regarding depression mood, exercise has been viewed as a cost-effective and non-invasive treatment alternative.

In the present literature analyses, we confirmed that exercise provides a small to moderate reduction in depression mood among breast cancer survivors. The average of ≥135 min per week for up to 12 weeks of supervised, moderate, aerobic exercise is more beneficial for depressive symptoms for patients under or after treatment. It is possible due to difficulty handling the burden of the disease, that women who suffer from depressive
symptoms either precancer or due to cancer diagnosis are not willing to participate in exercise interventions. Cancer survivors should try to avoid inactivity. Physicians and medical care providers should suggest physical activity in order to optimise physical and psychological symptoms that are related to breast cancer. Nevertheless, exercise can be safely recommended to women with mild or clinical levels of depressive symptoms as there are no negative side effects of exercise participation throughout the course of cancer survivorship.

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