ORIGINAL RESEARCH

Effects of exercise intervention in breast cancer survivors: a meta-analysis of 33 randomized controlled trails

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Background: Exercise is associated with favorable outcomes in cancer survivors. The purpose of this meta-analysis is to comprehensively summarize the effects of exercise intervention in breast cancer survivors.

Methods: A systematic search of PubMed, Elsevier, and Google scholar was conducted up to March 2015. References from relevant meta-analyses and reviews were also checked.

Results: Thirty-three randomized controlled trials were included in this meta-analysis, including 2,659 breast cancer survivors. Compared with the control group, quality of life was significantly improved in exercise intervention group, especially in mental health and general health subscales of short form 36 questionnaire, as well as emotion well-being and social well-being subscales of the Functional Assessment of Cancer Therapy. Besides, exercise alleviated the symptoms of depression and anxiety in the exercise group. Furthermore, exercise was also associated with positive outcomes in body mass index, lean mass, and muscle strength. In addition, the serum concentration of insulin, insulin-like growth factor-II, and insulin-like growth factor binding protein-1 was significantly reduced in exercise intervention group. However, based on the current data of this meta-analysis, there were no significant differences in sleep dysfunction or fatigue between groups.

Conclusion: Our study suggested that exercise intervention was beneficial to breast cancer survivors. Therefore, exercise should be recommended to this patient group.

Keywords: exercise, quality of life, depression, BMI, insulin

Introduction

Breast cancer is one of the main causes of cancer deaths in women,[1] which was responsible for 23% of total cancer cases and 14% of cancer deaths.[2] With the improvements in early detection and treatment, the number of cancer survivors continued to increase, in which women with breast cancer accounted for 22% of total cancer survivors in 2012.[3] However, the problems related to breast cancer and cancer treatment, such as cardiac toxicity of adjuvant systemic therapy,[4,5] arm or shoulder problems, body image,[6] change in social life, fear,[7] and poorer quality of life[8] were negatively associated with the overall well-being of breast cancer survivors.

A growing body of evidence indicated that exercise intervention results in beneficial outcomes in cancer patients. Some studies had suggested that exercise increased cardiorespiratory fitness,[9] physical performance,[10] and reduced overall mortality.[11] There were also studies demonstrating that exercise was associated with improvements in the symptom of depression,[12] body image, self-esteem,[13] and quality of life,[14–16] though some conclusions were not inconsistent in terms of fatigue.[17]

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Previously, these effects of exercise intervention in breast cancer patients had been assessed in several meta-analyses and systematic reviews.[18–22] However, some of them only summarized some of effects related to intervention,[18,19] or compared the effects of group exercise with individual exercise.[20] Others either only focused on one special symptom,[21] or evaluated the efficacy of Tai Chi Chuan alone.[22] Moreover, new evidences in recent years have not been included. Thus, we aim to comprehensively summarize the effects of exercise intervention on breast cancer patients based on the available data from randomized controlled trials.

Methods
Literature search
We searched PubMed, Elsevier, and Google Scholar up to March 2015. The reference lists of relevant systematic reviews and meta-analyses were also examined to identify additional studies. The search terms used in this meta-analysis were related to breast cancer (breast neoplasm, cancer, tumour, tumor, carcinoma) and exercise (exercise, physical activity, sport, weight training).

Inclusion criteria
Studies were considered eligible if they met the following criteria: 1) were written in English; 2) adopted a randomized controlled trial design, comparing exercise intervention group with control group (usual care, maintain current activity level, or waitlist); 3) included adults diagnosed with breast cancer; and 4) evaluated the effects of exercise in breast cancer patients.

Studies were excluded if: 1) included mixed cancer populations, including other types of cancer patients; 2) included other types of intervention (exercise intervention combined with diet); and 3) exercise merely focused on upper limb or arm.

Data extraction
Relevant data were independently extracted by GQ Zhu and X Zhang with a standard excel template, including 1) characteristics of the study and participants (first author, year of publication, mean age, sample size); 2) content of exercise intervention: exercise type, timing (before, during, or after treatment), and the frequency, intensity, and duration of intervention; 3) outcomes of intervention (quality of life, depression, anxiety, fatigue, muscle strength, body composition, physiological markers); and 4) assessment methods. Any disagreements were checked and discussed until a consensus was reached.

Methodological quality assessment
The methodological quality of the studies were independently assessed by two reviewers (GQ Zhu and YL Wang) using the Delphi criteria list,[23] which is a set of nine criteria for quality assessment of randomized controlled trials. It was hard to blind the participants and providers in the interventional study. Therefore, participants blinding and provider blinding were not rated, and we only assessed the blinding of the outcome assessors. Each item was scored as yes (+) or no (−).

Statistical analysis
The outcomes were assessed if the data were available in at least two studies. For continuous outcomes, standardized mean differences with 95% confidence intervals (CIs) were calculated, with $P<0.05$ considered statistically significant. Statistical heterogeneity among studies was measured by I^2 test, in which values above 25% and 50% were considered as the indicative of moderate and high heterogeneity, respectively.[24] A fixed-effect model was adopted when $I^2<50\%$; otherwise, a random-effect model was used.

In the presence of heterogeneity, subgroup analysis was performed based on the measurement methods or the type of exercise. Besides, sensitivity analysis was carried out to evaluate the influence of a single study to the overall estimate. Publication bias was estimated through Begg's test and Egger's linear regression, with $P<0.10$ consumed as an indication of publication bias.[25] All analyses were conducted using Review Manager Version 5.3 (Cochrane Collaboration, Copenhagen, Denmark) and Stata 12.0 (College Station, TX, USA).

Results
Study selection
A total of 3,429 records were identified from the database (Figure 1). After screening the titles and abstracts, the full texts of 161 articles were further reviewed for eligibility. Finally, 33 articles[26–58] were included and assessed for methodological quality, with 128 articles excluded in which the aim, intervention type, or design of the study failed to meet the inclusion criteria.

Characteristics of the exercise interventions
There were 2,659 breast cancer patients, with the mean age of 54 (46.3–60.6) years (Table 1). The main types of exercise interventions reported in this meta-analysis were aerobic, resistance, and stretching exercises. Besides, there were also six studies on yoga intervention,[28,39,42,4,50,52] two studies on tai chi chuan,[35,55] and one on dancing.[46] Twenty Five studies
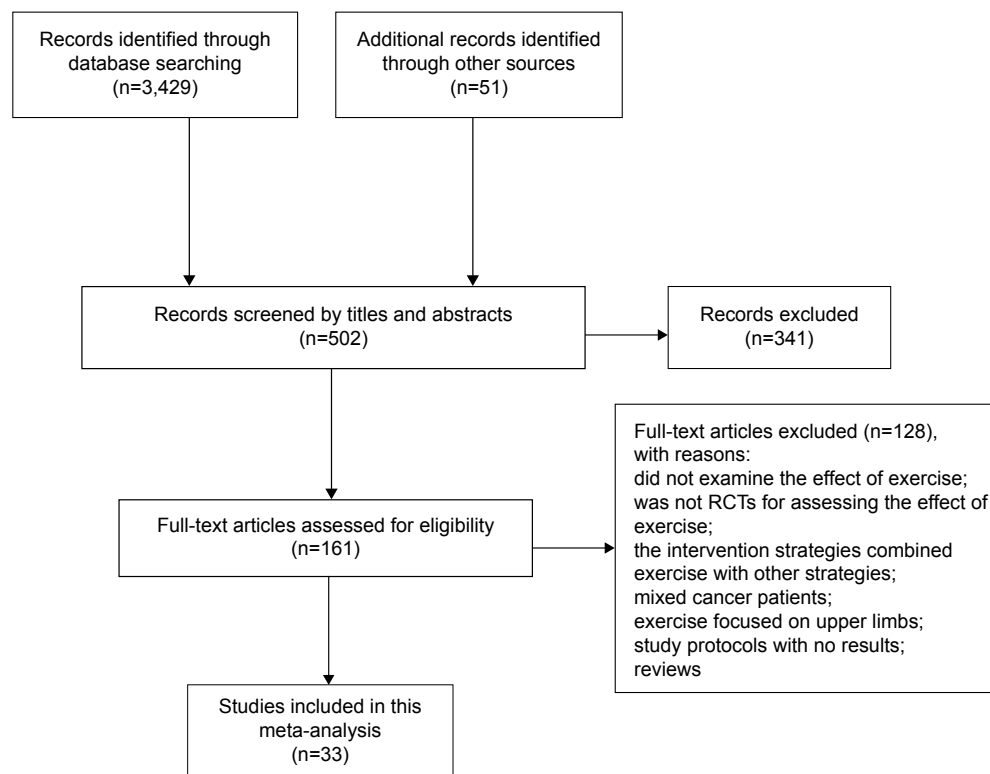
Figure 1 Flow diagram of study selection.
Abbreviation: RCT, randomized controlled trial.

performed intervention after treatment,[26,28,29,31,33–36,38,40,41,44,46–58] seven studies during treatment,[20,27,32,37,43,45,51] and the remaining two studies before treatment.[39,42] The duration of intervention lasted from 6 weeks to 12 months, with the frequency of intervention varying from two times a week to every day. The intensity of exercise also varied from low to vigorous in different situations, among which the moderate intensity was most frequently reported.

Methodological quality of included studies

We assessed 33 articles according to the Delphi criteria list, and seven criteria were examined in each of the study. In all, 14 studies met five criteria,[26,30,35,38–41,51–54,56–58] 12 studies more than five criteria,[29,31,33,34,36,37,42,44,46,48–50] and the remaining 7 studies less than five criteria.[27,28,32,43,45,47,55] Of these, 19 studies failed to conceal the allocation,[26–28,32–34,38–40,43,45,47,52–58] and 22 studies did not blind the outcome assessor.[27–28,30–32,35–36, 38–41,43,45–47,51–55,57,58] Besides, 14 studies were not intention-to-treat analysis (Table 2).[26–28,30,32,35,37,41,43,45,47,49,55,56]

Pooled effect estimates for outcome measures

In this meta-analysis, we examined the effects of exercise intervention on quality of life, psychological outcomes,

body composition, physical function and symptom, and physiological markers of breast cancer survivors. A total of 53 outcomes were evaluated, which were reported in at least two studies (Table 3).

Results of quality of life

The quality of life was reported as an outcome in 18 studies,[26,30,31,36,37,42,45,51–58] among which 10 studies used the Functional Assessment of Cancer Therapy-Breast (FACT-B) and the Functional Assessment of Cancer Therapy–General (FACT-G) questionnaire,[31,36,37,41,45,46,51,53–55] 4 studies the Medical Outcomes Study Short Form health survey (SF-36) questionnaire,[26,46,51,57] and two studies Treatment of Cancer-Quality of Life questionnaire (EORTCQoLC30).[42,58] The other 4 studies used SF-12 health survey (SF-12),[52] the Functional Assessment of Cancer Therapy–Anemia,[30] the World Health Organization Quality of Life (WHOQOL-BREF),[45] and the Cancer Rehabilitation Evaluation System-Short Form,[56] respectively. We only pooled the outcomes that data could be extracted in at least two studies. Therefore, the data of 12 studies, involving 15 quality life domains, were included in this meta-analysis.[26,31,36,37,41,45,46,51,53–55,57]

Measured by SF-36 or MOS SF-36, the exercise intervention significantly improved the mental health (I^2=0%,

Table 1 Characteristics of 33 studies included in this meta-analysis

Year	Study	Author	Mean age (SD) Intervention/control	The exercise type of intervention/control	Number of subjects in intervention/control groups
2006	26	Basen-Engquist et al	55.7 (11.1)/54.4 (11.7)	Lifestyle program/standard care	35/25
2007	27	Battaglini	56.6 (16)/57.5 (23)	Cardiovascular, resistance, flexibility/control group	10/10
2014	28	Bower et al	54 (5.4)	Iyengar yoga/health education	16/15
2011	29	Cantarero-Villanueva et al	48 (9)/49 (9)	Aerobic, resistance, neck–shoulder mobility, self-massage/usual care	38/40
2007	30	Courneya et al	49.5/49/49	Aerobic/resistance/usual care	82/78/82
2007	31	Daley et al	51.6 (8.8)/50.6 (8.7)/51.1 (8.6)	Aerobic exercise/exercise–placebo/usual care	34/46/38
2006	32	Drouin et al	49.4 (7.0)/51.9 (10)	Walking/placebo stretching	8/13
2009	33	Irwin et al	56.5 (9.5)/55.1 (7.7)	Walking/usual care	37/38
2009	34	Irwin et al	56.5 (9.5)/55.1 (7.7)	Walking/usual care	37/38
2011	35	Janelsins et al	54.33 (10.64)/52.7 (6.67)	Tai Chi Chuan/no exercise control	9/10
2008	36	Milne et al	55.2 (8.4)/55.1 (8.0)	Aerobic, resistance, stretching: immediate/delayed exercise group	29/29
2007	37	Mutrieet et al	51.3 (10.3)/51.8 (8.7)	Group exercise program: aerobic, resistance/usual care	101/102
2007	38	Nikander et al	52.5 (6.4)/51.3 (7.3)	Aerobic exercise/daily activity	14/14
2009	39	Rao et al	NR	Yoga/brief supportive therapy	45/53
2013	40	Rogers et al	58.0 (6.1)/53.7 (13.9)	Aerobic, resistance/usual care	15/13
2009	41	Rogers et al	52 (15)/54 (8)	Walking/usual care	21/20
2009	42	Vadiraja et al	NR	Yoga/brief supportive therapy	45/53
2009	42	Vadiraja et al	NR	Yoga/brief supportive therapy	45/53
2008	43	Battaglini	57.5 (23)/56.6 (16)	Cardiovascular, stretching, resistance/control group	10/10
2003	44	Courneya et al	59 (5)/58 (6)	Cycle ergometers/no train	24/28
2008	45	Hwang et al	46.3 (7.5)/46.3 (9.5)	Stretching, aerobic exercise/self-shoulder stretching	17/23
2005	46	Sandel et al	59.7 (9.8)/59.5 (13.3)	Dance and movement program/a waitlist control group	19/19
2007	47	Moadel et al	55.11 (10.07)/54.23 (9.81)	Yoga/waitlist control group	84/44
2003	48	Fairey et al	59 (5)/58 (6)	Cycle ergometers/control group	25/28
2005	49	Schmitz et al	53.3 (8.7)/52.8 (7.6)	Weight training: immediate/delayed group trained	42/43
2012	50	Bower et al	54.4 (5.7)/53.3 (4.9)	Lyengar yoga/health education	16/15
2009	51	Cadmus et al	54.5 (8.2)/54 (10.9)	Home-based exercise program: phone guide/usual care	25/25
2009	51	Cadmus et al	56.5 (9.5)/55.1 (7.7)	Supervised exercise intervention/usual care	37/37

Timing	Intensity	Frequency	Duration	Outcomes
Posttreatment	Moderate	NR	6 months	Physical performance, QoL
During treatment	Low-moderate: 40%–60% of predicted maximum exercise capacity	2 times/week, ≤60 minutes	21 weeks	Body composition, muscle strength
Posttreatment	NR	NR	12 weeks	Inflammation-related gene expression, circulating markers of proinflammatory cytokine, salivary cortisol
Posttreatment	Aerobic: ACSM recommendations; resistance; 75% maximum load and increase	3 times/week; 90 minutes	8 weeks	Fatigue, cortisol, IgA salivary levels, α-amylase activity, cervical–shoulder range of motion
During treatment	AET: 60%–80% of VO2 max; RET: 60%–70% of their estimated one repetition maximum	3 times/week	Mean 17 (9–24) weeks	QoL, physical fitness, body composition, psychosocial functioning, fatigue
Posttreatment	Moderate-intensity (65%–85% of age-adjusted HR maximum and RPE of 12–13)	3 times/week, 50 minutes	8 weeks	QoL, depression, fatigue exercise behavior, aerobic fitness
During treatment	50%–70% of measured maximum HRs	3–5 times/week, 20–45 minutes	7 weeks	Erythrocyte measures: RBC, HCT, HB, peak VO2
Posttreatment	Moderate (60%–80% of predicted maximal HR)	3 times (supervised) +2 times (own)/week, 150 minutes	6 months	Body composition, physical activity levels
Posttreatment	Moderate (60%–80% of predicted maximal HR)	3 times (supervised) +2 times (own)/week, 150 minutes	6 months	Insulin, IGF-1, IGFBP-3
Posttreatment	Moderate	3 times/week, 60 minutes	12 weeks	Insulin, insulin-related molecules and cytokines, body composition
Posttreatment	NR	3 times/week	12 weeks	QoL, fatigue, social physical anxiety, aerobic fitness
During treatment	Moderate (50%–75% of age adjusted maximum HR)	3 times/week, 45 minutes	12 weeks	QoL, depression, physical activity, shoulder mobility
Posttreatment	Vigorous	3 times/week	12 weeks	Feasibility, efficacy, physical performance
Before treatment	NR	Daily/60 minutes		QoL
Posttreatment	Moderate	150 minutes weekly aerobic, 2 sessions/week resistance	3 months	Inflammatory-related serum markers, cardiorespiratory fitness, muscle strength, body composition, fatigue, sleep
Posttreatment	Moderate	150 minutes/week	12 weeks	Feasibility, healthy outcome: aerobic fitness, muscle strength, body composition, QoL, sleep
Before treatment	NR	Daily/60 minutes	NR	QoL
Before treatment	NR	Daily/60 minutes	NR	The total caloric intake, fatigue, body composition, aerobic fitness
During treatment	40%–60% of predicted maximum exercise capacity	2 times/week, ≤60 minutes	6 months	Peak oxygen consumption, QoL, fatigue, self-esteem, happiness, body composition
Posttreatment	70%–75% of maximal oxygen consumption in untrained subjects	3 times/week, 15–35 minutes	15 weeks	QoL, fatigue, ROM of shoulder, pain
During treatment	50%–70% of the age-adjusted HR maximum	3 times/week, 50 minutes	5 weeks	QoL, shoulder (ROM), body image
Posttreatment	NR	2 times/weeks for 6 weeks, 1 time/week for 6 weeks, 50–60 minutes	12 weeks	QoL, fatigue, distressed mood, spiritual well-being
Posttreatment	NR	1.5-hour weekly classes	12 weeks	Fasting insulin, glucose, insulin resistance, IGFs, IGFBPs
Posttreatment	(70%–75%) of peak oxygen consumption	3 times/week, 15–35 minutes	15 weeks	Body composition, insulin, glucose, IGF axis variables
Posttreatment	Upper body: symptoms allowed; lower body: the most weight lift	2 times/week, 60 minutes	12/6 months	Vigor, depression, sleep, stress, physical performance
During treatment	Moderate-vigorous: 60%–80% of predicted maximal HR	5 times/week, 30 minutes	6 months	Happiness, depression, anxiety, stress, self-esteem, QoL
Posttreatment	Moderate-vigorous: 60%–80% of predicted maximal HR	5 times/week, 30 minutes	6 months	Happiness, depression, anxiety, stress, self-esteem, QoL

(Continued)

Table 1 (*Continued*)

Year	Study	Author	Mean age (SD) Intervention/control	The exercise type of intervention/control	Number of subjects in intervention/control groups
2009	52	Danhauer et al	54.3 (9.6)/57.2 (10.2)	Yoga class group/waitlist group	13/14
2012	53	Hayes et al	51.2 (8.8)/52.2 (8.6)/53.9 (7.7)	Face-to-face/telephone exercise: aerobic strength intervention/ usual care	67/67/60
2012	54	Littman et al	60.6 (7.1)/58.2 (8.8)	Facility-based and home-based Viniyoga intervention/waitlist control group	27/27
2004	55	Mustian et al	52(9)	Tai Chi Chuan/psychosocial support	11/10
2006	56	Ohira et al	53.3 (8.7)/52.8 (7.6)	Weight training/control group	43/43 (39/40)
2012	57	Sprod et al	54.33 (3.55)/52.7 (2.11)	Tai Chi Chuan exercise/standard support therapy	9/10
2012	58	Saarto et al	52.3/52.4	Step aerobics class and circuit training class (supervised), endurance training (home)/control group	263/237

Abbreviations: ACSM, American college of sports medicine; AET, aerobic exercise training; BMI, body mass index; HB, hemoglobin; HCT, hematocrit; HR, heart rate; IFGBP, insulin-like growth factor binding protein; IGF, insulin-like growth factor; IL, interleukin; NR, not reported; QoL, quality of life; RBC, red blood cell; RET, resistance exercise training; VO2 peak, peak oxygen consumption; IgA, immunoglobulin A; SD, standard deviation; ROM, range of motion; RPE, rating of perceived exertion.

$P=0.006$, 95% CI: 0.11, 0.62, Figure 2) and general health ($I^2=95\%$, $P=0.02$, 95% CI: 0.70, 8.48, Figure 2) compared with the control groups. Besides, exercise was associated with a significant increase in emotion well-being ($I^2=2\%$, $P=0.0006$, 95% CI: 0.12, 0.43, Figure 2) and social well-being subscales ($I^2=0\%$, $P=0.01$, 95% CI: 0.19, 1.69, Figure 2) of the Functional Assessment of Cancer Therapy. The pooled results of five studies showed a significant increase in breast cancer subscale of the Functional Assessment of Cancer Therapy from exercise ($I^2=15\%$, $P=0.000001$, 95% CI: 1.85, 4.04) (Table 3).[36,37,44,54,57]

However, substantial heterogeneity was observed for some outcomes. There was no evidence of publication bias except for SF-36 role-emotion ($P=0.062$, Table 3).

Results of psychological outcomes
Pooled data from three studies indicated that the self-esteem score was higher in the intervention group ($I^2=0\%$, $P=0.02$, 95% CI: 0.18, 2.22), measured by the Rosenberg Self-Esteem Scale (Table 3).[29,44,51] Meanwhile, exercise intervention reduced depression ($I^2=2\%$, $P=0.001$, 95% CI: −3.36, −0.80, Figure 3) and anxiety score ($I^2=0\%$, $P<0.0001$, 95% CI: −4.76, −1.58, Figure 3), which were of clinical importance. However, the pooled results showed no difference in happiness and stress between intervention and control groups, assessed by the 2-item Fordyce Happiness Measure and the Perceived Stress Scale (Table 3).

Furthermore, exercise led to improvement in the positive and negative attitudes in breast cancer survivors, measured by the Positive and Negative Affect Schedule (PANAS), of

which the PANAS negative score decreased by 3.51 points ($I^2=76\%$, $P=0.02$, 95% CI: −9.92, −0.71) and the PANAS positive score increased by 4.46 points ($I^2=0$, $P<0.00001$, 95% CI: 2.48, 6.44) (Table 3). In addition, measured by the Functional Assessment of Chronic Illness Therapy–Spiritual, exercise was associated with positive effect in spirit compared with control groups ($I^2=0\%$, $P=0.02$, 95% CI: 0.76, 7.13) (Table 3).

No publication bias were detected in any of the results, except the Pittsburgh Sleep Quality Index ($P=0.082$). High heterogeneity was only found for PANAS negative (Table 3).

Results of body compositions
Seven parameters were included in this meta–analysis (Table 3). Body mass index (BMI) was examined in nine studies, and the pooled results indicated it reduced significantly with exercise ($I^2=0\%$, $P<0.00001$, 95% CI: −1.09, −0.47, Figure 4).[34,35,37,38,40,41,44,49,54] Besides, the pooled results of four studies showed that exercise was associated with significant increase in lean mass compared with control groups ($I^2=57\%$, $P=0.04$, 95% CI: 0.08, 2.25) (Table 3).

Similarly, body fat percentage ($I^2=57\%$, $P=0.02$, 95% CI: −3.33, −0.35) and fat mass ($I^2=0\%$, $P=0.05$, 95% CI: −4.83, −0.04) were significantly reduced in the exercise intervention groups (Table 3). However, there were no significant differences on waist circumference, hip circumference, and waist-to-hip ratio between intervention and control groups.

No publication bias was observed, with only moderate heterogeneity for lean mass and body fat (Table 3).

Timing	Intensity	Frequency	Duration	Outcomes
Posttreatment	NR	1 times/week, 75 minutes	10 weeks	Feasibility, aerobic fitness, muscle strength, body composition, QoL, fatigue, sleep
Posttreatment	Individually tailored	4 times/week, 45 minutes	8 months	QoL, body function, fatigue, lymphedema, BMI, menopausal symptoms, anxiety, depression, pain
Posttreatment	NR	5 times/week, ≥75 minutes	6 months	QoL, fatigue, body composition
Posttreatment	Moderate	3 times/week, 60 minutes	12 weeks	QoL, self-esteem
Posttreatment	NR	2 times/week	6 months	QoL, depression, body composition, upper and lower body strength
Posttreatment	NR	3 times/week, 60 minutes	12 weeks	IL-6, IL-8, IGF-I, glucose, insulin, cortisol, IGFBP-1, IGFBP-3, QoL
Posttreatment	86%–92% of maximal HR, 76%–85% of maximal VO2	3–4 times/week: 1 supervised +2/3 home, 60 minutes	12 months	QoL, fatigue, physical fitness, physical activity

Table 2 Methodological quality assessment of 33 randomized controlled trials

Study	Randomization	Conceal allocation	Similarity of baseline	Specified eligibility criteria	Blinding of outcome assessor	Point estimates and measures of reliability of primary outcome	Intention-to-treat analysis
Basen-Engquist et al, 2006[26]	+	−	+	+	+	+	−
Battaglini, 2007[27]	+	−	−	+	−	+	−
Bower et al, 2014[28]	+	−	+	+	−	+	−
Cantarero-Villanueva et al, 2011[29]	+	+	+	+	+	+	+
Courneya et al, 2007[30]	+	+	+	+	−	+	−
Daley et al, 2007[31]	+	+	+	+	−	+	+
Drouin et al, 2006[32]	+	−	+	+	−	+	−
Irwin et al, 2009[33]	+	−	+	+	+	+	+
Irwin et al, 2009[34]	+	−	+	+	+	+	+
Janelsins et al, 2011[35]	+	+	+	+	−	+	−
Milne et al, 2008[36]	+	+	+	+	−	+	+
Mutrieet et al, 2007[37]	+	+	+	+	+	+	−
Nikander et al, 2007[38]	+	−	+	+	−	+	+
Rao et al, 2009[39]	+	−	+	+	−	+	+
Rogers et al, 2013[40]	+	−	+	+	−	+	+
Rogers et al, 2009[41]	+	+	+	+	−	+	−
Vadiraja et al, 2009[42]	+	+	+	+	+	+	+
Battaglini, 2008[43]	+	−	+	+	−	+	−
Courneya et al, 2003[44]	+	+	+	+	+	+	+
Hwang et al, 2008[45]	+	−	+	+	−	+	−
Sandel et al, 2005[46]	+	+	+	+	−	+	+
Moadel et al, 2007[47]	+	−	−	+	−	+	−
Fairey et al, 2003[48]	+	+	+	+	+	+	+
Schmitz et al, 2005[49]	+	+	+	+	+	+	−
Bower et al, 2012[50]	+	+	+	+	+	+	+
Cadmus et al, 2009[51]	+	+	−	+	−	+	+
Danhauer et al, 2009[52]	+	−	+	+	−	+	+
Hayes et al, 2012[53]	+	−	+	+	−	+	+
Littman et al, 2012[54]	+	−	+	+	−	+	+
Mustian et al, 2004[55]	+	−	−	+	−	+	−
Ohira et al, 2006[56]	+	−	+	+	+	+	−
Sprod et al, 2012[57]	+	−	+	+	−	+	+
Saarto et al, 2012[58]	+	−	+	+	−	+	+

Table 3 Meta-analysis of the effect of exercise intervention in breast cancer survivors

Outcomes	Study	Number of subjects in intervention/control groups	I^2 (%)	P-value	95% CI	Publication bias (P-value)
The quality of life (SF-36)	10					
Mental health	4	125/116	18	0.03	1.04 (0.09, 2.00)	0.917
Role (physical)	4	125/116	95	0.95	0.11 (−3.54, 3.76)	0.829
Social function	3	106/97	0	0.18	−0.36 (−0.88, 0.16)	0.289
Vitality	3	106/97	61	0.16	1.35 (−0.53, 3.23)	0.936
Pain	3	106/97	98	0.33	2.58 (−2.65, 7.81)	0.418
General health	3	106/97	95	0.02	4.59 (0.70, 8.48)	0.113
Role (emotion)	3	106/97	13	0.6	−0.10 (−0.46, 0.26)	0.062
FACT-G	6	237/200	87	0.08	6.02 (−0.73, 12.76)	0.482
TACT: TOI	2	54/57	96	0.23	13.04 (−8.13, 34.20)	
FACT-G: social well-being	8	343/316	0	0.01	0.94 (0.19, 1.69)	0.889
FACT-G: function well-being	8	343/316	83	0.07	0.37 (−0.03, 0.77)	0.589
FACT-G: emotion well-being	8	343/316	2	0.0006	0.27 (0.12, 0.43)	0.889
FACT-G: physical well-being	8	343/316	88	0.15	1.53 (−0.57, 3.63)	0.574
FACT-B subscale	5	225/238	15	<0.00001	2.96 (1.87, 4.04)	0.906
FACT-B	6	241/230	85	0.08	0.46 (−0.05, 0.97)	0.235
Psychological outcomes						
The Rosenberg Self-Esteem Scale	3	185/192	0	0.02	1.02 (0.18, 2.22)	
The 2-item Fordyce Happiness Measure	2	87/90	0	0.66	1.34 (−4.64, 7.32)	
Depression	6	378/373	2	0.001	−2.08 (−3.36, −0.80)	0.236
Anxiety	5	341/361	0	<0.0001	−3.17 (−4.76, −1.58)	0.200
Positive and negative affect scale	3					
PANAS negative	3	142/150	76	0.02	−5.31 (−9.92, −0.71)	
PANAS positive	3	142/150	0	<0.0001	4.46 (2.48, 6.44)	
FACIT−Spiritual	2	97/58	0	0.02	4.04 (0.76, 7.13)	
The Perceived Stress Scale	2	78/77	0	0.08	−1.94 (−4.11, 0.22)	
Sleep dysfunction						
The Pittsburgh Sleep Quality Index	4	64/62	0	0.58	0.32 (−0.82, 1.46)	0.082
Body composition						
Body mass index	9	270/283	0	<0.0001	−0.78 (−1.09, −0.47)	0.599
Lean body mass/lean mass	4	246/252	57	0.04	1.17 (0.08, 2,25)	0.140
Body fat %	5	267/272	57	0.02	−1.84 (−3.33, −0.35)	0.376
Fat mass	2	169/174	0	0.05	−2.44 (−4.83, −0.04)	0.212
Waist-to-hip ratio	2	36/33	21	0.19	−0.02 (−0.04, 0.01)	
Waist circumference	3	103/105	0	0.71	0.17 (−0.70, 1.03)	
Hip circumference	2	64/65	0	0.94	−0.16 (−4.27, 3.94)	
Physical performance and function						
Fatigue	10	841/800	83	0.69	0.30 (−1.16, 1.75)	0.387
FACT−Fatigue subscale	3	120/134	46	0.17	2.75 (−1.22, 6.71)	
Fatigue Symptom Inventory	2	31/28	68	0.04	−0.85 (−1.68, −0.02)	
FACIT−Fatigue	4	469/410	0	0.96	0.04 (−1.2, 1.27)	
Muscle strength	5	235/236	48	0.0009	4.27 (1.76, 6.78)	0.272
VO2 peak, mL/kg/min	2	185/192	52	0.21	0.68 (−0.38, 1.75)	
VO2 peak, mL/min	2	185/192	46	0.19	0.06 (−0.03, 0.14)	
Physiological markers						
IL-6	4	46/45	70	0.36	1.01 (−1.14, 3.15)	
IL-6 change	4	46/45	69	0.02	1.46 (0.27, 2.65)	0.046
IL-8	2	21/20	76	0.07	1.38 (−0.09, 2.86)	
Glucose	3	71/77	0	0.35	0.27 (−0.29, 0.82)	
Glucose change	3	71/77	99	<0.00001	1.73 (1.36, 2.11)	0.687
Insulin	5	117/126	95	0.05	−6.79 (−13.64, 0.06)	
Insulin change	5	117/126	97	0.04	−4.98 (−9.26, −0.33)	0.353
IGF-1	5	119/126	99	0.47	7.46 (−12.94, 27.87)	
IGF-1 change	5	119/126	99	0.53	6.5 (−13.88, 26.89)	0.957
IGF-II	2	64/68	88	0.94	4.36 (−110.03, 118.75)	

(*Continued*)

Table 3 (*Continued*)

Outcomes	Study	Number of subjects in intervention/control groups	I^2 (%)	P-value	95% CI	Publication bias (P-value)
IGF-II change	2	64/68	0	<0.0001	−54.21 (−61.41, −47.00)	
IGFBP-1	4	82/88	46	<0.0001	−3.16 (−4.40, −1.91)	
IGFBP-1 change	4	82/88	0	<0.0001	−2.93 (−3.93, −1.93)	0.639
IGFBP-3	5	119/126	93	0.9	−0.2 (−3.24, 2.48)	0.830
IGFBP-3 change	5	119/126	86	0.55	0.49 (−1.11, 2.08)	

Abbreviations: FACT-B, Functional Assessment of Cancer Therapy–Breast Questionnaire; FACT-G, Functional Assessment of Cancer Therapy-General; FACIT–Spiritual, Functional Assessment of Chronic Illness Therapy–Spiritual well-being scale; IGF-I, insulin-like growth factor-I; IGF-II, insulin-like growth factor-II; IGFBP-1, insulin-like growth factor binding protein-1; IGFBP-3, insulin-like growth factor binding protein-3; IL, interleukin; PANAS, Positive and Negative Affect Schedule; SF-36, short form 36 questionnaire; VO2 peak, peak oxygen consumption; CI, confidence interval; TOI, Trial Outcome Index; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy–Fatigue Scale.
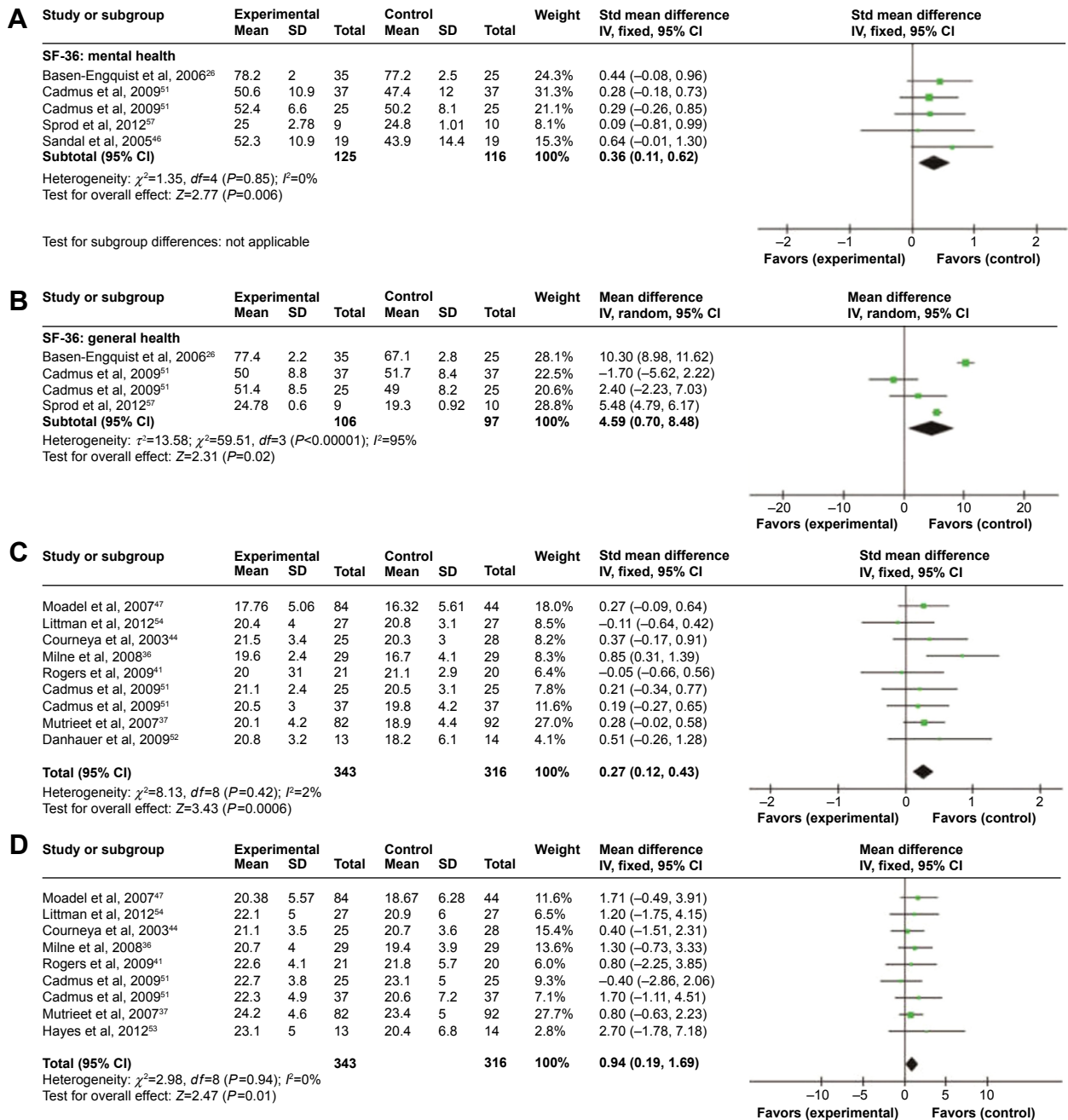

Figure 2 The association between exercise intervention and quality of life in breast cancer survivors.
Notes: (**A**) SF-36 mental health, (**B**) SF-36 general health, (**C**) FACT emotion well-being, and (**D**) FACT social well-being.
Abbreviations: CI, confidence interval; FACT, Functional Assessment of Cancer Therapy; SD, standard deviation; SF-36, short form 36 questionnaire; df, degree of freedom.

Results of physical function and symptom

Muscle strength was reported in five studies, which indicated significant improvement (I^2=48%, P=0.0009, 95% CI: 1.76, 6.78, Figure 5) in exercise intervention group. Besides, no significant improvement was showed on peak oxygen consumption, based on the data from two studies (Table 3).[27,30,34,40,41]

Fatigue was assessed in 12 studies, the pooled results of which indicated that there was no difference on fatigue between the intervention and control groups (Figure 6).[29,30,36,37,40,47,50,52–54,58] In the present of high heterogeneity, we performed the subgroup analysis stratified by the measurement method and the type of exercise intervention (Figure 6). However, the effect of exercise on the symptom of fatigue still remained insignificant in both of the subgroups, except small reduction in Fatigue

Symptom Inventory (I^2=68%, P=0.04, 95% CI: −1.68, −0.02). No evidence of publication bias was detected in any of the results (Table 3).

Results of physiological markers

Eight physiological markers were examined in this meta-analysis (Table 3). When the data of postintervention were used, only insulin (I^2=95%, P=0.05, 95% CI: −13.64, 0.06) and insulin-like growth factor binding protein (IGFBP)-1 (I^2=46%, P<0.00001, 95% CI: −4.40, −1.91) were significantly reduced after exercise intervention. However, based on the changed serum concentration of physiological markers after intervention (postintervention minus baseline), exercise significantly reduced the serum concentration of insulin (I^2=97%,
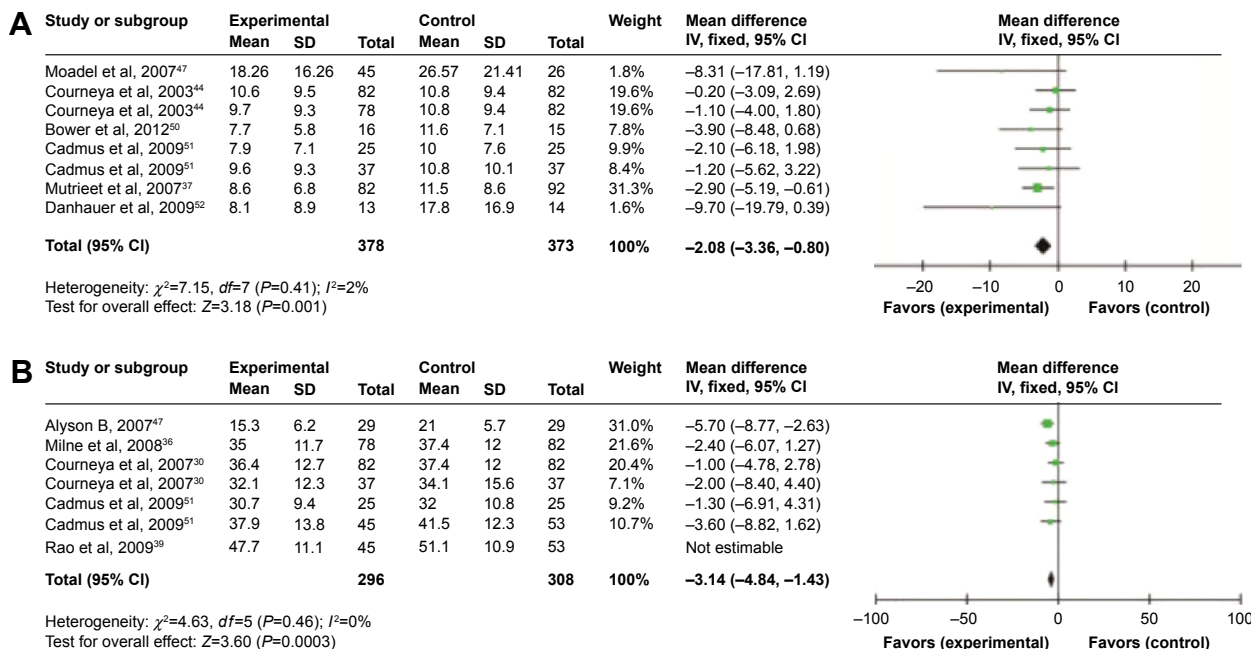
Figure 3 The association between exercise intervention and depression and anxiety in breast cancer survivors.
Notes: (**A**) Depression and (**B**) anxiety.
Abbreviations: CI, confidence interval; SD, standard deviation; *df*, degree of freedom.

Figure 4 The association between exercise intervention and body mass index in breast cancer survivors.
Abbreviations: CI, confidence interval; SD, standard deviation; *df*, degree of freedom.

Study or subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, fixed, 95% CI	Mean difference IV, fixed, 95% CI
Battaglini, 2008[43]	295.59	22.65	10	260.89	38.76	10	0.8%	34.70 (6.88, 62.52)	
Milne et al, 2008[36]	66.2	10.2	29	61.7	11	29	21.2%	4.50 (−0.96, 9.96)	
Courneya et al, 2003[44]	28.2	14.2	78	27.1	14.1	82	32.8%	1.10 (−3.29, 5.49)	
Courneya et al, 2003[44]	32.8	12.6	82	27.1	14.1	82	37.7%	5.70 (1.61, 9.79)	
Rogers et al, 2009[41]	68.4	15.5	15	67.1	16.2	13	4.5%	1.30 (−10.49, 13.09)	
Rogers et al, 2013[40]	80.3	27	21	64.9	19.7	20	3.0%	15.40 (0.98, 29.82)	
Total (95% CI)			**235**			**236**	**100%**	**4.27 (1.76, 6.78)**	

Heterogeneity: χ^2=9.61, df=5 (P=0.09); I^2=48%
Test for overall effect: Z=3.33 (P=0.0009)

Favors (experimental) Favors (control)

Figure 5 The association between exercise intervention and muscle strength in breast cancer survivors.
Abbreviations: CI, confidence interval; SD, standard deviation; df, degree of freedom.

A

Study or subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, random, 95% CI	Mean difference IV, random, 95% CI
FACIT-fetigue									
Moade et al, 2007[47]	36.56	10.85	45	34.77	13.58	26	3.7%	1.79 (−4.32, 7.90)	
Littman et al, 2012[54]	45	5.3	27	43.1	10.3	27	5.7%	1.90 (−2.47, 6.27)	
Courneya et al, 2003[44]	8.3	7.9	25	8.8	8.1	28	5.8%	−0.50 (−4.81, 3.81)	
Milne et al, 2008[36]	11.9	3.2	29	17.4	4.7	29	10.4%	−5.50 (−7.57, −3.43)	
Cantarero-Villanueva et al, 2011[29]	6.04	1.89	32	3.54	1.74	35		Not estimable	
Bower et al, 2014[28]	3.4	1.8	16	4.9	1.3	15	12.6%	−1.50 (−2.60, −0.40)	
Courneya et al, 2007[30]	36.3	9.4	82	34.9	12.5	82	7.4%	1.40 (−1.99, 4.79)	
Courneya et al, 2007[30]	36.8	10.4	78	34.9	12.5	82	7.1%	1.90 (−1.66, 5.46)	
Rogers et al, 2013[40]	4.2	1.8	15	4.2	1.6	13	12.3%	0.00 (−1.26, 1.26)	
Mutrieet et al, 2007[37]	40.3	10.4	82	36	12.1	92	7.5%	4.30 (0.96, 7.64)	
Hayes et al, 2012[53]	40.4	9.8393	67	41.8	10.0647	60	7.3%	−1.40 (−4.87, 2.07)	
Hayes et al, 2012[53]	41.7	10.2493	67	41.8	10.0647	60	7.1%	−0.10 (−3.64, 3.44)	
Danhauer et al, 2009[52]	39.8	12.4	13	32.6	15.5	14	1.5%	7.20 (−3.35, 17.75)	
Saarto et al, 2012[58]	2.4	9.0597	263	2.4	8.5958	237	11.7%	0.00 (−1.55, 1.55)	
Subtotal (95% CI)			**809**			**765**	**100%**	**−0.06 (−1.42, 1.30)**	

Heterogeneity: τ^2=3.52; χ^2=41.21, df=12 (P<0.0001); I^2=71%
Test for overall effect: Z=0.08 (P=0.93)

| **Total (95% CI)** | | | **809** | | | **765** | **100%** | **−0.06 (−1.42, 1.30)** | |

Heterogeneity: τ^2=3.52; χ^2=41.21, df=12 (P<0.0001); I^2=71%
Test for overall effect: Z=0.08 (P=0.93)
Test for subgroup differences: not applicable

Favors (experimental) Favors (control)

B

Study or subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, random, 95% CI	Mean difference IV, random, 95% CI
Yoga									
Moade et al, 2007[47]	36.56	10.85	45	34.77	13.58	26	2.7%	1.79 (−4.32, 7.90)	
Littman et al, 2012[54]	45	5.3	27	43.1	10.3	27	4.5%	1.90 (−2.47, 6.27)	
Bower et al, 2014[28]	3.4	1.8	16	4.9	1.3	15	12.3%	−1.50 (−2.60, −0.40)	
Danhauer et al, 2009[52]	39.8	12.4	13	32.6	15.5	14	1.0%	7.20 (−3.35, 17.75)	
Subtotal (95% CI)			**101**			**82**	**20.5%**	**0.49 (−2.46, 3.43)**	

Heterogeneity: τ^2=4.05; χ^2=5.55, df=3 (P=0.14); I^2=46%
Test for overall effect: Z=0.32 (P=0.75)

Aerobic + resistance + strenching									
Courneya et al, 2003[44]	8.3	7.9	25	8.8	8.1	28	4.5%	−0.50 (−4.81, 3.81)	
Milne et al, 2008[36]	11.9	3.2	29	17.4	4.7	29	9.4%	−5.50 (−7.57, −3.43)	
Cantarero-Villanueva et al, 2011[29]	3.54	1.74	32	3.92	1.96	35	12.8%	−0.38 (−1.27, 0.51)	
Rogers et al, 2013[40]	4.2	1.8	15	4.2	1.6	13	11.9%	0.00 (−1.26, 1.26)	
Mutrieet et al, 2007[37]	40.3	10.4	82	36	12.1	92	6.2%	4.30 (0.96, 7.64)	
Hayes et al, 2012[53]	40.4	9.8393	67	41.8	10.0647	60	5.9%	−1.40 (−4.87, 2.07)	
Hayes et al, 2012[53]	41.7	10.2493	67	41.8	10.0647	60	5.8%	−0.10 (−3.64, 3.44)	
Saarto et al, 2012[58]	2.4	9.0597	263	2.4	8.5958	237	11.0%	0.00 (−1.55, 1.55)	
Subtotal (95% CI)			**580**			**554**	**67.6%**	**−0.59 (−2.10, 0.91)**	

Heterogeneity: τ^2=3.11; χ^2=31.71, df=7 (P<0.0001); I^2=78%
Test for overall effect: Z=0.77 (P=0.44)

Aerobic									
Courneya et al, 2003[44]	36.3	9.4		82	34.9	12.5	6.1%	1.40 (−1.99, 4.79)	
Subtotal (95% CI)				**82**			**6.1%**	**1.40 (−1.99, 4.79)**	

Heterogeneity: not applicable
Test for overall effect: Z=0.81 (P=0.42)

Resistance									
Courneya et al, 2003[44]	36.8	10.4		78	34.9	12.5	5.8%	1.90 (−1.66, 5.46)	
Subtotal (95% CI)				**78**			**5.8%**	**1.90 (−1.66, 5.46)**	

Heterogeneity: not applicable
Test for overall effect: Z=1.05 (P=0.30)

| **Total (95% CI)** | | | | **841** | | **800** | **100%** | **−0.19 (−1.31, 0.92)** | |

Heterogeneity: τ^2=2.33; χ^2=41.50, df=13 (P<0.0001); I^2=69%
Test for overall effect: Z=0.34 (P=0.73)
Test for subgroup differences: χ^2=2.43, df=3 (P=0.49); I^2=0%

Favors (experimental) Favors (control)

Figure 6 The association between exercise intervention and fatigue in breast cancer survivors.
Notes: (**A**) Overall effect and (**B**) subgroup analysis based on the type of exercise intervention.
Abbreviations: CI, confidence interval; FACIT, Functional Assessment of Chronic Illness Therapy; SD, standard deviation; df, degree of freedom.
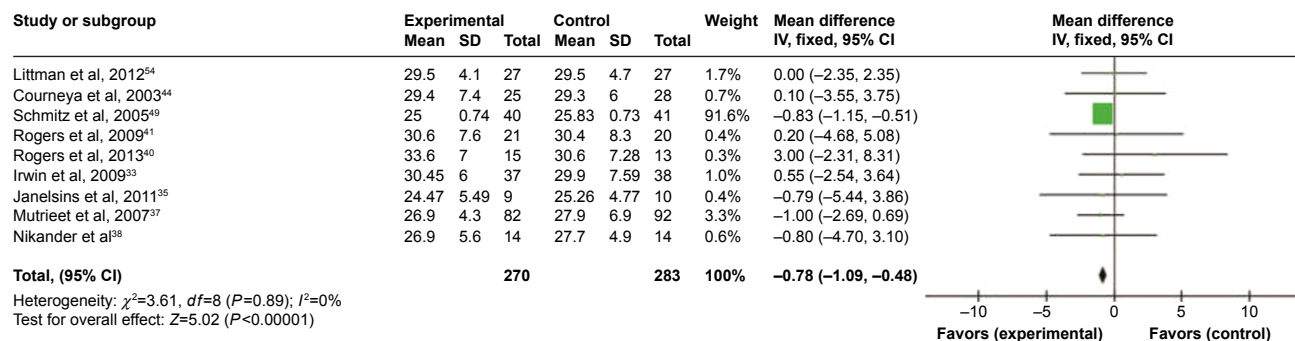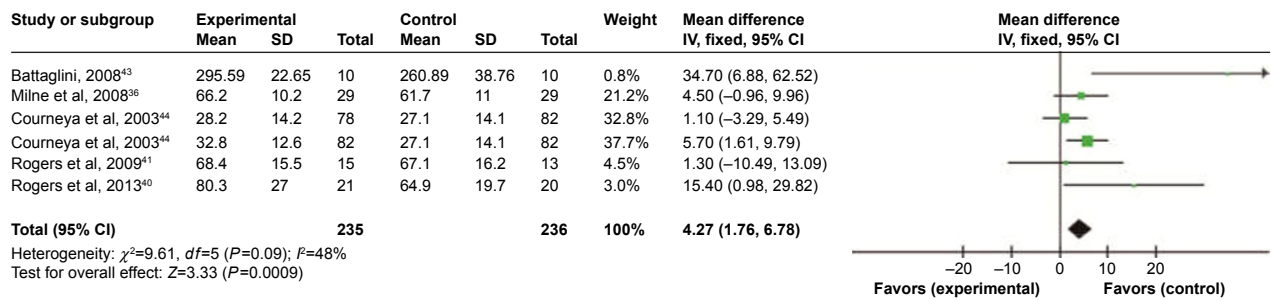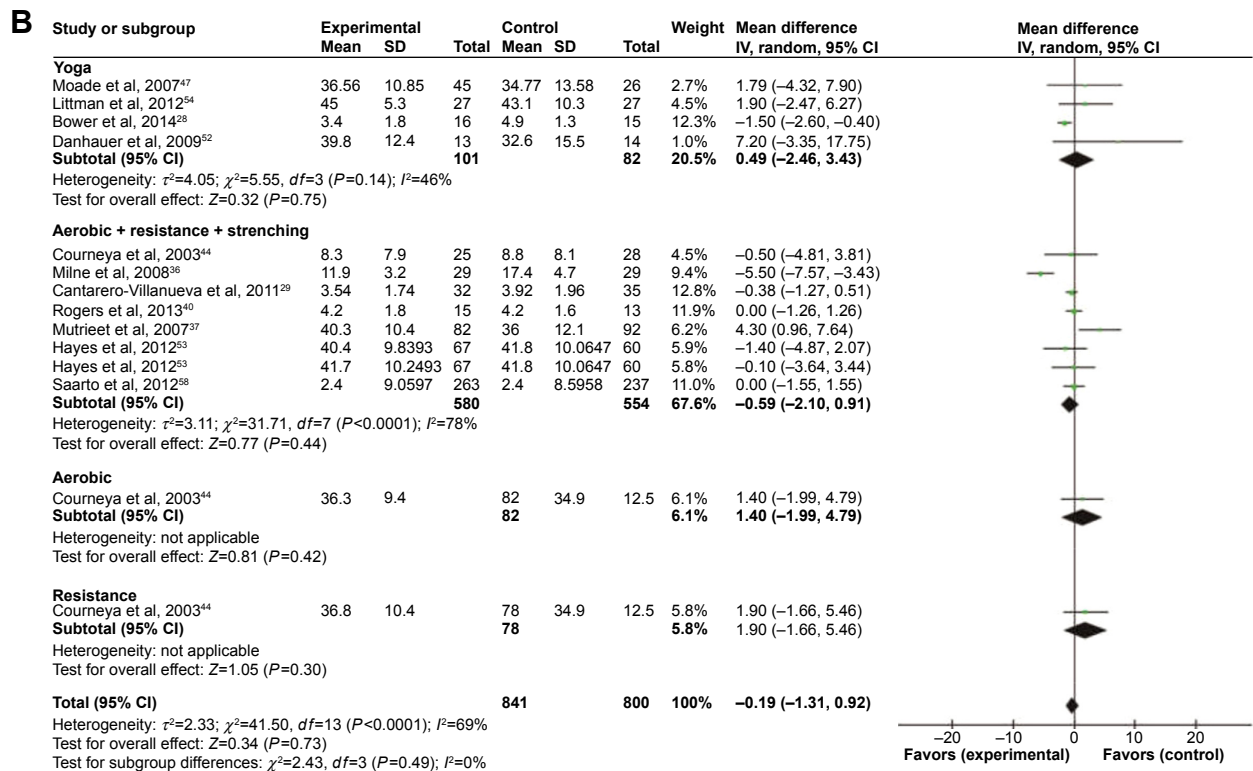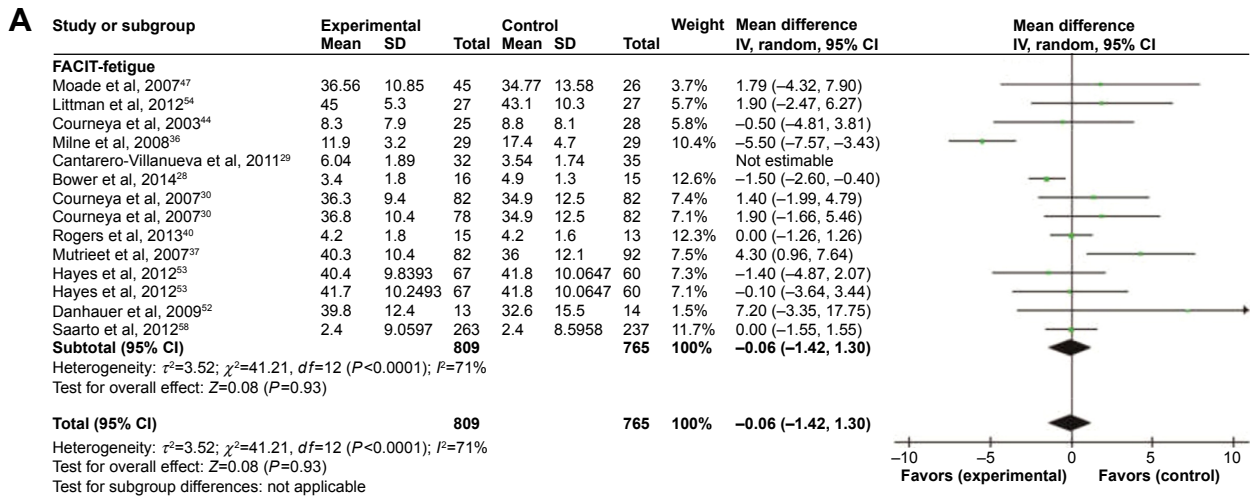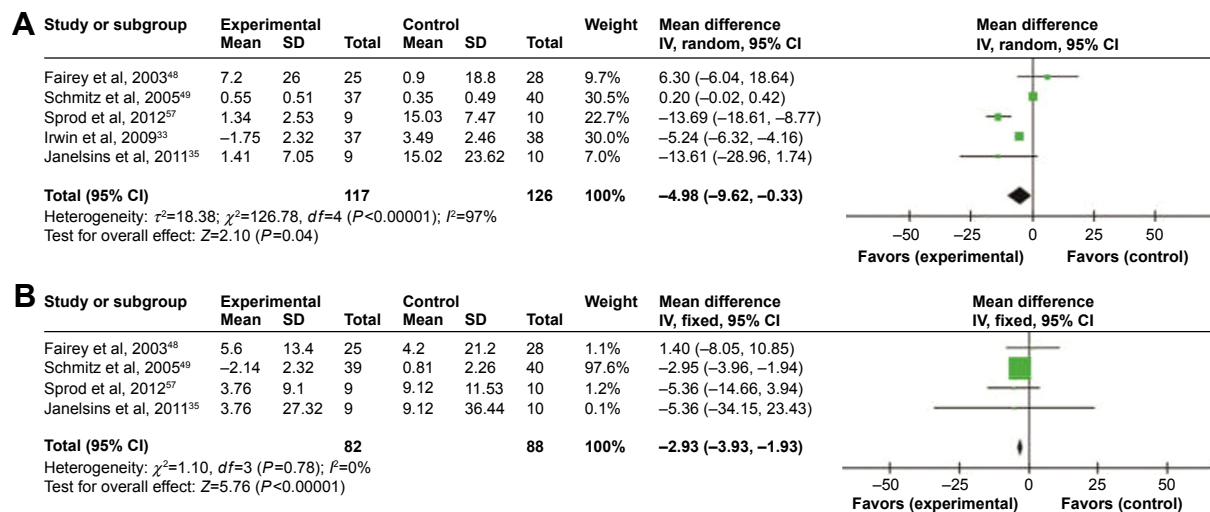
Figure 7 The association between exercise intervention and insulin and IGFBP-1 in breast cancer survivors.
Notes: (**A**) Insulin and (**B**) IGFBP-1.
Abbreviations: CI, confidence interval; IFGBP-1, insulin-like growth factor binding protein-1; SD, standard deviation; *df*, degree of freedom.

$P<0.00001$, 95% CI: -9.26, -0.33, Figure 7), IGFBP-1 ($I^2=0\%$, $P<0.00001$, 95% CI: -3.93, -1.93, Figure 7), and insulin-like growth factor (IGF)-II ($I^2=0\%$, $P<0.00001$, 95% CI: -61.41, -47.00). Significant increases were shown in interleukin (IL)-6 ($I^2=69\%$, $P=0.02$, 95% CI: 0.27, 2.65) and glucose ($I^2=99\%$, $P<0.00001$, 95% CI: 0.27, 2.65). There were substantial heterogeneity in some of the physiological markers, and evident publication bias was only observed in IL-6 ($P=0.046$) (Table 3).

Discussion

In this meta-analysis, we summarized the effects of exercise intervention on breast cancer survivors, including 53 outcomes reported from 33 articles. Results showed that exercise was associated with significant improvements in quality of life, self-esteem, and the response attitude toward life. Besides, it alleviated the symptoms of depression and anxiety in breast cancer survivors. In addition to the beneficial outcome in body composition, exercise also increased muscle strength in the intervention groups. Furthermore, the serum concentration of some physiological markers, such as insulin, IGF-II, and IGFBP-1, was significantly reduced after exercise intervention.

In line with previous meta-analyses,[19,59,60] the pooled results supported the evidences that exercise improved the quality of life in cancer patients. However, a significant improvement was shown in general health subscale of SF-36 in our meta-analysis, but not in general health scale of the Functional Assessment of Cancer Therapy.

Similarly, a statistically significant increase was only detected in the social function and emotion function scales of the Functional Assessment of Cancer Therapy, but not in the role emotion and social function subscales of SF-36. It was the same as the evidence of Fong who discovered that exercise improved SF-36 scores in physical function, social function, and mental health with mixed type of cancer survivors.[61] Thus, despite the fact that exercise was proved to improve quality of life, there were slight differences in the domains of quality life, owing to the differences in the features of patients and exercise, as well as measurement methods.

According to the sensitivity analysis of the Functional Assessment of Cancer Therapy, the study by Mustian was identified as an outlier: the timing of intervention was during treatment in the study by Milne, whereas, the other studies were posttreatment.[36] When excluding this outliers from analysis, the heterogeneity in the Functional Assessment of Cancer Therapy subscales (social well-being, function well-being, emotion well-being, physical well-being) decreased evidently ($I^2=0\%$, 27%, 20%, 0%, 8%, respectively).

The study by Basen-Engquist was also identified as an outlier, based on the sensitivity analysis of SF-36 subscales: in this study, the exercise intervention was lifestyle intervention, which encouraged participants to integrate activity into daily routine and perform activities they choose.[26] When this study was excluded, the heterogeneity was evidently decreased in vitality ($I^2=0\%$), body pain of SF-36 ($I^2=0\%$), and general health ($I^2=86\%$).

In our current meta-analysis, we only calculated the effect size of outcomes reported in at least two studies. Therefore, the data of life quality measured by the Functional Assessment of Cancer Therapy–Anemia,[30] the European Organization

for the Research and Treatment of Cancer-Quality of Life (EORTCQoLC30 questionnaire),[42,58] the Cancer Rehabilitation Evaluation System-Short Form,[56] and the WHOQOL-BREF were not pooled.[45] Even though all the five studies favored exercise intervention, only three of them reported a clinical significant improvement in quality of life on breast cancer survivors,[42,45,56] and the results in other two studies failed to reach statistical significance.[30,58]

We observed a significant improvement in depression, anxiety, and self-esteem in breast cancer patients, which were frequently reported in pervious meta-analyses and systematic reviews with mixed cancer patients.[59,61–64] We also discovered that the attitude toward life in intervention group was more positive than control group. The positive attitude played a critical role in the emotion well-being, which might have some correlation with improved quality of life in breast cancer survivors.

There was no clinical significant change on the symptom of fatigue between groups, based on the pooled results in our meta-analysis, which was consistent with a previous meta-analysis.[61] However, physical activity was reported to be associated with improvement on the symptom of fatigue in several meta-analyses, both breast and other cancer survivors.[19,59,62,65,66]

In the subgroup analysis based on the measurement methods, a significant decrease of fatigue was only observed in the Fatigue Symptom Inventory. We then stratified the results by the types of intervention, the results of which still remained insignificant. Even yoga, a "mind–body" exercise, had no significant effect on fatigue, which had been suggested to be associated with a moderate reduction of fatigue in a previous study.[67] We further performed sensitivity analysis, the results of which indicated the studies by Bower and Milne exerted substantial influence to the overall estimate.[28,36] However, when excluding the two studies, the fatigue level was increased in exercise intervention groups (I^2=50%, P=0.05, 95% CI: 0.02, 2.19), which had not been reported in previous meta-analysis. Given the current inconsistent conclusions, more researches are needed to further examine this effect.

Several system reviews and meta-analyses had suggested positive effects of exercise on peak oxygen consumption.[18,19,61,66] However, the pooled results of two studies observed no statistical significance change of peak oxygen consumption between groups, which might be attributed to the small size in our meta-analysis. Furthermore, owing to the lack of sufficient data, the outcomes, such as the 3-minute step test[52] and the figure-8 running test,[38] were not included in our meta-analysis, which also showed improvements compared with control groups.

Results indicated that exercise led to a statistically significant reduction in BMI and insulin. Each 5 kg weight gain might increase the breast cancer-specific mortality by 13% and all-caused mortality by 12%.[68] Besides, research showed that insulin was associated with BMI, and the increase of insulin was related to a twofold increased risk of breast cancer recurrence.[69] Thus, the decreased BMI and insulin from exercise might potentially contribute to a reduced risk of mortality and recurrence on breast cancer survivors.

Additionally, one study suggested that IGFBP-1 and IGFBP-5 as IGF-I antagonists might block mammary gland development.[70] However, pooled results showed that IGFBP-1 was significantly decreased in exercise intervention group, while the change of IGF-1 was insignificant. Contrary to previous results, two meta-analyses reported only IGF-I was reduced significantly, and no evidences of significant change were found in insulin, IGFBP-1, and glucose in both breast cancer patients or mixed cancer patients.[61,62] Therefore, given this inconsistency, we should treat the association between exercise and the change of physiological markers with caution, and more researches are needed before making a confirmed conclusion.

The sensitivity analysis of physiological markers identified two outliers: the study by Schmitz and Melinda, in which the duration of intervention lasted for 6 to 12 months, while the durations were 12 to 15 weeks in other studies.[34,39] Therefore, it is likely that the duration of exercise intervention is the source of heterogeneity among these results.

Limitations

In our meta-analysis, we only included published randomized control trails in two databases, though we further searched the relevant reference lists for potential articles, which may increase the risk of publication bias. Besides, there was a lack of consistency in terms of the outcomes reported and measurement methods among the studies. The outcomes, such as erythrocyte Levels,[32] salivary cortisol,[29] were reported in only one study respectively, and we, therefore, failed to calculate their effect sizes in present meta-analysis.

Similarly, the quality of life was measured by different methods, which made it difficult to combine the diverse outcomes. Therefore, we only pooled the outcomes of quality life components measured by the Functional Assessment of Cancer Therapy and SF-36, respectively, which were used in most of the studies.

Furthermore, some data could not be extracted in several studies, and we did not try to contact the authors for detailed information. In addition, we used the mean and

standard deviation of postintervention to calculate the effect sizes for most of the data, rather than the changes after the intervention, the results of which may be influenced by the differences at baselines.

Implications for future research and practice

The differences of intervention type, intensity, and duration might account for some variations in the effects of exercise, and we could have performed subgroup analysis based on these differences. However, it would lead to insufficient data to calculate the effect sizes of some outcomes. Therefore, future research should further explore the correlation between intervention effects and the exercise type, intensity, and duration.

Additionally, the survival outcomes in breast cancer survivors are likely to have some correlation with exercise intervention.[71,72] However, the studies included in our current meta-analysis failed to examine this association. Therefore, it is recommended that future studies examine the effects of exercise intervention on survival outcomes and determine whether exercise will provide benefit to the survival outcomes.

Taken together, the present evidences support the idea that exercise intervention is beneficial to breast cancer survivors, although it fails to identify the optimal type, timing, and intensity of exercise intervention. In addition, previous studies demonstrated that it was feasible and safe for various cancer patients to exercise during treatment,[73] without increasing the risk or exacerbating the symptom of lymphedema.[74] Nevertheless, some prospective longitudinal studies showed that the physical activity decreased during treatment.[75,76] The frequency of exercise was also lower off-treatment than prediagnosis in breast cancer patients.[77] Therefore, exercise intervention should be prescribed to breast cancer survivors, encouraging them to continue their established exercise habits or adopt a right type of exercise.

Conclusion

Though with some limitations, there are evidences that exercise was associated with beneficial outcomes in breast cancer survivors. Based on the results from 33 studies, exercise improved the quality of life and alleviated the symptoms of depression and anxiety in breast cancer survivors. There were also benefits on muscle strength and body composition. Besides, exercise intervention was associated with reduced serum concentration of insulin, IGF-II, and IGFBP-1. Therefore, on the basis of our current evidences, exercise should be recommended to breast cancer survivors.

Disclosure

The authors report no conflicts of interest in this work.

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