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A systematic review and meta-analysis of the safety, feasibility and effect of exercise in women with stage II+ breast cancer.

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Abstract

Objective: To systematically evaluate the safety, feasibility and effect of exercise among women with stage II+ breast cancer. **Data Sources:** CINAHL, Cochrane, Ebscohost, MEDLINE, Pubmed, ProQuest Health and Medical Complete, ProQuest Nursing and Allied Health Source, Science Direct and SPORTDiscus were searched for articles published prior to March 1, 2017. **Study selection:** Randomised, controlled, exercise trials involving at least 50% of women diagnosed with stage II+ breast cancer were included. **Data Extraction:** Risk of bias was assessed and adverse event severity was classified using the Common Terminology Criteria. Feasibility was evaluated by computing median (range) recruitment, withdrawal and adherence rates. Meta-analyses were performed to evaluate exercise safety and effects on health outcomes only. The influence of intervention characteristics (mode, supervision, duration and timing) on exercise outcomes were also explored. **Data Synthesis:** There were no differences in adverse events between exercise and usual care (risk difference: <0.01 [95% CI: –0.01, 0.01]), p=0.38). Median recruitment rate was 56% (1%–96%), withdrawal rate was 10% (0%–41%) and adherence rate was 82% (44%–99%). Safety and feasibility outcomes were similar, irrespective of exercise mode, supervision, duration, or timing. Effects of exercise for quality of life, fitness, fatigue, strength, anxiety, depression, body mass index and waist circumference compared with usual care were significant (standardised mean difference range: 0.17–0.77, p<0.05). **Conclusion**: The findings support the safety, feasibility and effects of exercise for those with stage II+ breast cancer, suggesting that national and international exercise guidelines appear generalizable to women with local, regional and distant breast cancer.

Key words: breast neoplasm, aerobic exercise, resistance exercise, exercise oncology.

There is growing scientific and community support to incorporate exercise into standard breast cancer care.[1] Previous systematic reviews have demonstrated a low risk of serious adverse events with exercise.[2-4] Specifically, no serious adverse events have been reported and over 80% of trials included in previous reviews have reported no exercise-related adverse events for individuals with cancer.[2-4] Exercise is also considered feasible. Previously reported recruitment rates have ranged between 20 to 70%[5], withdrawal rates have been low (<10%) and exercise adherence rates have been high (80–90%).[2-5] The health benefits of exercise both during and following treatment have also been well described in systematic reviews and meta-analyses.[3, 6, 7] Specifically, exercise improves fatigue, aerobic fitness, muscular strength, anxiety, body image and self-esteem, cognitive health, psychosocial distress and overall quality of life (QOL).[1, 3, 4, 7-10] Observational evidence also indicates that among women with breast cancer, exercise reduces the risk of subsequent chronic disease (including diabetes, osteoporosis, cardiovascular disease), reduces the risk of cancer recurrence and improves survival.[7, 10-12]

Most studies included in systematic reviews on exercise and breast cancer have comprised of a sample primarily with early-stage and localised breast cancer.[13, 14] However, population-based statistics suggest that approximately 50% of women with breast cancer are diagnosed with regional or distant disease (Stage II+).[13, 15] As such, it is plausible that women with stage II+ disease are underrepresented in the body of evidence, which currently supports exercise as being safe, feasible and effective during and following breast cancer treatment. This is of note since breast cancer stage influences the types of treatment prescribed. More invasive surgery and higher doses of adjuvant treatment are associated with more frequent and severe treatment-related sequelae.[16-20] Further, five-year relative survival declines with advancing stage (Stage I: 99%; Stage II: 93%, Stage III: 72%; Stage IV: 22%[15, 21, 22]). As such, compared with early stage breast cancer, the higher disease and treatment-related

burden associated with later stage breast cancer may also influence safety, feasibility and exercise outcomes.

The aim of this systematic review and meta-analysis was to assess the safety, feasibility and effect of exercise in women with stage II, III or IV disease (i.e., II+). Specifically, this review evaluated: 1) the number, type and severity of adverse events (safety): 2) study recruitment, withdrawal and adherence rates (feasibility); and 3) effect of exercise (as assessed immediately post-intervention) on survivorship outcomes including QOL, aerobic fitness and fatigue. This analysis was performed by evaluating findings derived from randomised, controlled trials (RCTs) that involved samples with >50% of women with stage II+ breast cancer. As a secondary objective, we also explored the relationship between safety, feasibility, effect, and intervention characteristics, including exercise mode, degree of intervention supervision, intervention duration and timing of intervention (during or following treatment).

Methods

Search strategy and selection criteria

Eligibility criteria were established using the Participants, Intervention, Comparator, and Outcome (PICO) framework[23] as follows: Participants: RCTs in which at least 50% of the sample was diagnosed with Stage II+ breast cancer, either undergoing or completed treatment. If a study involved multiple intervention arms, groups consisting of less than 50% of participants with Stage II+ disease were excluded. Intervention: Exercise intervention trials were eligible for inclusion. Exercise was defined as any form of planned, structured, and repetitive bodily movements performed in order to improve or maintain fitness, performance or health.[24, 25] Exercise mode was classified as aerobic, resistance or other. 'Other exercise'

was considered a form of exercise that: 1) was not specified as aerobic or resistance (e.g., yoga); and 2) did not constitute complete decongestive therapy-based exercise, or common forms of lymphoedema treatment (e.g., stretching, passive, assistive, remedial or range of motion exercise performed against no resistance). Trials were eligible regardless of the level of supervision provided, mode of intervention delivery, intervention duration or intensity. Studies that involved multiple intervention groups consisting of different exercise intensities or modes were eligible if they included a control group. Studies that involved exercise in addition to other interventions such as dietary or other lifestyle interventions were excluded if the outcomes of the exercise could not be isolated. Comparators: Studies were included if they involved a usual care or control group (i.e., any type of control group not involving exercise therapy).

The following electronic databases were searched by one reviewer (BS): CINAHL, Cochrane, Ebscohost, MEDLINE, Pubmed, ProQuest Health and Medical Complete, ProQuest Nursing and Allied Health Source, Science Direct and SPORTDiscus. A faculty liaison librarian was consulted in the development of search terms. Titles and abstracts were searched for the following terms: 'breast neoplasm' or 'breast cancer' 'or 'breast' and '(cancer or neoplasm)' and/or 'advanced' or 'metastatic' or 'stage II, III, IV' or 'late stage' or 'palliative' and 'physical activity' or 'aerobic' or 'exercise' or 'training' or 'fitness' or 'physical' or 'jogging' or 'walking' or 'running' or 'swim*' or 'bik*' or 'bicyc*' or 'cycl*' or 'weight lifting' or 'aerobics' or '(strength or resistance)' or 'hydrotherapy' or 'water*' or 'yoga' and/or 'exercise' or 'movement' or 'exercise tolerance' or 'exercise therapy'. Database searches were limited to peer-reviewed scholarly journal articles published in English-language prior to March 1, 2017. There was no registered protocol for this review.

Outcomes of interest

Safety

Adverse events were defined as any undesirable medical or health-related event that occurred during study participation. They were classified as either non-exercise adverse events (adverse events reported to have occurred during study participation, but considered unrelated to exercise) or exercise-related adverse events (events which occurred during, or as a direct result of exercise). Adverse events were categorised according to the Common Terminology Criteria for Adverse Events, Version 4[26] as grade 1: asymptomatic or mild symptoms, clinical or diagnostic observations only and/or intervention not indicated; grade 2: moderate, minimal, local or non-invasive intervention required and/or limiting age-appropriate activities of daily living; grade 3: severe or medically significant but not immediately life-threatening, hospitalisation and/or prolongation of hospitalisation indicated, disabling and limiting self-care activities of daily living; grade 4: life-threatening consequences and urgent intervention indicated, or; grade 5: death. Serious adverse events were considered any "adverse medical event that required hospitalization, resulted in significant disability, was life threatening or resulted in death".[27] The lack of reporting and categorisation of health-related withdrawals as adverse events is common in exercise trials, and is suggestive of under-reporting of adverse events.[28] Therefore, we considered any withdrawal that occurred due to health-related reasons as an adverse event (e.g., illness or cancer recurrence). However, if participants withdrew for reasons such as time constraints, travel or family reasons, these were not considered adverse events (i.e., non-health-related reasons). If the severity of an adverse event was not reported, and the event resulted in study withdrawal, or if a participant withdrew from a trial due to unspecified health or medical reasons, these events were categorised as grade 3. If a study did not report on the occurrence of adverse events, and no health-related withdrawals occurred, it was considered that no adverse events had occurred. If a study involved more than one intervention group and did

not specify in which intervention group an adverse event occurred, the data were not included in the meta-analysis.

Feasibility

Feasibility was determined by computing recruitment rate, withdrawal rate, reason for withdrawals, and exercise adherence rate. Recruitment rates were computed as the proportion of those who were eligible and consented to participate in the study. Withdrawal rates were calculated as the percentage of those enrolled who did not complete the study. Exercise adherence rates were calculated as a percentage of the scheduled number of exercise sessions that were completed by participants.

Health outcomes

Health outcomes that were reported in a minimum of two studies were included in a meta-analysis. These included QOL, aerobic fitness, fatigue, upper-body strength, anxiety, depression, body mass index, body fat percentage, body mass index and waist circumference.

Data extraction and management

The titles and abstracts of all articles identified through an electronic database search were screened for eligibility by one reviewer (BS). Reference lists of all eligible and original manuscripts, and reviews were manually checked to identify additional articles (BS). Relevant records were then retrieved in full-text and screened further against the eligibility criteria (BS). Study and participant characteristics, intervention features and outcomes assessed from included articles were extracted into tabular format using predefined data fields (BS).

The quality of methods used in each RCT was assessed independently by two investigators (CS and BS) using the Physiotherapy Evidence Database (PEDro scale). The PEDro scale is a valid and reliable tool for evaluating risk of bias and quality in RCTs.[29, 30]

The scale consists of 11 items (eligibility criteria, random allocation, allocation concealment, baseline differences between groups, subject blinding, therapist blinding, assessor blinding, attrition, intention-to-treat analyses, between-group statistical comparisons and reporting of measures), with the total PEDro score ranging from 0 to 10 points (item 1 not contributing to the total score). RCTs with a score 6 or higher were considered high quality. RCTs receiving less than 6 were classified as low quality.[29, 31] Discrepancies in ratings were resolved by discussion and consultation with a third reviewer (SH) when required.

Statistical analyses

Meta-analysis of adverse events

Adverse events were treated as a count variable for inclusion in the meta-analysis. The number of adverse events that occurred in the exercise participants compared to the usual care participants was pooled and analysed, using a Mantel-Haenszel random effects model. The risk difference (RD) and 95% confidence interval was calculated as the effect measure. The RD was considered most appropriate since there were studies included in this review that reported no adverse events in either group. Performing a meta-analysis using risk ratio as the effect measure would also exclude all studies with zero adverse events.[32, 33] A negative value for RD indicates a lower risk of an adverse event with exercise compared with usual care. Meta-analysis was performed only for adverse events that were grade 3 or higher. This was considered appropriate because evaluation of grade 3 or higher adverse events was more likely to be consistent across the intervention versus usual care groups. Conversely, reporting of grade 1–2 events may not have been comprehensively evaluated for those in the usual care groups due to reduced contact with study staff. Further, some grade 1–2 events may reflect normal physiological responses to exercise (e.g., mild muscle stiffness or soreness) as

compared to potentially avoidable adverse events.[34, 35] All adverse events (grade 1–5) were also evaluated descriptively.

Feasibility

Feasibility was evaluated by calculating study recruitment rate, withdrawal rate and exercise adherence rate (all as a percentage); median, interquartile range, minimum and maximum rates were reported to ensure adequate description of data and to account for skewed data. We defined feasibility of exercise as achievement of a recruitment rate of ≥25%[36], a withdrawal rate of <25% (i.e., retention of ≥75%[37]) and adherence of ≥75%.[37] These values were determined *a priori* as clinically relevant cut-offs to establish feasibility based on previous literature.[38, 39]

Meta-analysis of health outcomes

All health outcomes of interest were analysed as continuous variables and involved comparisons of post-intervention means and standard deviations (SDs) between exercise and usual care participants. To allow comparison of data from different scales, pooled statistics were calculated using standardised mean differences (SMDs) using RevMan software (version 5.3). Forest plots were created using R statistical software (version 3.4.1). When means and SDs were not available (n=9 studies), authors were contacted (two responded), or means and/or SDs were calculated using reported data (e.g., using median, range and sample size) and recommended formulas.[40] If authors could not be contacted, and means or SDs could not be calculated (because of insufficient data or data being reported in graph format only), the study was not included in meta-analyses (n=7). When two or more methods of assessing outcomes were used in a study, the method defined as being the gold standard or the method/instrument with demonstrated validity and reliability was used.

Data were combined at the study level for each meta-analysis. Publication bias was assessed by plotting RDs or SMDs against corresponding standard errors and determining the presence of asymmetries or missing sections within the funnel plot when ten or more studies were available.[41] Statistical heterogeneity was assessed using Cochran's Q test and the I^2 statistic to quantify the proportion of the overall outcome attributed to variability.[42, 43] The following values were used to determine level of heterogeneity: I^2=0–25%: low heterogeneity; I^2=>25–50%: moderate heterogeneity; I^2=>75–100%.[3, 43] Planned subgroup analyses were performed to assess the influence of: 1) exercise mode (aerobic, resistance, combined and 'other' exercise); 2) degree of intervention supervision (supervised and unsupervised); 3) intervention duration (12 weeks or less and greater than 12 weeks), and; 4) timing of the intervention with respect to treatment status of participants (during treatment, post-treatment and mixed [i.e., samples consisting of those currently receiving and completed treatment]) on adverse events, recruitment, withdrawal and adherence rates, and effect of exercise on health outcomes. Sensitivity analyses were also performed by repeating all meta-analyses with: 1) only trials rated as high quality using the PEDro scale, and; 2) only trials with 100% of samples with stage II+ disease. Standardised classifications for the magnitude of effect were used, with less than 0.20 representing a small effect; >0.20–0.50 representing a moderate effect; and >0.50 representing a large effect.[44] A p-value of less than 0.05 was considered statistically significant.

Results

Literature search

Following a search of databases, 2,391 articles were identified (Supplementary Material 1). After removal of duplicates and screening of titles and abstracts, 406 publications were

retrieved and examined. Of these, 345 were excluded (with 60% of exercise and breast cancer trials excluded as they comprised samples with <50% of participants with stage II+ breast cancer). After these exclusions, 61 trials were included in the systematic review (low quality, n=24, 39%; high quality, n=37, 61%, Supplementary Material 2).

Participant characteristics

Median sample size was 63 (range: 10–377), with a participant mean age of 53 years (SD=3.6, see Online Supplementary Material 3). The period since breast cancer diagnosis ranged between 8 months[45] and 6 years[46, 47]; 41% (n=25) of trials involved participants who were currently undergoing treatment, including neoadjuvant, adjuvant or palliative treatment. The median proportion of the samples with stage II+ disease was 72% (range: 50% (n=2 studies[48, 49]) to 100% (n=10 studies,[50-59]). Within the ten trials that involved only participants with stage II+ disease[50-59], one trial included only participants with stage II disease[54], seven trials included only those with stage II or III disease[50, 55-59], and two trials included only women with stage IV disease.[51, 53]

Intervention characteristics

Details of intervention characteristics are shown in Table 1. Approximately one-third of studies (n=20[45, 47, 48, 50, 52-54, 59-71]) evaluated aerobic exercise only, whereas another third (n=21[9, 55, 57, 72-89]) evaluated combined aerobic and resistance exercise. The remaining studies evaluated resistance exercise only (n=6 studies[46, 49, 90-93]), or other modes of exercise (n=11,[51, 56, 58, 94-101]), and three trials involved separate aerobic and resistance exercise arms (n=3,[102-104]). Home-based exercise was prescribed for approximately one-third of the interventions (n=20 studies, 32%[9, 50, 53, 61, 64, 65, 67-72, 75, 79, 81, 84, 88, 89, 103, 104]), while the other two-thirds involved interventions conducted at a range of facilities including local gymnasiums, hospital, clinical, university or rehabilitation settings. Approximately half of the interventions

involved supervised exercise sessions (i.e., over half of the exercise sessions involved face-to-face supervision, n=31[45-49, 52, 54, 57, 59, 60, 62, 73, 74, 76-78, 80, 82, 83, 85, 86, 90, 92-99, 102]), with one trial evaluating a supervised and an unsupervised intervention group.[87] Supervision in these trials was provided by an accredited exercise physiologist (n=9,[46-48, 52, 60, 80, 85, 86, 102]), other exercise trainers with or without tertiary qualifications (n=10,[49, 57, 76, 78, 82, 83, 90, 93, 95, 96]), or other allied health professionals such as an occupational therapist or physical therapist (n=8,[45, 73, 78, 87, 92, 95-97]). The interventions in 29 trials were classified as unsupervised (i.e., less than half of the prescribed exercise sessions involved face-to-face supervision: n=29,[9, 50, 51, 53, 55, 56, 58, 61, 63-72, 75, 79, 81, 84, 88, 89, 91, 100, 101, 103, 104]). Of these 29 trials, nine involved predominantly unsupervised exercise sessions, supplemented with some face-to-face contact or supervision, commonly once per week.[9, 53, 55, 56, 58, 66, 91, 100, 101] Eleven trials involved telephone contact with an exercise specialist[75], research staff member[61, 68-70, 81, 104], accredited exercise physiologist[72], nurse[63] or a physical activity counsellor[64, 65] throughout the intervention. The remaining nine unsupervised trials involved other forms of intervention support such as provision of guidebooks or print materials[50, 67, 71, 89, 103], emails with support from an e-counsellor exercise physiologist[79], a website[88] or exercise instructional videos or CDs.[51, 84] Intervention durations ranged between 6 weeks and 1 year (median 12 weeks, Table 1).

Safety - summary of adverse events

Adverse events in exercise participants

From 61 studies included in this review, 41% (n=25) explicitly reported that no adverse events had occurred, while 34% (n=21) did not mention adverse events (see Online Supplementary Material 4). There were a total of 116 adverse events among participants allocated to exercise reported in 15 trials[52, 55, 64, 65, 68, 70, 72, 73, 81, 87, 93, 95-97, 103] (grade 1: n=42 events; grade 2: n=20 events; grade 3: n=52 events; grade 4: n=0 events; grade 5: n=2 events, Table 2). The most common adverse events among exercise participants were unspecified

health or medical problems or illness leading to withdrawal (n=20 events, grade 3), discomfort or low-level muscle pain, stiffness or soreness after an exercise session (n=18 events, grade 1) and musculoskeletal injuries (e.g., sprains: n=8 events, grade 1). While 58% (n=66) of reported adverse events were considered unrelated to exercise, 42% (n=50) were exercise-related. Of these events, most (n=43, 88%) were classified as grade 1 or 2 (grade 1: n=34 events; grade 2: n=9 events; grade 3: n=6 events). Of the six exercise-related adverse events that were grade 3, five of these events resulted in participant withdrawal. These were severe headaches (n=1 event), an unspecified physical accident (n=1 event), severe discomfort (n=1 event), dizziness (n=1 event) and foot pain requiring surgery (n=1 event).

Adverse events in usual care participants

Seventeen studies[45, 49, 52, 53, 58, 60, 62, 83, 86-88, 90-93, 100, 101] reported a total of 40 adverse events in those allocated to usual care (grade 1: n=2 events; grade 2: n=1 event; grade 3: n=34 events; grade 4: n=0; grade 5: n=3, Table 2). The most common adverse events among usual care participants were unspecified health or medical problems or illness leading to withdrawal (n=11 events, grade 3), infections, secondary suturing, seroma discharge or uncontrollable pain (not reported individually, n=8 events, grade 3) and breast cancer progression (n=4 events, grade 3).

Meta-analyses of adverse events

Adverse event data from one trial[66] (n=5: wheezing requiring physician evaluation for asthma, cholinergic urticarial, herpes zoster, sinusitis, and back pain related to a fall) were not included in the meta-analysis since group allocation was unclear. Further, adverse event data (n=2: shoulder tendonitis and foot tendonitis) from another trial[103] involving two exercise

intervention groups were excluded from subgroup analyses of exercise mode due to a lack of clarity of intervention group allocation.

Pooled analyses of 60 RCTs involving 5,200 participants (exercise: n=2,621; usual care: n=2,579) showed no difference in the risk of a grade 3–5 adverse event between exercise and usual care (n=91 adverse events [exercise: n=54 events; usual care: n=37 events], RD: <0.01 [95% CI= –0.01, 0.01]; p=0.38; I^2=0%: low heterogeneity, Figure 1). Evaluation of funnel plots indicated there was no evidence of publication bias (data not shown). The results of subgroup analyses suggested that results were similar irrespective of exercise mode (aerobic, resistance, combined and other exercise), intervention supervision (supervised and unsupervised), intervention duration (12 weeks or less and longer than 12 weeks) and intervention timing (during and after treatment). The RD remained unchanged following sensitivity analyses involving only high-quality trials and trials with 100% of samples with stage II+ disease (Figure 1).

Feasibility outcomes: recruitment, withdrawals, and exercise adherence

Recruitment, withdrawal and adherence rates are shown in Table 3. *Recruitment rates:* Study recruitment rates were calculated for 48 studies (data from 13 studies were unavailable). Median recruitment rate met the pre-defined criterion of ≥25%, with an overall rate of 45%. Recruitment rates varied based on exercise mode, with aerobic exercise studies showing the lowest rates (32%) and studies evaluating 'other' modes of exercise showing the highest rates (65%). *Withdrawals:* Overall withdrawal rate was 11%, across a total of 69 intervention groups, with similar rates irrespective of subgroup (Table 3). Lower withdrawal rates occurred in studies with a high-quality rating compared with low quality studies (exercise groups: 18% [low-quality studies] versus 9% [high-quality studies]; usual care groups: 16% [low-quality studies] versus 11% [high-quality studies]). Health-related reasons

for withdrawal were similar between exercise and usual care groups. Unspecified health or medical reasons were the most common reason (see Online Supplementary Material 5 for all reasons for withdrawals). *Exercise adherence:* Overall median adherence to the scheduled number of exercise sessions was 82% (Table 3), and rates were similar irrespective of subgroup.

Health Outcomes: assessment of outcomes.

An overview of all instruments and methods used to assess specific health outcomes, including QOL, aerobic fitness, fatigue, upper-body strength, anxiety, depression and body composition, body mass index, body weight and waist circumference is shown in Supplementary Material 6.

Meta-analyses results of health outcomes: exercise versus usual care

Large effects in favour of exercise compared with usual care were observed for aerobic fitness (SMD=0.62 [95% CI: 0.42, 0.81], p<0.01, I^2=75%; moderate heterogeneity, n=31 trials, Figure 2), anxiety (SMD=0.77 [95% CI: 0.64, 0.91]; p<0.01, I^2=89%; high heterogeneity, n=14 trials, see Supplementary Content 7) and depression (SMD=0.66 [95% CI: 0.52, 0.80]; p<0.01, I^2=90%; high heterogeneity, n=14 trials, see Supplementary Content 8). Compared with usual care, there were moderate effects in favour of exercise for QOL (SMD=0.40 [95% CI: 0.33, 0.47]; p<0.01, I^2=78%; high heterogeneity, n=40 trials, Figure 3), fatigue (SMD=0.30 [95% CI: 0.23, 0.38], p<0.01, I^2=75%; moderate heterogeneity, n=31 trials, Figure 4), upper-body strength (SMD=0.43 [95% CI: 0.33, 0.53]; p<0.01, I^2=49%; moderate heterogeneity, n=22 trials, see Supplementary Content 9) and waist circumference (SMD=0.22 [95% CI: 0.02, 0.43]; p=0.03, I^2=0%; low heterogeneity, n=8 trials, see

Supplementary Content 10). Small effects from exercise were observed for body mass index (SMD=0.17 [95% CI: 0.01, 0.32]; p=0.03, I^2=0%; low heterogeneity, n=13 trials, see Supplementary Content 11), body weight (SMD=0.08 [95% CI: –0.04, 0.20]; p=0.22, I^2=0%; low heterogeneity, n=15 trials) and body fat (SMD=0.11 [95% CI: –0.02, 0.24]; p=0.11, I^2=0%; low heterogeneity, n=13 trials), with effect on only body mass index also being supported statistically (see Supplementary Content 12–13).

The results of subgroup analyses showed that exercise mode significantly influenced exercise effect on QOL (χ^2=26.36, df=3, p<0.01), with evidence of small-to-moderate effects in favour of aerobic (SMD=0.22 [95% CI: 0.10, 0.33], p<0.01), resistance (SMD=0.29 [0.09, 0.49], p<0.01) and combined exercise (SMD=0.51 [95% CI: 0.39, 0.62] p<0.01), and large effects in favour of 'other' exercise (SMD=0.75 [95% CI: 0.55, 0.95], p<0.01) compared with usual care. Subgroup analysis suggested that exercise mode influenced the effect on aerobic fitness (χ^2=6.05, df=3, p=0.05), with aerobic (SMD=0.62 [95% CI: 0.43, 0.81], p<0.01) and combined exercise (SMD=0.65 [95% CI: 0.26, 1.03]) having a large effect, and resistance exercise having a small to moderate effect (clinically), although not supported statistically (SMD=0.23 [95% CI: –0.07, 0.53], p=0.13). Exercise mode also influenced upper-body strength (χ^2=12.44, df=2, p<0.01), anxiety (χ^2=40.91, df=3, p<0.01) and depression (χ^2=40.54, df=3, p<0.01). For upper-body strength, a large effect was observed for resistance exercise (SMD=0.68 [95%CI: 0.05, 0.85]; p<0.01). For anxiety and depression, large effects were observed for combined exercise (anxiety: SMD=1.36 [95% CI: 1.10, 1.62]; p<0.01; depression: SMD=0.62 [95% CI: 0.18, 1.06]; p<0.01) and 'other' exercise (anxiety: SMD=0.83 [95% CI: 0.61, 1.06]; p<0.01 depression: SMD=1.16 [95% CI: 0.94, 1.38); p<0.01) compared with small-to-moderate effects for aerobic exercise (anxiety: SMD=0.37 [95% CI: 0.09, 0.65]; p=0.01; depression: SMD=0.53 [95% CI: 0.24, 0.82]; p<0.01) and no

effect for resistance exercise (anxiety: SMD=0.08 [95% CI:–0.30, 0.45]; p=0.68; depression: SMD=0.04 [95% CI: –0.23, 0.31]; p=0.79).

Intervention supervision influenced the effect of exercise on QOL (χ^2=13.74, df=1, p<0.01), fatigue (χ^2=5.87, df=1, p=0.02), anxiety (χ^2=5.26, df=1, p=0.02,) and depression (χ^2=16.51, df=1, p<0.01). Supervised interventions had large effects on QOL (SMD=0.59 [95% CI: 0.46, 0.71], p<0.01) and fatigue (SMD= 0.44 [95% CI: 0.30, 0.57]; p<0.01), while small effects were observed for unsupervised interventions (QOL: SMD=0.30 [95% CI: 0.22, 0.39], p<0.01; fatigue: SMD= 0.24 [95% CI: 0.15, 0.33]; p<0.01). In contrast, large effects were observed during unsupervised interventions for anxiety and depression (anxiety: SMD=0.93 [95% CI: 0.74, 1.13], p<0.01; depression: SMD=1.18 [95% CI: 0.89, 1.47], p<0.01), while moderate-to-large effects were observed during supervised interventions (anxiety: SMD=0.62 [95% CI: 0.43, 0.81], p<0.01; depression: SMD=0.50 [95% CI: 0.34, 0.66], p<0.01). Neither the timing of the interventions (i.e., during or following treatment) nor the intervention duration influenced the effect on outcomes, except in the case of depression. Intervention duration had an effect on depression (χ^2=7.93, df=1, p<0.01), with interventions lasting longer than 12 weeks producing a large effect (SMD=0.84 [95% CI: 0.65, 1.03]; p<0.01) and interventions lasting 12 weeks or less having a moderate effect (SMD=0.44 [95% CI: 0.23, 0.65]; p<0.01).

Sensitivity analyses

High quality trials: Results remained unchanged after performing meta-analyses with only high-quality trials, except for body mass index and waist circumference, for which the effect of exercise became smaller compared with results from meta-analyses using all available data. That is, exercise had no effect on body mass index (SMD=0.12 [95% CI: –0.86, 0.73], p=0.87, I^2=0%: low heterogeneity) and waist circumference (SMD= –0.07 [95%

CI: –0.09, 0.33], p=0.27, I^2=2%; low heterogeneity) when analysis was restricted to including data only from high quality trials. *Trials with 100% of samples with stage II+ disease:* Compared with results from meta-analyses using all available data, effect sizes of exercise tended to be larger in trials involving only women with stage II+ breast cancer for QOL (0.78 vs. 0.40), fatigue (0.41 vs. 0.30) and depression (0.80 vs. 0.66).

Discussion

These findings suggest that exercise is safe, feasible and effective for improving health outcomes among women with stage II+ breast cancer. More specifically, adverse events reported as a consequence of participating in exercise during or following treatment for stage II+ breast cancer were uncommon (occurring in <5% of women, Table 2). When adverse events were reported, they were typically mild in nature and represented acute and normal physiological adaptations to exercise. These results are similar to findings reported in previous reviews and meta-analyses, which had underrepresentation of women with regional and advanced breast cancer.[2-4] Nonetheless, caution and care with exercise prescription remains relevant because about one-third of studies (n=21) provided no comment on the occurrence (or lack thereof) of adverse events. Studies that did report adverse events, mostly did not comprehensively describe monitoring and recording procedures. Similar to our findings, Speck *et al.*[3] reported in their review of mixed-cancer types that only 44% (n=36) of studies documented the presence or absence of adverse events, with 81% (n=29) of these studies reporting no harm as a result of exercise. These findings highlight the need for standardised recording of adverse events to be incorporated into the design of RCTs. While only a minimal amount of events that occurred in the exercise intervention group (5%) were classified as severe (grade 3), these results nonetheless suggest a need for a thorough health

and medical history evaluation prior to exercise prescription, as well as individualised exercise approaches and patient education to ensure that individuals can take appropriate action, should an adverse event occur.

The safety findings were similar irrespective of the mode of exercise evaluated, the degree of supervision provided, intervention duration and whether the intervention was conducted during or following breast cancer treatment. However, caution is advised when interpreting these results. For example, the exercise intensity of unsupervised interventions was generally less vigorous compared with supervised exercise interventions. This difference in intensity may have been intentional, or it may suggest that individuals are more cautious when exercising unsupervised. Also, compared with aerobic interventions, which were mostly home-based walking programs, resistance exercise interventions were more commonly performed at a supervised facility, involving specialised equipment (e.g., pin-loaded machines), instruction of technique and monitoring and progression of intensity (e.g., progressing from 50 to 80% of 1RM). As such, paying particular attention to the provision of safety information when prescribing unsupervised resistance-based exercise is paramount to maintaining safety in this setting. Low withdrawal rates (approximately 11%) and high adherence (approximately 80%) identified in this review suggest that exercise during and following treatment for stage II+ breast cancer is highly feasible. These findings may in part reflect recruitment bias (e.g., exercise readiness tends to be higher in those who agree to participate in exercise trials compared with those who do not[5]). Alternately, the findings may reflect the perceived or real physical and psychosocial benefit achieved through exercise during the breast cancer survivorship period.[1] Specifically, the outcomes from this meta-analysis also demonstrated that for women with stage II+ breast cancer, exercise during and following treatment led to improvements in QOL (SMD=0.4), fatigue (SMD=0.3), aerobic

fitness (SMD=0.6), upper-body strength (SMD=0.4), anxiety (SMD=0.8), depression (SMD=0.7), waist circumference (SMD=0.2) and body mass index (SMD=0.2).

The magnitude of the effects reported here is similar to those reported in previous reviews that likely overrepresented women with early-stage disease.[2-4, 105-111] However, greater effects of exercise were observed for depression and anxiety in this review. When analyses were restricted to include data only from those studies involving all participants with stage II+ disease, the effect was also higher for QOL, fatigue and depression. In contrast to previous findings that showed larger effects of exercise when conducted following compared with during adjuvant treatment[3], our findings showed similar effects irrespective of intervention timing. It seems plausible that these differences are influenced by capacity for change. That is, compared with those women with early-stage breast cancer, those with stage II+ disease experience poorer health and greater morbidity (e.g., higher rates of depression and anxiety are observed in women with more advanced disease compared with local disease during and after treatment[112]). Women with more advanced breast cancer may therefore experience greater benefits of exercise for improving their mental health and wellbeing. Irrespective, the consistent message from findings reported here and that of others previously, is that exercise is effective for preventing treatment-related morbidity and health declines, and can be used to facilitate recovery post-treatment.[113]

Exercise, irrespective of intervention characteristics, led to favourable effects, yet there was some evidence to suggest that the magnitude of effect differed for some outcomes depending on exercise mode, degree of supervision, timing (during versus following treatment) and duration of the intervention. For example, stronger effects for QOL were evident for supervised compared with unsupervised exercise, and when the intervention involved more than one exercise mode compared with only one mode. In contrast, greater benefits in psychological outcomes (anxiety and depression) occurred during unsupervised

interventions, compared with supervised interventions. Resistance exercise was more effective for improving strength compared with other modes of exercise, whereas interventions that included aerobic exercise were more effective at improving fitness, anxiety and depression. Finally, interventions lasting longer than 12 weeks produced larger effects on depression than shorter interventions. This provides support for the important role of exercise in longer term management of psychosocial wellbeing post-diagnosis. These findings also support the notion that best clinical practice includes an exercise prescription that considers a patient's physical and psychosocial needs, as well as their personal interests and preferences.

Limitations

Key limitations of this review include the poor reporting of adverse events by over 60% of included studies, and the likelihood of a response bias. The mean age of the study participants was 53 years, whereas the international average age of breast cancer diagnosis is between 56 and 62 years.[114] The samples included in this review were also likely healthier compared with the wider breast cancer population. Most (79%; n=48) of the trials excluded participants with various comorbidities, yet 90% of women with breast cancer report at least one comorbidity.[115] Consenting women were also likely to live in more urban environments with easier access to care, and have a history of exercise participation. In contrast, approximately 60% of the wider breast cancer population is sedentary or insufficiently active at time of breast cancer diagnosis.[116] Considering these limitations, we advise caution against over-interpreting the results of this review. Another potential limitation of this review is the inclusion of studies that involved women with early-stage, local disease. However, these women represented less than 50% of the data. Further, findings from the sensitivity analyses (which involved only RCTs with 100% of the sample being women with stage II+ disease) were consistent with those findings when all studies were included. Finally, exercise effects were examined based on immediately post-intervention results and the longest intervention

length was 1 year. As such, the longer term effects of exercise among women with stage II+ breast cancer remain unknown.

Conclusions

This review highlights the need for improved and standardised recording and monitoring of adverse events, which is relevant in both clinical and research settings. Further, demonstrating exercise that exercise is safe, feasible and effective in women with stage II+ disease represents an important contribution to the literature. Future research will lead to greater understanding of the role of exercise with respect to survival outcomes, and will help to refine optimal exercise prescription and the diagnosis, treatment, personal and behavioural characteristics that influence exercise safety, feasibility and effectiveness. Until this information is available, the findings reported here indicate that most individuals with Stage II+ breast cancer should be able to participate safely in exercise, according to established general guidelines that are available and promoted to women with breast cancer. Specifically, exercise should include mixed exercise modes (including aerobic- and resistance-based exercise), and should be performed at moderate or higher intensities, three to five times per week, for a total of at least 150 minutes per week of exercise.[1, 117]

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Table 1: Summary of exercise intervention characteristics separated by exercise mode (n=61).

	Intervention details	
Aerobic exercise studies (n=20)[1]		
Mode	Continuous and interval training: cycle ergometer, outdoor cycling, elliptical trainer, treadmill, brisk walking, jogging, rowing ergometer, stair-climbing machine (stair-master).	
Intensity	40–85 HR_{max}; 60–80% of age-adjusted HR_{max}; 35–85% HRR; up to 90% of the HR reached in the 6MWT; 60–80% VO_{2max}; 55–100% VO_{2peak} (Interval training: <2 min intervals at >80 % VO_{2peak}); 12–14 RPE (6–20 scale); 4–6 RPE (0–10 Scale, "breathing hard but able to talk"); ≤3–6 METS.	
Session duration	15–60 minutes' overall duration (5–10 min warm-up and cool-down).	
Frequency	2–7 sessions per week (range 6 weeks to 1 year).	
Supervision	Supervised interventions[2]: 2–3 supervised sessions per week. Unsupervised interventions[3]: 2–5 unsupervised sessions per week; weekly supervised exercise sessions and/or in-person contact; weekly telephone contact; exercise instruction guidebook; weekly to fortnightly in-person and telephone physical activity counselling sessions; tailored-physical activity print-materials; physical activity booklet.	
Resistance exercise studies (n=21)[1]		
Mode	Resistance machines, free weights (dumbbells and barbells), weighted vests, resistance-bands. Exercises included upper- and lower-body exercises targeting all major muscle groups (e.g., squat, lunge, leg extension, leg curl, leg press, calf raises, chest press, seated row, triceps extension, biceps curls, and modified curl-ups, lat-pulldown, shoulder press, lateral raise, shoulder flexion, hip flexion, hip extension, abdominal crunches, lower back hyperextensions and 2 footed jumps with weighted vests).	
Intensity	50–85% of 1RM; 15 RPE (6–20 scale), 3–8 RPE (0–10 scale); 0–10% of body weight (weighted vests). 6–20 repetitions per set. 1–3 sets per exercise.	
Session duration	30–60 min overall session duration (5–10 min warm-up and cool-down).	
Frequency	1–4 sessions per week (range 4 weeks to 12 months).	
Supervision	Supervised interventions[2]: In-person supervision 2–3 sessions per week; 1 unsupervised session per week. Unsupervised interventions[3]: 2–4 unsupervised sessions per week; 1 supervised session per week; exercise instruction guidebook.	
Combined exercise studies (n=6)		
Mode	Aerobic-based, resistance-based, circuit training (including pump class and boot camp style training), stretching and flexibility exercises, mobility exercises, floor-based exercises, Pilates, hydrotherapy and patient-specific rehabilitation performed either on separate days or in combination (e.g., aerobic exercise followed by resistance exercises in the same session). Aerobic exercise: Same as aerobic exercise studies plus aerobics classes, running, hiking, Nordic walking, floor-based aerobic exercise to music, water-based aerobic exercise, dragon boat rowing, mini-trampoline, step-up blocks, antigravity treadmill, floor-based aerobic exercise to music, jumping jacks, running-on-the-spot. Resistance exercise: Same as resistance exercise studies plus Flexband exercises, water-based resistance exercises, strength training exercises with Nordic walking poles, strength exercises using steps and balls, small soft ball, mats, fit-balls and bodyweight exercises. Upper- and lower body exercises targeting all major muscle groups including lower back and abdominals. Exercises targeting all major muscle groups.	
Intensity	Aerobic exercise: 12–16 RPE (6–20 scale), 7–8 RPE (0-10 RPE scale); 40–75% VO_{2max}; 55–75% VO_{2peak}; 55–85% HR_{max} (intervals ranged from 30 secs [100% HR_{max})] to 6 mins [90%–95% of HR_{max}]); 40–65% HRR; 3-6 METS; 60 RPM (cycle ergometer); ≥ 50% bodyweight (antigravity treadmill).	Resistance exercise: 40–90% 1RM; 13–15 RPE (6–20 scale), 4–7 RPE (0–10 scale). 6–20 repetitions per set. 1–4 sets per exercise.
Session duration	15–90 min overall session duration (5–10 min warm-up and cool-down).	
Frequency	1 to 7 sessions per week (range 6 weeks to 12 months).	
Supervision	Supervised interventions[2]: In-person supervised 1–3 sessions per week; unsupervised sessions 2–3 times per week. Unsupervised interventions[3]: 1–7 unsupervised sessions per week; weekly to monthly supervised sessions; weekly to monthly telephone calls, instructional exercise videos; weekly email messages; internet-based support (telehealth).	
Other exercise (n=11)		
Mode	Yoga (n=5): Stretching and isometric floor-based and standing exercises, whole-body postures, breathing exercises, meditation and relaxation techniques and post-operative shoulder mobility exercises involving use of a mat, bolsters, chairs, blankets, blocks, and a ≤1kg hand weights. Pilates (n=1): Whole-body, standing, seated and floor based-exercises (including pelvic floor exercises) comprising of stretching, breathing, running and mobility exercises using resistance bands, foam rollers, ≤1kg hand weights; floor-based, seated and standing movements.	

	Hydrotherapy (n=3): Various whole body aerobic-based, strength-based, mobility and stretching movements targeting all major muscle groups including running in water and swimming, forward and backward jogging with arms pushing, pulling and pressing, leaps, leg crossovers and movements using pool noodles, swimming boards, and swimming belts. Seated exercise (n=1): Stretching and repeated flexion and extension of the arms, head, upper-torso, and legs while seated. Nia exercise (n=1): Aerobic-based and whole-body conditioning program that integrates strength, flexibility, mobility, agility, and stability exercises incorporating martial arts, dance and yoga style movements.
Intensity	Yoga: Low–moderate, low-impact and gentle stretching and postures; moderate (<12 RPE); Individual poses were held from 20 seconds to 5 minute. Pilates: Low–moderate. Hydrotherapy: Aerobic-based components performed at 60% HR_{max} and strength-based components performed for 2–3 sets of 8–12 repetitions. Seated exercise: Low–moderate.
Session duration	15–120 min overall session duration (including 5-10 min warm up, cool down and stretching).
Frequency	1–7 sessions per week for 4 weeks up to 24 weeks.
Supervision	Supervised interventions[2]: In-person supervision 1–3 sessions per week. Unsupervised interventions[3]: 1–7 sessions per week unsupervised; weekly supervised sessions; instructional exercise videos and audiotapes.
Studies involving separate aerobic and resistance exercise arms (n=3)	
	See aerobic and resistance exercise studies for details

[1] N=3 additional trials involved separate aerobic and resistance exercise arms,
[2] Supervised were interventions whereby 50% or more of prescribed exercise was supervised in-person.
[3] Unsupervised were interventions whereby less than 50% of prescribed exercise was supervised in-person.
HR: Heart rate; HR_{max}: Heart rate maximum; HRR: Heart rate reserve; METS: Metabolic equivalents; RPE: Rating of perceived exertion; RPM: Revolutions per minute; VO_{2max}: Maximal oxygen consumption; VO_{2peak}: Peak oxygen consumption; 6MWT: 6-minute walk test.

Table 2. Adverse events by grade of severity described for those in the exercise and usual care groups.

Adverse event grade[1]	Exercise group (116 adverse events, 2621 participants) Total number of adverse events[2] / exercise-related adverse events		Usual care group (40 adverse events, 2579 participants) Total number of adverse events[2] / exercise-related adverse events	
Grade 1	**Grade 1 adverse events: 42/34**		**Grade 1 adverse events: 2/0**	
	Low-severity musculoskeletal symptoms (pain/stiffness/soreness/tendonitis) (18/18) Lymphoedema onset or worsening (8/3) Increase in fatigue (4/4) Mild cardiac symptoms or angina (7/6)	Unspecified minor injuries (3/2) Acute illness (1/0) Vertigo (1/1)	Acute illness (1/0) Lymphoedema onset (1/0)	
Grade 2	**Grade 2 adverse events: 20/10**		**Grade 2 adverse events: 1/0**	
	Musculoskeletal injuries (mild fractures, strains, tendinitis) (9/6) High blood pressure (>140/90 mmHg) (4/3) Gynaecologic complication or urinary tract infection (2/0)	Influenza or upper respiration tract infection (2/0) Hypoglycaemia (1/1) Haemorrhoids (1/0) Diabetes mellitus (1/0)	Shingles secondary to varicella zoster infection (1/0)	
Grade 3[3]	**Grade 3 adverse events: 52/6**		**Grade 3 adverse events: 34/0**	
	Unspecified health/medical problems or illness leading to withdrawal (20/0) Infections/secondary suturing/seroma, discharge/uncontrollable pain (2/0)[4] Breast cancer progression (3/0) Breast cancer recurrence (2/0) Cancer[5] or developed other cancer (n=5) Hospitalisation (4/0) Lymphoedema (3/0) Musculoskeletal symptoms or injuries leading to withdrawal (2/0) Discomfort with exercise (1/1)	Dizziness and dyspnoea (1/1) Unspecified physical accident (2/1) Foot pain requiring surgery (1/1) Mild chest pain during exercise (1/1) Gastrointestinal complication (1/0) Deep vein thrombosis and pulmonary embolism (1/0) Diverticulosis (1/0) Syncope (1/1)	Unspecified health/medical problems or illness leading to withdrawal (12/0) Infections/secondary/suturing/seroma/ discharge/uncontrollable pain (8/0) Breast cancer progression (4/0) Breast cancer recurrence (3/0) Uncontrolled cardiac disease and hypertension leading to withdrawal (2/0)	Gynaecologic problems (1/0) Anaemia leading to withdrawal (1/0) Foot fracture (1/0) Chemotherapy-induced severe discomfort leading to withdrawal (1/0) Bronchitis (1/0)
Grade 4	**Grade 4 adverse events: 0/0**		**Grade 4 adverse events: 0/0**	
	Nil		Nil	
Grade 5	**Grade 5 adverse events: 2/0**		**Grade 5 adverse events: 3/0**	
	Death (2/0)		Death (3/0)	

[1] Adverse events were classified using the Common Terminology Criteria[26] as; grade 1: asymptomatic or mild symptoms; grade 2: moderate, minimal, local or non-invasive intervention indicated and limiting age-appropriate instrumental activities of daily living; grade 3: severe or medically significant but not immediately life-threatening; grade 4: life-threatening consequences and urgent intervention indicated, or; grade 5: death.

[2] Includes all adverse events (both exercise- and non-exercise related).

[3] Adverse events in which the severity was not reported were considered Grade 3 or higher if the event led to study withdrawal.

[4] Not reported individually.

[5] Reported as "cancer" with no further detail provided on whether the withdrawals were due to cancer progression, recurrence or development of other cancer.

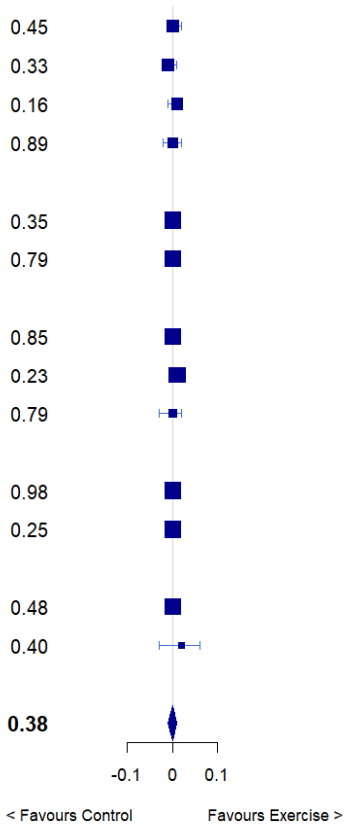
Table 3. Study recruitment rate, withdrawal rate and exercise adherence by exercise mode, treatment status, intervention supervision and intervention duration.

	Recruitment rate (%) Median (minimum, maximum [IQR])	Withdrawal rate (%)[2] Median (minimum, maximum [IQR])		Adherence rate (%) Median[2] (minimum, maximum [IQR])
		Exercise	Usual care	
Overall	45 (1, 96 [40]), n=48	11 (0, 41 [15.5]), n=69	12 (0, 49 [13]), n=69	81 (44, 99 [21]), n=52
Exercise mode				
Aerobic exercise	32 (1, 96 [45]), n=22	11 (0, 41 [14]), n=26	12 (0, 49 [20]), n=26	86 (71, 99 [18]), n=16
Resistance exercise	40 (28, 83 [50]), n=6	7 (0, 34 [19]), n=10	11 (4, 43 [15]), n=10	84 (44, 96 [32]), n=9
Combined exercise	49 (33, 95 [23]), n=13	11 (0, 32 [24]), n=23	7 (0, 32 [16]), n=23	79 (55, 93.9 [20]), n=17
Other exercise	65 (15, 85 [32]), n=7	17 (0, 41 [19]), n=10	15 (0, 36 [19]), n=10	81 (58, 92 [34]), n=10
Treatment status				
During treatment	48 (14, 96 [35]), n=17	9 (0, 41 [14]), n=29	14 (0, 49 [16]), n=29	80 (58, 99 [15]), n=19
Post treatment	46 (1, 95 [41]), n=27	12 (0, 41 [20]), n=36	11 (0, 43 [17]), n=36	84 (44, 98 [20]), n=30
Mixed	26 (13, 47 [-[4]]), n=4	12 (5, 32 [23]), n=4	16.5 (7, 25 [14.75]), n=4	84 (71, 92 [-[4]]), n=3
Supervision				
Supervised	45 (14, 83 [41]), n=24	7 (0, 41 [19]), n=33	14 (0, 49 [IQR]), n=33	79 (44, 98 [20]), n=31
Unsupervised	46 (1, 96 [48]), n=24	12 (0, 38 [38]), n=36	10 (0, 36 [IQR]), n=36	84 (55, 99 [14]), n=21
Intervention duration				
≤12 weeks	45 (1, 95 [47]), n=27	12 (0, 41 [15]), n=37	14 (0, 49 [14]), n=37	85 (58, 99 [16]), n=27
>12 weeks	47 (14, 96 [46]), n=21	9 (0, 38 [21]), n=32	11 (0, 43 [16]), n=32	79 (44, 98 [17]), n=25
Study quality rating[3]				
Low	61 (15, 81 [26]) n=14	17 (0, 41 [30]), n=27	16 (0, 49 [25]), n=27	79 (55, 98 [20]), n=20
High	38 (1, 96 [36]), n=34	9 (0, 34 [12]), n=42	11 (0, 43 [10]), n=42	84 (44, 99 [20]), n=32

[1] n= values represent number of studies.
[2] n= values represent number of groups. Withdrawal and adherence rates reported by intervention groups because n=7 studies involved multiple intervention groups.
[3] Low quality: PEDro scale score of less than 6; high quality: PEDro scale score of 6 or higher.
[4] Interquartile range not computable
IQR: Interquartile range.

Figure 1. Meta-analysis of all grade 3 to 5 adverse events in exercise compared to usual care presented as overall and separated by exercise mode, treatment status, intervention duration and degree of supervision.

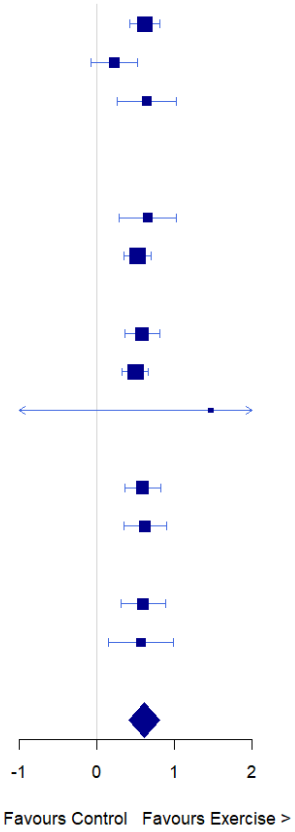
Subgroup	Studies (n=)	Participants (n=) Intervention vs. Control	Total adverse events (n=) Intervention vs. Control	RD (95% CI)	P-value
Exercise mode					
Aerobic exercise	22	960 vs. 938	22 vs. 11	0.00 (-0.01, 0.02)	0.45
Resistance exercise	9	389 vs. 383	3 vs. 9	-0.01 (-0.02, 0.01)	0.33
Combined exercise	27	846 vs. 871	22 vs. 7	0.01 (-0.01, 0.02)	0.16
Other exercise	11	426 vs. 387	6 vs. 10	0.00 (-0.02, 0.02)	0.89
Supervision [1]					
Supervised interventions	42	1136 vs. 1125	29 vs. 14	0.00 (-0.01, 0.01)	0.35
Unsupervised interventions	27	1485 vs. 1454	25 vs. 23	0.00 (-0.01, 0.01)	0.79
Intervention timing					
During treatment	29	1128 vs. 1145	24 vs. 17	0.00 (-0.01, 0.01)	0.85
Post-treatment	36	1273 vs. 1213	25 vs. 16	0.01 (-0.01, 0.02)	0.23
Mixed	4	220 vs. 221	5 vs. 4	0.00 (-0.03, 0.02)	0.79
Duration					
<12 week interventions	36	1578 vs. 1469	20 vs. 19	0.00 (-0.01, 0.01)	0.98
>12 week interventions	33	1043 vs. 1110	34 vs. 18	0.01 (-0.01, 0.01)	0.25
Sensitivity analyses [2]					
High quality studies only	42	1862 vs. 1888	40 vs. 31	0.00 (-0.00, 0.01)	0.48
Stage II+ only	10	257 vs. 258	16 vs. 10	0.02 (-0.03, 0.06)	0.40
Overall	**69**	**2621 vs. 2579**	**54 vs. 37**	**0.00 (-0.01, 0.01)**	**0.38**



[1] Supervised intervention were classed as interventions where ≥50% of prescribed exercise involved face-to-face supervision and unsupervised interventions involved <50% of prescribed exercise involving face-to-face supervision.
[2] Sensitivity analyses were performed only on i) high quality studies, and ii) studies with 100% of samples with stage II+ disease.

Figure 2. Meta-analyses results of aerobic fitness with subgroup analyses for exercise mode, intervention supervision, timing and duration, and sensitivity analyses (positive SMD values favour exercise).

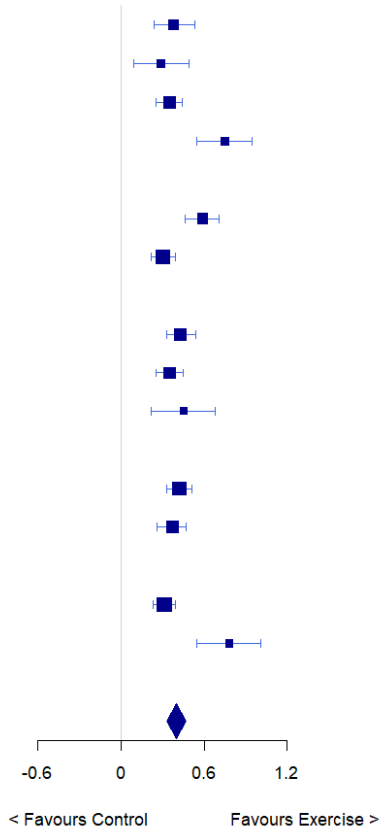
Subgroup	Studies (n=)	Participants (n=)	I^2 (%)	SMD (95% CI)	P-value
Exercise mode		Intervention vs. Control			
Aerobic exercise	15	395 vs. 355	31%	0.62 (0.43, 0.81)	<0.01
Resistance exercise	3	108 vs. 76	0%	0.23 (-0.07, 0.53)	0.13
Combined exercise	13	487 vs. 498	87%	0.65 (0.26, 1.03)	<0.01
Other exercise	0	-	-	-	-
Supervision [1]					
Supervised interventions	15	491 vs. 413	84%	0.66 (0.29, 1.03)	<0.01
Unsupervised interventions	16	499 vs. 516	43%%	0.53 (0.35, 0.70)	<0.01
Intervention timing					
During treatment	14	611 vs. 546	68%	0.58 (0.36, 0.81)	<0.01
Post-treatment	15	279 vs. 278	0%	0.50 (0.33, 0.67)	<0.01
Mixed	2	100 vs. 105	98%	1.47 (-1.01, 3.95)	0.25
Duration					
<12 week interventions	13	255 vs. 250	34%	0.59 (0.36, 0.83)	<0.01
>12 week interventions	18	724 vs. 642	83%	0.62 (0.35, 0.90)	<0.01
Sensitivity analyses [2]					
High quality studies only	18	714 vs. 663	84%	0.60 (0.32, 0.89)	<0.01
Stage II+ only	4	83 vs. 81	34%	0.57 (0.15, 0.99)	<0.01
Overall	**31**	**990 vs. 929**	**75%**	**0.62 (0.42, 0.81)**	**<0.01**



[1] Supervised intervention were classed as interventions where ≥50% of prescribed exercise involved face-to-face supervision and unsupervised interventions involved <50% of prescribed exercise involving face-to-face supervision.
[2] Sensitivity analyses were performed only on i) high quality studies, and ii) studies with 100% of samples with stage II+ disease.

Figure 3. Meta-analyses results of quality of life with subgroup analyses for exercise mode, intervention supervision, timing and duration and sensitivity analyses (positive SMD values favour exercise).

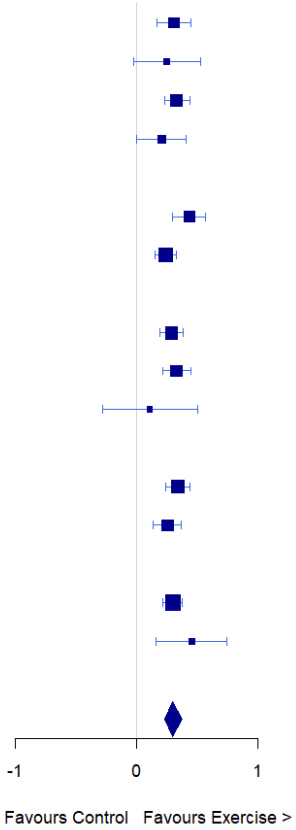
Subgroup	Studies (n=)	Participants (n=)	I^2 (%)	SMD (95% CI)	P-value
Exercise mode		Intervention vs Control			
Aerobic exercise	9	653 vs. 645	80%	0.38 (0.24, 0.53)	<0.01
Resistance exercise	5	247 vs. 171	3%	0.29 (0.09, 0.49)	<0.01
Combined exercise	20	646 vs. 609	82%	0.35 (0.25, 0.44)	<0.01
Other exercise	6	231 vs. 202	75%	0.75 (0.55, 0.95)	<0.01
Supervision [1]					
Supervised interventions	19	643 vs. 521	75%	0.59 (0.46, 0.71)	<0.01
Unsupervised interventions	21	1134 vs. 1076	79%	0.30 (0.22, 0.39)	<0.01
Intervention timing					
During treatment	16	849 vs. 714	79%	0.43 (0.33, 0.54)	<0.01
Post-treatment	21	776 vs. 727	81%	0.35 (0.25, 0.45)	<0.01
Mixed	3	152 vs. 156	27%	0.45 (0.22, 0.68)	<0.01
Duration					
<12 week interventions	24	1053 vs. 955	82%	0.42 (0.33, 0.51)	<0.01
>12 week interventions	16	724 vs. 642	71%	0.37 (0.26, 0.47)	<0.01
Sensitivity analyses [2]					
High quality studies only	24	1345 vs. 1202	80%	0.31 (0.23, 0.39)	<0.01
Stage II+ only	6	128 vs. 144	77%	0.78 (0.55, 1.01)	<0.01
Overall	**40**	**1777 vs. 1597**	**78%**	**0.40 (0.33, 0.47)**	**<0.01**



[1] Supervised intervention were classed as interventions where ≥50% of prescribed exercise involved face-to-face supervision and unsupervised interventions involved <50% of prescribed exercise involving face-to-face supervision.
[2] Sensitivity analyses were performed only on i) high quality studies, and ii) studies with 100% of samples with stage II+ disease.

Figure 4. Meta-analyses results of fatigue with subgroup analyses for exercise mode, intervention supervision, timing and duration and sensitivity analyses (positive SMD values favour exercise).

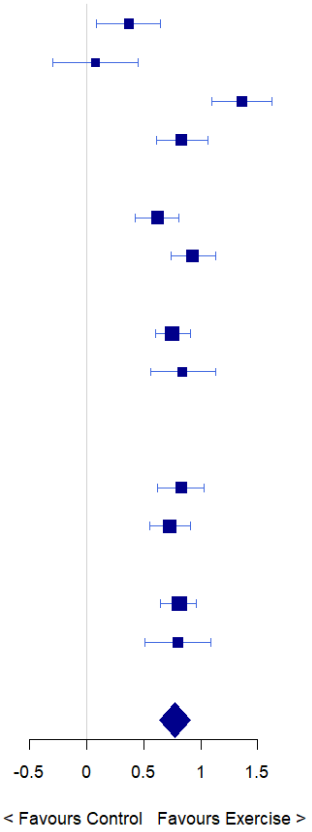
Subgroup	Studies (n=)	Participants (n=)	I² (%)	SMD (95% CI)	P-value
Exercise mode		Intervention vs. Control			
Aerobic exercise	11	671 vs. 628	80%	0.31 (0.17, 0.45)	<0.01
Resistance exercise	2	128 vs. 90	0%	0.25 (-0.02, 0.53)	0.07
Combined exercise	12	470 vs. 481	64%	0.33 (0.23, 0.44)	<0.01
Other exercise	6	225 vs. 185	87%	0.21 (0.00, 0.41)	0.04
Supervision [1]					
Supervised interventions	14	534 vs. 451	79%	0.44 (0.30, 0.57)	<0.01
Unsupervised interventions	17	960 vs. 933	70%	0.24 (0.15, 0.33)	<0.01
Intervention timing					
During treatment	17	829 vs. 737	79%	0.29 (0.19, 0.39)	<0.01
Post-treatment	13	618 vs. 596	74%	0.33 (0.22, 0.45)	<0.01
Mixed	1	47 vs. 51	-	0.11 (-0.28, 0.51)	0.25
Duration					
<12 week interventions	18	843 vs. 798	84%	0.34 (0.24, 0.44)	<0.01
>12 week interventions	13	651 vs. 586	13%	0.26 (0.14, 0.37)	<0.01
Sensitivity analyses [2]					
High quality studies only	21	407 vs. 422	67%	0.30 (0.22, 0.38)	<0.01
Stage II+ only	4	92 vs. 95	73%	0.46 (0.16, 0.75)	<0.01
Overall	**31**	**1494 vs. 1384**	**75%**	**0.30 (0.23, 0.38)**	**<0.01**



[1] Supervised intervention were classed as interventions where ≥50% of prescribed exercise involved face-to-face supervision and unsupervised interventions involved <50% of prescribed exercise involving face-to-face supervision.
[2] Sensitivity analyses were performed only on i) high quality studies, and ii) studies with 100% of samples with stage II+ disease.

Supplementary Content 7. Meta-analyses results of anxiety with subgroup analyses for exercise mode, intervention supervision, timing and duration and sensitivity analyses (positive SMD values favour exercise).

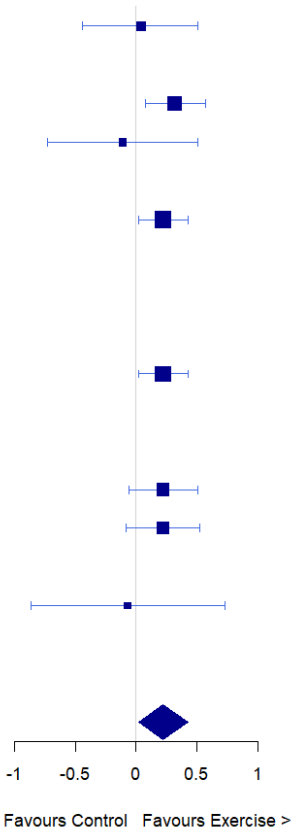
Subgroup	Studies (n=)	Participants (n=)	I² (%)	SMD (95% CI)	P-value
Exercise mode		Intervention vs. Control			
Aerobic exercise	4	84 vs. 127	0%	0.37 (0.09, 0.65)	0.01
Resistance exercise	1	41 vs. 82	-	0.08 (-0.30, 0.45)	0.68
Combined exercise	4	143 vs. 143	59%	1.36 (1.10, 1.62)	<0.01
Other exercise	5	168 vs. 217	94%	0.83 (0.61, 1.06)	<0.01
Supervision [1]					
Supervised interventions	7	213 vs. 299	92%	0.62 (0.43, 0.81)	<0.01
Unsupervised interventions	7	223 vs. 270	82%	0.93 (0.74, 1.13)	<0.01
Intervention timing					
During treatment	10	328 vs. 465	92%	0.75 (0.60, 0.91)	<0.01
Post-treatment	4	108 vs. 104	14%	0.84 (0.56, 1.13)	<0.01
Mixed	0	-	-	-	-
Duration					
<12 week interventions	7	198 vs. 254	91%	0.83 (0.62, 1.03)	<0.01
>12 week interventions	7	238 vs. 315	89%	0.73 (0.55, 0.91)	<0.01
Sensitivity analyses [2]					
High quality studies only	10	341 vs. 433	91%	0.81 (0.65, 0.96)	<0.01
Stage II+ only	4	102 vs. 98	84%	0.80 (0.51, 1.09)	<0.01
Overall	**14**	**436 vs. 569**	**89%**	**0.77 (0.64, 0.91)**	**<0.01**



[1] Supervised intervention were classed as interventions where ≥50% of prescribed exercise involved face-to-face supervision and unsupervised interventions involved <50% of prescribed exercise involving face-to-face supervision.
[2] Sensitivity analyses were performed only on i) high quality studies, and ii) studies with 100% of samples with stage II+ disease.

Supplementary Content 10. Meta-analyses results of waist circumference with subgroup analyses for exercise mode, intervention supervision, timing and duration and sensitivity analyses (positive SMD values favour exercise).

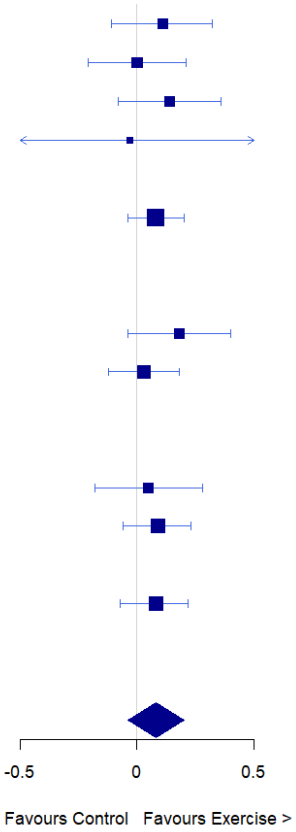
Subgroup	Studies (n=)	Participants (n=)	I^2 (%)	SMD (95% CI)	P-value
Exercise mode		Intervention vs Control			
Aerobic exercise	3	30 vs. 39	0%	0.04 (-0.44, 0.51)	0.89
Resistance exercise	0	0 vs. 0	-	-	-
Combined exercise	4	120 vs. 152	0%	0.32 (0.08, 0.57)	<0.01
Other exercise	1	20 vs. 20	-	-0.11 (-0.73, 0.51)	0.72
Supervision [1]					
Supervised interventions	8	170 vs. 211	0%	0.22 (0.02, 0.43)	0.03
Unsupervised interventions	0	-	-	-	-
Intervention timing					
During treatment	0	-	-	-	-
Post-treatment	8	170 vs. 211	0%	0.22 (0.02, 0.43)	0.03
Mixed	0	-	-	-	-
Duration					
<12 week interventions	6	84 vs. 123	0%	0.22 (-0.06, 0.51)	0.12
>12 week interventions	2	170 vs. 211	0%	0.22 (-0.08, 0.52)	0.14
Sensitivity analyses [2]					
High quality studies only	1	10 vs. 16	-	-0.07 (-0.86, 0.73)	0.87
Stage II+ only	0	-	-	-	-
Overall	**8**	**170 vs. 211**	**0%**	**0.22 (0.02, 0.43)**	**0.03**



[1] Supervised intervention were classed as interventions where ≥50% of prescribed exercise involved face-to-face supervision and unsupervised interventions involved <50% of prescribed exercise involving face-to-face supervision.
[2] Sensitivity analyses were performed only on i) high quality studies, and ii) studies with 100% of samples with stage II+ disease.

Supplementary Content 11. Meta-analyses results of body weight with subgroup analyses for exercise mode, intervention supervision, timing and duration and sensitivity analyses (positive SMD values favour exercise).

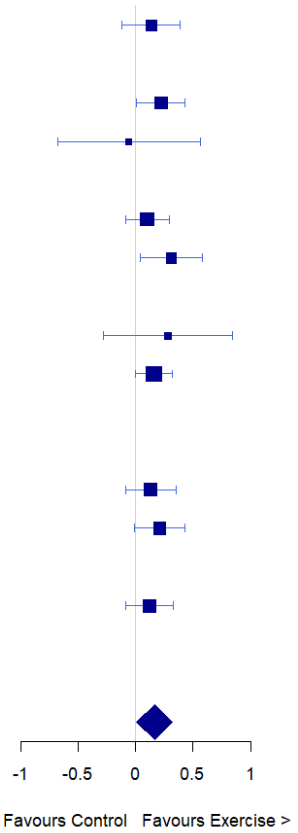
Subgroup	Studies (n=)	Participants (n=)	I^2 (%)	SMD (95% CI)	P-value
Exercise mode		Intervention vs. Control			
Aerobic exercise	6	172 vs. 164	0%	0.11 (-0.11, 0.32)	0.32
Resistance exercise	3	172 vs. 169	0%	0.00 (-0.21, 0.21)	0.99
Combined exercise	5	162 vs. 160	0%	0.14 (-0.08, 0.36)	0.22
Other exercise	1	20 vs. 20	-	-0.03 (-0.65, 0.59)	0.92
Supervision [1]					
Supervised interventions	15	526 vs. 513	0%	0.08 (-0.04, 0.20)	0.22
Unsupervised interventions	0	-	-	-	-
Intervention timing					
During treatment	2	164 vs. 160	0%	0.18 (-0.04, 0.40)	0.11
Post-treatment	13	362 vs. 353	0%	0.03 (-0.12, 0.18)	0.67
Mixed	0	-	-	-	-
Duration					
<12 week interventions	7	148 vs. 145	0%	0.05 (-0.18, 0.28)	0.65
>12 week interventions	8	378 vs. 368	20%	0.09 (-0.06, 0.23)	0.24
Sensitivity analyses [2]					
High quality studies only	8	373 vs. 361	0%	0.08 (-0.07, 0.22)	0.29
Stage II+ only	0	-	-	-	-
Overall	**15**	**526 vs. 513**	**0%**	**0.08 (-0.04, 0.20)**	**0.22**



[1] Supervised intervention were classed as interventions where ≥50% of prescribed exercise involved face-to-face supervision and unsupervised interventions involved <50% of prescribed exercise involving face-to-face supervision.
[2] Sensitivity analyses were performed only on i) high quality studies, and ii) studies with 100% of samples with stage II+ disease.

Supplementary Content 12. Meta-analyses results of body mass index with subgroup analyses for exercise mode, intervention supervision, timing and duration and sensitivity analyses (positive SMD values favour exercise).

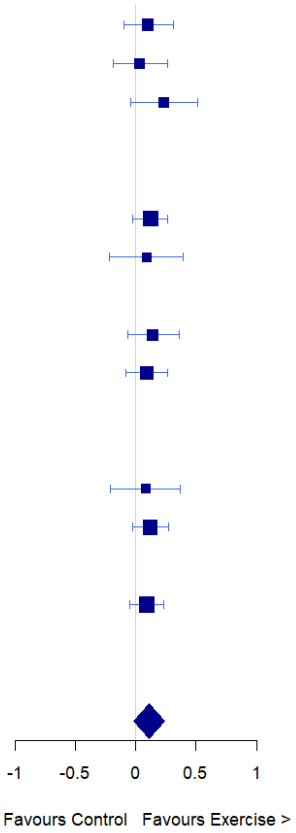
Subgroup	Studies (n=)	Participants (n=)	I^2 (%)	SMD (95% CI)	P-value
Exercise mode		Intervention vs. Control			
Aerobic exercise	4	123 vs. 119	0%	0.14 (-0.12, 0.39)	0.29
Resistance exercise	0	-	-	-	-
Combined exercise	8	165 vs. 204	5%	0.22 (0.01, 0.43)	0.04
Other exercise	1	20 vs. 20	-	-0.06 (-0.68, 0.56)	0.86
Supervision [1]					
Supervised interventions	8	205 vs. 232	0%	0.10 (-0.09, 0.29)	0.31
Unsupervised interventions	5	103 vs. 111	0%	0.31 (0.04, 0.58)	0.03
Intervention timing					
During treatment	2	27 vs. 27	83%	0.28 (-0.28, 0.84)	0.33
Post-treatment	11	281 vs. 316	0%	0.16 (-0.00, 0.32)	0.05
Mixed	0	-	-	-	-
Duration					
<12 week interventions	6	149 vs. 178	0%	0.13 (-0.09, 0.35)	0.24
>12 week interventions	7	159 vs. 165	20%	0.21 (-0.01, 0.43)	0.07
Sensitivity analyses [2]					
High quality studies only	6	177 vs. 175	2%	0.12 (-0.09, 0.33)	0.27
Stage II+ only	0	-	-	-	-
Overall	**13**	**308 vs. 343**	**0%**	**0.17 (0.01, 0.32)**	**0.03**



[1] Supervised intervention were classed as interventions where ≥50% of prescribed exercise involved face-to-face supervision and unsupervised interventions involved <50% of prescribed exercise involving face-to-face supervision.
[2] Sensitivity analyses were performed only on i) high quality studies, and ii) studies with 100% of samples with stage II+ disease.

Supplementary Content 13. Meta-analyses results of body fat with subgroup analyses for exercise mode, intervention supervision, timing and duration and sensitivity analyses (positive SMD values favour exercise).

Subgroup	Studies (n=)	Participants (n=)	I² (%)	SMD (95% CI)	P-value
Exercise mode		Intervention vs Control			
Aerobic exercise	5	185 vs. 177	0%	0.10 (-0.10, 0.31)	0.33
Resistance exercise	4	150 vs. 150	0%	0.03 (-0.19, 0.26)	0.78
Combined exercise	4	104 vs. 106	0%	0.23 (-0.04, 0.51)	0.09
Other exercise	0	-	-	-	-
Supervision [1]					
Supervised interventions	9	352 vs. 350	0%	0.12 (-0.03, 0.26)	0.13
Unsupervised interventions	4	87 vs. 83	0%	0.09 (-0.22, 0.39)	0.57
Intervention timing					
During treatment	2	164 vs. 160	0%	0.14 (-0.07, 0.36)	0.20
Post-treatment	11	275 vs. 273	0%	0.09 (-0.08, 0.26)	0.29
Mixed	0	-	-	-	-
Duration					
<12 week interventions	5	95 vs. 91	0%	0.08 (-0.21, 0.37)	0.59
>12 week interventions	8	344 vs. 342	20%	0.12 (-0.03, 0.27)	0.12
Sensitivity analyses [2]					
High quality studies only	10	384 vs. 378	0%	0.09 (-0.05, 0.23)	0.21
Stage II+ only	0	-	-	-	-
Overall	**13**	**439 vs. 433**	**0%**	**0.11 (-0.02, 0.24)**	**0.11**



[1] Supervised intervention were classed as interventions where ≥50% of prescribed exercise involved face-to-face supervision and unsupervised interventions involved <50% of prescribed exercise involving face-to-face supervision.
[2] Sensitivity analyses were performed only on i) high quality studies, and ii) studies with 100% of samples with stage II+ disease.

Supplementary Content 3: Overview of samples and exercise details of included studies (n=61)

	Sample	Exercise	Intervention setting	Supervision[1]
Ahmed 2006	N=46: 0–III BC with lymphoedema Exercise group: DCIS: 1 (4.4%); Stage I: 6 (26.1%); Stage II: 13 (56.5%) Stage III: 3 (13.0%)	Type: Resistance exercise Frequency: 2/week for 6 months Intensity: 3 sets per exercise of 8–12 repetitions Time: ~60 minutes	Recreation centre	Supervised: ACSM certified fitness professional.
Anderson 2012	N=104 stage I–III BC Exercise group I: n=25 (48%); II: n=19 (37%); III: n=8 (15%); N/A: n=0. Usual care I: n=26 (50%); II: n=21 (40%); III: n=4 (8%); N/A: n=1 (2%).	Type: Combined aerobic and resistance Frequency: 2/week for 12 months Intensity: Resistance exercise: >50%1RM, 12 repetitions 14–16 RPE Time: ~60 min total session (30min continuous walking)	University health and exercise research centre	Supervised: Occupational or physical therapist.
Banerjee 2007	N=68 undergoing RT; Stage II–III Exercise group (n=23): II: 17 (48%) III: 18 (52%)	Type: Other (Yoga) Frequency: 6 weeks Intensity: Low Time: 90 min	Hospital outpatient setting and home	Supervised: Yoga instructors
Campbell 2017	N=19 completed chemotherapy for stages I-IIIA BC I: 0 II: 10 (100%) III: 0	Type: Aerobic Frequency: 4/week for 24 weeks Intensity: 60–80% of HRR Time: 30–45 min	Research gym and home	Supervised: Not reported by whom Unsupervised
Cantarero-Villanueva 2012a	N=40 BC; Stage I–IIIA currently receiving HT. Exercise group n=20 I: 6 (30) II: 8 (40) IIA: 6 (30)	Frequency: 3/week for 8 weeks Intensity: Not specified Time: 60 min (5 minutes of warm-up, 15–20 min of aerobic exercise, 15 min of mobility exercise and 20 min of recovery techniques. Type: Other, hydrotherapy	University medical centre outpatient clinic and swimming pool	Supervised: Exercise trainer specialist and physiotherapists
Cantarero-Villanueva 2012b	n=78 BC survivors; stage I–IIIA Exercise group n=32: I: 4 (12.5) II: 23 (71.9) IIIA: 5 (15.6)	Frequency: 3/week for 8 weeks Intensity: Aerobic exercise[]: Resistance exercise: 75% maximum load, 2–3 sets of 10–15 repetitions, Time: 90 min Type: Aerobic, resistance & mobility exercise (Core Stability Exercises; all major muscle groups; small soft ball, mats, fit-ball & resistance bands).	University medical centre outpatient clinic and swimming pool	Supervised: not reported
Cantarero-Villanueva 2012c;	N=66; stage I–IIIA Exercise group (n=33) I: 16 (48) II: 10 (30) IIIA: 7 (22)	Frequency: 3/week for 8 weeks Intensity: Low-intensity Time: 60 min (10-min warm-up, 35 min, 15 min cool-down) Type: Hydrotherapy	University medical centre outpatient clinic and swimming pool	Supervised: Physical therapist
Cantarero-Villanueva	N=68 (stages I–IIIA), post-treatment excluding	Frequency: 3/ week for 8 weeks	University medical centre outpatient	Supervised: Exercise specialist and

2013	hormone therapy Exercise group: n=32 I: 4 (12.5) II: 23 (72) IIIA: 5 (15.5)	Intensity: Moderate; 2–3 sets of 8–12 repetitions Time: 60 min (10 min warm-up, 40 min aerobic & endurance exercises, 10 min cool-down). Type: Hydrotherapy	clinic and swimming pool	physical therapists
Chandwani 2014	N=109 stage 0–III breast undergoing RT Exercise group: 0: 5 10 I: 16 30 II: 15 28 III: 17 32	Frequency: 3/week for 6 weeks Intensity: Low Time: 60 min Type: Yoga	Cancer treatment centre	Supervised: certified yoga instructor
Cormie 2013	N=63; stage I–III BC; High-load exercise: I: 2 (9.1) II: 18 (81.8) III: 2 (9.1) Low-load exercise: I: 5 (23.8) II: 10 (47.6) III: 6 (28.6)	Frequency: 2/wk for 12 weeks Intensity: 12–16 RPE; High load: 75–85 % of 1RM using 10–6 RM Low load: 55–65 % of 1RM using 20–15 RM Time: 60 min (inc. 10 min warm-up & 5 min cool-down) Type: Resistance exercise	Hospital, health clinic	Supervised: Accredited exercise physiologist
Cornette 2016	N=44; stage I–IIIB during CT Exercise group (n=20) I: 3 (15%) IIA: 8 (40%) IIB: 3 (15%) IIIA: 5 (25%) IIIB: 1 (5%)	Frequency: ≥3/week for 1 year Intensity: Aerobic: 60RPM; 70–80% HRmax; 3-6 METS; Resistance: 2 sets per exercise of 8–12RM Time: Aerobic: 20–40 min (+5 min warm-up and 5 min cool down); Resistance: Not specified. Type: Resistance- and aerobic-based.	Home–based	Unsupervised: Weekly telephone contact from an exercise specialist
Courneya 2003	N=53; stage I–IIIa; completed treatment Exercise group: I: 10 (42%) IIa: 6 (25%) IIb: 6 (25%) IIIa: 2 (8%)	Frequency: 3/week for 15 weeks Intensity: 70–75% VO_2max Time: 15–35 mins (+5 min warm-up & 5 min cool down) Type: Aerobic; cycle ergometer	University Cancer institute	Supervised: Accredited exercise physiologist
Courneya 2007	N=242; stage I–IIIa; BC initiating adjuvant CT Aerobic exercise group: I: 18 (23.1%) IIa: 33 (42.3%) IIb: 17 (21.8%) IIIa: 10 (12.8%) Resistance exercise group: I: 22 (26.8%) IIa: 36 (43.9%) IIb: 9 (11.0%) IIIa: 15 (18.3%)	Frequency: 3/week for 15 weeks Intensity: Aerobic exercise group: 60–80%VO_2max Resistance exercise group: 2 sets of 8–12 repetitions at 60-70% 1RM Time: Aerobic exercise group: 15–45 min (+5 min warm-up and 5 min cool down) Resistance exercise group: Not specified. Type: Aerobic exercise (cycle ergometer, treadmill, or elliptical) or resistance exercise	University Cancer institute	Supervised: Accredited exercise physiologist

Danhauer 2009	N=44; DCIS– stage VI Exercise group: DCIS: 13.6 (3%) I: 22.7 (5%) II: 45.5 (10%) III: 13.6 (3%) IV: 4.6 (1%)	Type: Other, yoga Frequency: 1/week for 10 weeks Intensity: Low Time: 75 mins	Yoga studio	Supervised: Certified yoga instructor
De Luca 2016	N=20; stage I–III completed treatment Exercise group n=10: I: 4 (x%) II: 5 (x%) III: 2 (x%)	Frequency: 2/ week for 24 weeks Intensity: Aerobic exercise: 70–80% HRmax; Resistance exercise: 2–4 sets per exercise, 6–10 repetitions at 40–60% 1RM. Time: 90 min (10 min warm-up, 40 min resistance exercise, 30 min aerobic exercise, 10 min cool down); Type: Aerobic and resistance exercise	University gymnasium	Supervised: Fitness professional and physician
Dethlefsen 2016	N= 74 diagnosed with operable (stage I–III); <6 months since completing CT Exercise group (n=37) I: 4% II: 60% III: 36%	Type: Aerobic and resistance exercise Frequency: 1/week for 6 months (supervised) Intensity: Aerobic exercise: Intervals ranged from 30 s (maximum intensity) to 6 min (90%–95% of HRmax); Resistance exercise: 3 sets of 8–12 repetitions at 70–90% of 1RM Time: 90 min (supervised), >3 h/week	Hospital	Supervised: not reported
Dolan 2016	N=33; stage 0–III; postmenopausal; Interval exercise group: 0: 0 I: 3 II: 5 III: 3 Other: 1 Continuous intensity exercise group: 0: 1 I: 2 II: 2 III: 5 Other: 1	Frequency: 3/week for 6 weeks Intensity: Interval exercise: 3.22–4.02 km; ≤2 min bouts at ≥80 % VO_2peak; Continuous exercise: 3.22–4.02 km at 55–70 % VO_2peak Time: Interval exercise: Continuous exercise: Type: Aerobic (treadmill)	Location not specified	Supervised: Accredited exercise physiologist
Drouin 2005	N=20 stage 0–IIIb; during RT Exercise group (n=13): 0: 3 I: 2 II: 6 III: 2	Frequency: 3–5/week for 7 weeks Intensity: 50–70% HRmax Time: 20–45 min Type: Aerobic, walking	Home-based	Unsupervised: Weekly contact (face-to-face or by telephone) with researcher
Eakin 2012	N=143; invasive BC, 6 weeks post-surgery Telephone group: 0–I: 26 (35.6%) II+: 38 (52.1%)	Frequency: ≥4/week for 8 months Intensity: Low–high Time: 20–45+ min Type: Aerobic & resistance exercise	Home-based	Unsupervised: Weekly to monthly telephone contact with an Accredited exercise physiologist

		(telephone-delivered exercise)		
Fernández-Lao 2013	N=98; stage I–IIIA) completed treatment (excluding HT) Land-based exercise group n=31: I: 5 II: 21 IIIa: 5 Water-based exercise group n=33: I: 13 II: 13 IIIa: 7	Frequency: 3/ week for 8 weeks Intensity: 60% HRmax (aerobic exercise) and 2–3 sets of 8–12 repetitions (resistance exercise) Time: 60 min (inc. 10 min warm-up and 10 min cool-down) Type: Aerobic and resistance exercise; land- or water-based	A gymnastic hall and heated swimming pool	Supervised: Fitness specialist and physical therapist
Galiano-Castillo 2017	N=81 completed adjuvant therapy (except hormone treatment) for stage I to IIIA breast cancer Exercise group n=40 I: 14 (35%) II: 18 (45%) IIA: 8 (20%)	Type: Combined aerobic and resistance Frequency: 3/week for 8 weeks Intensity: Moderate Time: 90 min	Home-based	Unsupervised: Internet-based (Tele-rehabilitation)
Gokal 2015	N=50; stage I–III BC N=25 exercise; n=25 control I: 0 0 II: 5 20 III: 20 80	Frequency: 5/week for 12 weeks Intensity: 12–14 RPE Time: 10–30 mins Type: Aerobic, Walking	Home-based	Unsupervised: Physical activity booklet
Guinan 2013	N=26 BC survivors Stage I–III Exercise group n=16: I: 3 (18.8) II: 10 (62.6) III: 3 (18.8)	Frequency: 2/week for 8 weeks Intensity: 35–65% HRR Time: 21–42 min Type: Aerobic (stationary bike, treadmill, rowing ergometer).	Centre- (unspecified) and home-based	Supervised: Physiotherapist and a research assistant
Hatchett 2013	N=85 stage I-IV BC completed treatment Intervention group (n=36) I: 10 II: 17 III: 6 IV: 3	Frequency: 3-7/week for 12 weeks Intensity: 12-14 RPE Time: 10-60 min (150 min/week total) Type: Aerobic and resistance exercise	Home-based	Unsupervised: email delivered intervention (e-counselor exercise physiologist)
Hayes 2012	N=194 Stage 0–III; 6-weeks post- surgery Face-to-face exercise (n=67) 0: 2 (3.0) I: 23 (34.3) II–III: 38 (56.7) Unknown: 4 (6.0) Telephone exercise (n=67) 0: 3 (4.5) I: 18 (26.9) II–III: 45 (67.2) Unknown: 1 (1.5)	Frequency: ≥4/week for 8 months Intensity: Low–high Time: 20–45+ min Type: Aerobic & resistance exercise	Home-based	Supervised and unsupervised: Accredited exercise physiologist
Headley 2004	n=32; stage IV BC. Exercise group (n=16)	Frequency[4]: 3/week for 12 weeks Intensity: “Low-to-moderate” (RPE not	Home-based	Unsupervised: exercise DVD

	IV: 16	reported) Time[5]: 30 min Type: Other; Stretching and repeated flexion and extension of the arms, head, upper torso, and legs while seated.		
Herrero 2005	N=16; stage I–II ductal breast carcinoma Exercise group; n=8 I: 3 II: 5	Frequency: 3/week for 8 weeks Intensity: Aerobic: 70–80% HRmax; Resistance: 1–3 sets of 8–20 repetitions; Time: 90 min (inc. 10 min warm-up & 10 min cool down) Type: Aerobic (cycle ergometer) & resistance exercise	Community fitness centre	Supervised: Exercise physiologists

Hornsby 2014	n=20; stage IIB–IIIC BC
	n=10 exercise;
	n=10 control;
		Frequency[4]: 3/week for 12 weeks
		Intensity: 60–100% VO_2peak
		Time[5]: 15–45 mins
		Type: Aerobic exercise (cycle ergometer; continuous and interval training)
			Cancer institute	Supervised: Exercise physiologist

Husebø 2014	N=67 stage I–III BC during CT Exercise group: I: 7 (24.2) II: 19 (65.5) III: 3 (10.3)	Frequency: Aerobic: Daily; Resistance exercise: 3/week for 6 months Intensity: Moderate Time: Aerobic exercise: 30 mins; Resistance exercise: Not specified Type: Aerobic & resistance exercise	Home-based	Unsupervised: fortnightly telephone calls from the research team
Hutnick 2005	N=49 stage I–III Exercise group: I: 6 (21.4%) II: 19 (67.9%) III: 2 (7.1%) Unknown: 1 (3.6%)	Frequency: 3/week for 6 months Intensity: Aerobic: 60–75% functional capacity; Resistance; 3 sets of 8-12 repetitions Time: 40–90 min Type: Aerobic & resistance exercise	University clinical setting and home	Supervised: exercise trainer
Kilbreath 2012	N=160 stage I–III BC Exercise group n=81 I: 17% II: 44% III: 38%	Type: Resistance exercise & stretching Frequency: ≥1/week for 8 weeks Intensity: Resistance exercises: 2 sets per exercise for 8–15 repetitions, 15 Borg RPE; Stretching: hold each stretch for 5–15 min Time: Not specified	Centre-based (unspecified) and home-based	Unsupervised and supervised: Not reported
Kim 2006	N=41 stage 0–III undergoing adjuvant therapy Exercise group: 0: 1 (4.5%) I: 10 (45.5%) II: 8 (36.4%) III: 3 (13.6%)	Type: Aerobic exercise Frequency: ≥3/week for 8 weeks Intensity: 60–70% HRR and/or VO_2peak Time: 30 min (+5 min warm-up and 5 min cool-down)	University exercise facility	Supervised: Exercise physiologists
Ligibel 2008	N=101 I–III Exercise group: I: 22 43 II: 22 43	Type: Aerobic & resistance exercise Frequency: >2/week for 16 weeks Intensity: Aerobic: 55–80% HRmax; Resistance: 80% 1RM, 2–4 sets per	Centre- (unspecified) and home-based,	Supervised: Personal trainer

	III: 6 12	muscle group Time: Aerobic exercise: 90 min; Resistance exercise: 50 min		

Ligibel 2016	n=101; metastatic BC.
	n=48 exercise;
	n=53 control;
		Frequency[4]: ≥ 150 min/week for 16 weeks
		Intensity: 55–80% HRmax
		Time[9]: ≥ 150 min/week
		Type: Aerobic exercise
			Home-based, supervised and unsupervised: Exercise physiologist	Unsupervised and supervised: Face-to-face and telephone contact with an exercise physiologist

Loudon 2014	N=28 stage 0–III BC Exercise group (n=15) 0: 0 I: 3 (25%) II: 6 (50%) III: 3 (25%)	Type: Yoga Frequency: 7/week for 8 weeks Intensity: Not specified Time: 40–90 min	Centre- (unspecified) and home-based,	Unsupervised and supervised: Yoga instructor and at home DVD
Macvicar 1989	n=45; stage II BC. n=18 exercise; age=45±10. n=11 stretching exercises); age=46±10. n=16 control; age=43±9	Type: Aerobic exercise (Interval cycle ergometry) Frequency[4]: 3/week for 10 weeks Intensity: 60–85% HRR Time[5]: Not reported	Centre-based (unspecified)	Supervised: Not reported
Maryam 2010	N=56 women with BC receiving CT stage I–III Exercise group I: 3 (10.7%) II: 20 (71.4%) III: 5 (17.9%)	Type: Aerobic & resistance Frequency: 3–5/week for 9 weeks Intensity: Light Time: 20–30 min	Home-based	Unsupervised: CD
Milne 2008	N = 58 within 2 years of completing adjuvant therapy stage I–IIIa Exercise group n=29: I: 15 (25.9%) IIa: 25 (43.1%) IIb: 16 (27.6%) IIIa: 2 (3.4%)	Type: Aerobic & resistance exercise Frequency: 3/week for 12 weeks Intensity: Aerobic exercise: Not specified; Resistance exercise: 12 exercises, 2 sets of 10–15 repetitions Time: Aerobic: 25 min (inc. 5 min cool-down).	Rehabilitation clinic	Supervised: Exercise physiologists
Moadel 2007	N=128 stages I to IV) BC Exercise group (n=84): I: 42 II: 36 III: 17 IV: 5	Frequency: 1/week for 12 weeks Intensity: Low Time: 90 min Type: Yoga	Cancer centre	Unsupervised and supervised: Oncologist and Yoga instructor
Mohan Rao 2015	N=98 stage II–III BC undergoing surgery followed by adjuvant RT and/or CT Exercise group n=45 II: 17 (54.83%) III: 16 (42.1%)	Frequency: 3/week for 24 weeks Intensity: Low Time: 60 min Type: Yoga	Hospital	Unsupervised and supervised: Yoga instructor
Mulero Portela 2008	N=44 Stage I–IV BC completed treatment Home exercise group: I: 3 II: 5	Home exercise group: Type: Aerobic & resistance exercise Frequency: 5/week for 26 weeks Intensity: Aerobic exercise: 12–16 RPE	Gymnasium or Home-based	Supervised and unsupervised: physical therapists

	III: 2 IV: 0 Unknown: 3 Gym exercise group: I: 0 II: 3 III: 6 IV: 0 Unknown: 3	(6–20 scale); Resistance exercise: 13–15 RPE (6–20 scale); 2–3 sets per exercise, 10–15 repetitions per set. Time: Aerobic exercise: 30 min; Resistance exercise: Not specified Gym exercise group: Type: Aerobic & resistance exercise Frequency: 5/week for 26 weeks Intensity: Aerobic exercise: 60–80% of HRmax; Resistance exercise: 13–15 RPE (6–20 scale); 2–3 sets per exercise, 10–15 repetitions per set. Time: Aerobic exercise: 30 min; Resistance exercise: Not specified		
Murtezani 2014	N=62 completed surgery, RT, and/or CT with or without current HT use stage I–IIIa. Exercise group (n=30) I: 10 (33%) IIa: 11 (37%) IIb: 6 (20%) IIIa: 3 (10%)	Type: Aerobic exercise Frequency: 3/week for 10 weeks Intensity: 50–75% HRR Time: 25–45 min	University clinical rehabilitation centre,	Supervised: Not reported
Musanti 2012	N=42 stage I–IIIB BC who had completed adjuvant chemotherapy Aerobic group: I: 5 II: 5 III: 2 Resistance group: I: 5 II: 10 III: 2	Aerobic group: Type: Aerobic exercise Frequency: 3/week for 12 weeks Intensity: 40–85 HRmax Time: 15–30 min Resistance group: Type: Resistance exercise Frequency: 3/week for 12 weeks Intensity: 3–5 RPE (0–10 scale, up to 8 RPE at the completion of 12 repetitions); 1 set of 10–12 repetitions Time: Not specified	Home-based	Unsupervised: Exercise booklet
Naraphong 2015	N=23 with postoperative stage I–IIIa breast cancer, scheduled to receive CT Exercise n=11: I: 1 (9.09%) II: 7 (63.64%) IIIA: 3 (27.27%)	Type: Aerobic exercise Frequency: 3–7/week for 10 weeks Intensity: 12–14 RPE (6–20 scale), 40–60% of HRmax; <3-6 METS Time: 20–30 min (plus 5 min warm-up & 5 min cool-down)	Home- and community-based	Unsupervised: Weekly telephone contact with a nurse
Naumann 2012	N=36 BC survivors stage I–III breast cancer, within 12 months of treatment completion Group-based exercise group (n=14) Stage (mean±SD): 2.0 ± 0.6	Type: Aerobic and resistance exercise Frequency: 3/week for 9 weeks Intensity: Moderate Time: 45–60 min	Gymnasium	Supervised: Accredited exercise physiologist
Pinto 2005	N=86: stage 0–II BC, completed treatment	Type: Aerobic	Home-based	Unsupervised: telephone support from

	0: 8 (18.6%) I: 17 (39.5%) II: 18 (41.9%)	Frequency: ≥5/week for 12 weeks Intensity: 55–65% HR_{max} Time: 30 min		research staff and pedometer
Pinto 2013	N=192: stage 0–IV BC currently undergoing treatment Exercise: 0: 12 (11%) I: 41 (39%) II: 44 (42%) III/IV: 9 (8%)	Type: Aerobic Frequency: ≥5/week for 12 weeks Intensity: 55–65% HR_{max} Time: 30 min	Home-based	Unsupervised: telephone counselling from a physical activity counsellor and pedometer
Pinto 2015	N=76 stage 0–III BC completed treatment 0: 3 (7.69%) I: 16 (41.03%) II: 16 (41.03%) III: 4 (10.26%)	Type: Aerobic (walking) Frequency: 5–7/week for 12 weeks Intensity: Moderate Time: ≥30 min	Home-based	Unsupervised: telephone counselling from a physical activity counsellor, pedometer and heart rate monitor
Raghavendra 2007	N=62 stage II–III BC on chemotherapy Exercise group n=28 II: 16 (57.1%) III: 12 (42.9%)	Frequency: 6/wk during the course of chemotherapy Intensity: Low Time: 60 min Type: Yoga	Hospital	Unsupervised and supervised: yoga instructor and home exercise video

Rao 2012	n=10; stage II-III BC.
	n=5 exercise;
	n=5 control;
		Frequency: 3/week for 16 weeks
		Intensity: Not specified
		Time: 60 min
		Type: Combined resistance- and aerobic exercise (involving bouts of jumping jacks, running in place, arm and leg exercises with exercise balls, bands and weights)
			Home- and community-based	Supervised: personal trainer

Rogers 2009	N=41 stage I–IIIA BC Intervention n=21: I: 6 (29) II: 11 (52) III: 4 (19)	Frequency: 3–5/week for 12 weeks Intensity: Moderate Time: 150 min/week Type: Walking	Centre- (unspecified) and home-based	Unsupervised and supervised: ACSM exercise specialist and/or certified exercise physiologist
Schmidt 2015	N=101 Stage I–IV BC starting CT Exercise group (n=49): I: 37 (38.9%) II: 41 (43.2%) III: 15 (15.8%) IV: 2 (2.1%)	Frequency: 2/week for 12 weeks Intensity: 3 sets, 8–12 repetitions at 60–80% of 1RM Time: 60 min Type: Resistance exercise (8 different machine exercises)	Hospital	Supervised: Physical therapists
Schwartz 2007	N=66 stage I–III BC beginning adjuvant CT Aerobic group n=22: I: 4 (18%) II: 13 (59%) III: 5 (12%) Resistance group n=21: I: 6 (28) II: 11 (52%) III: 4 (19%)	Aerobic group: Frequency: 4/week for 6 months Intensity: Moderate intensity (“breathing hard but able to talk”) Time: 15–30 min Type: Self-selected (e.g., walking or jogging) Resistance group: Frequency: 4/wk for 6 months	Home-based	Unsupervised: telephone contact from research staff

		Intensity: 2 sets of 8–10 repetitions Time: ~30 min Type: Thera-Band™ exercises (4 upper body & 4 lower body exercises).		
Short 2015	Tailored group n=109 0: 3 (2.9%) I: 27 (26.5%) II: 32 (31.4%) III: 23 (22.6%) IV: 2 (1.9%) Unknown: 15 (14.7%) Targeted group n=110 0: 3 (2.8%) I: 22 (20.8%) II: 45 (42.5%) III: 20 (18.8%) IV: 1 (0.9%) Unknown: 15 (14.5%)	Frequency: 4–7/week for 12 weeks Intensity: Moderate Time: ≥30 min Type: Aerobic and resistance (Tailored-print intervention: three computer-tailored physical activity newsletters; targeted-print group: physical activity booklet)	Home-based	Unsupervised; tailored-physical activity print materials or targeted physical activity booklet
Vallance 2007	N=377 stage I–III BC completed treatment Pedometer group (n=94) I: 38 (40.4%) II: 50 (53.2%) III: 6 (6.4%)	Frequency: ≥5/week for 12 weeks Intensity: Moderate Time: ≥30 min Type: Aerobic	Home-based	Unsupervised.
Vallance 2015	N=95 stage I–III BC receiving adjuvant chemotherapy Intervention group (n=49) I: 10 (20%) II: 31 (63%) III: 8 (16%)	Frequency: ≥5/week for 12 weeks Intensity: Moderate Time: ≥30 min Type: Aerobic	Home-based	Unsupervised: tailored print materials and pedometer
Van Waart 2016	N=230 stage I–III undergoing adjuvant chemotherapy OnTrack (n=76) I: 5 (7) II: 32 (42) III: 39 (51) Onco-Move (n=77) I: 2 (3) II: 40 (52) III: 35 (45)	Onco-Move (n=77) Frequency: 5/week for duration of chemotherapy Intensity: 12–14 RPE Time: >30 min Type: Combined resistance and aerobic OnTrack (n=76) Frequency: 5/week for duration of chemotherapy Intensity: Aerobic: 50% to 80% of the maximal workload; Resistance: 6 exercises, 2 sets, 8 repetitions 80% of 1RM Time: 50 min Type: Combined resistance and aerobic	Home-based, or Centre-based (unspecified)	Unsupervised, or Supervised: physical therapists
Wang 2011	N=72 Stage I–II undergoing CT Exercise group (n=35) I: 9 (25.7%) II: 26 (74.3%)	Type: Aerobic exercise, walking Frequency: 3–5/week for 6 weeks Intensity: 40–60% HR_{max} or Time: 30 min	Home-based	Unsupervised: weekly telephone calls

Winters Stone 2011	N=106 >1 year post-RT and/or CT 0: 7.7% I: 38.5% II: 48.1% IIIa: 1.9%	Type: Resistance exercise (+impact training) Frequency: 2–3/week for 12 months Intensity: 60–70% of 1-RM for 1–3 sets of 8–12 repetitions Time: 45–60 min	University setting and home-based	Unsupervised and supervised: certified exercise instructors
Winters-Stone 2013	71 BCS Stage I–IIIa: prematurely menopausal Impact + resistance group (N=35) I: 22.9 % II: 65.7 % III: 11.4 %	Frequency: 3/week for 12 months (2 supervised + 1 unsupervised) Intensity: 8–15 repetition maximum Time: 30–60 min/session Type: Free weights (e.g., dumbbells, barbells, resistance bands, and weighted vests Jump: 0–10% BW, 3–10 sets, 10 repetitions; Upper and lower-body RE: 2–3 sets per exercise, 6–14 repetitions (6-14RM; upper body RE); 0–10% BW (lower body RE)	University setting	Supervised: certified exercise instructors
Yang 2010	N=40 stage I–II BC receiving adjuvant chemotherapy I: 9 (47.4%) II: 10 (52.6%)	Type: Aerobic Frequency: 3/week for 12 weeks Intensity: 60–80% of age-adjusted maximal heart rate Time: 30 min (plus 5 min warm-up and 5 min cool-down)	Home-based	Unsupervised: weekly telephone calls

[1] Interventions were considered supervised if 50% or more of the prescribed exercise involved face-to-face supervision.

Supplementary Content 4: Summary of study recruitment, retention, adherence, reasons for withdrawal, intervention settings and supervision and exercise related events (n=61)

Study	Recruitment (eligible / total number screened)	Retention	Reasons for withdrawal	Adherence (to scheduled exercise sessions)	Location and supervision	Adverse events
Ahmed 2006	85/238 eligible & consented[2] 64%	Exercise: 100% Baseline: n=23 Completed: n=23 Control: 96% Baseline: n=23 Completed: n=22	Exercise: n=0 Control n=1 Breast cancer recurrence n=1	92%	Recreation centre, supervised: ACSM certified fitness professional.	Exercise: Not reported Control: Not reported
Anderson 2012	104/625 eligible & consented 16%	Exercise: 83% Baseline: n=52 Completed: n=43 Control: 75% Baseline: n=52 Completed: n=39	Not reported by group: Feeling overwhelmed or a lack of time to participate (38%), lost to follow-up (19%), lack of interest (10%), family issues (10%), death (n=2, 10%), and other reasons (10%).	71.2%	University health and exercise research centre, supervised: Occupational or physical therapist.	Exercise: N=2 exercise related adverse events (n=1 pectoral muscle pain; n=1 stress fracture in foot). Control: Not reported
Banerjee 2007	Not reported	Exercise: 100% Baseline: n=35 Completed: n=35 Control: 70% Baseline: n=33 Completed: n=23	Exercise: n=0 Control: n=10 Reason not reported	Not reported.	Hospital outpatient, supervised: Yoga instructors + Home, unsupervised	Exercise: Not reported Control: Not reported
Campbell 2017	19/102 eligible and consented 18.6%	Exercise: 100% Baseline: n=10 Completed: n=10 Control: 100% Baseline: 9 Completed: n=9	Exercise: n=0 Control: n=0	Overall: 87.5% Supervised gym: 88% Unsupervised home: 87%	Research gym, supervised: not reported by whom + Home, unsupervised	Exercise: No adverse events occurred. Control: No adverse events occurred.
Cantaro-Villanueva 2012a	40/62 eligible & consented 65%	Exercise: 100% Baseline: n=20 Completed: n=20 Control: 100% Baseline: n=20 Completed: n=20	Exercise: n=0 Control: n=0	79%	University medical centre outpatient clinic and swimming pool, supervised: Exercise trainer specialist and physiotherapists	Exercise: N=4 in the hydrotherapy group showed a temporal (1–3 days) increase of pain after one session, but this event did not stop them continuing the programme. Control: No further adverse events were reported.
CantarerVillanueva 2012b	78/238 eligible and consented 33%	Exercise: 84% Baseline: n=38 Completed: n=32 Control: 88% Baseline: n=40 Completed: n=35	Exercise: n=6 (health problems n=1; family problems n=1; never started program n=2; too busy n=2) Control: n=5 (not contactable n=1; absent from test n=4)	Overall: 83.5% Completed treatment ≤6 months: 79.6% Completed treatment >6 months:	University medical centre outpatient clinic and swimming pool, supervised: not reported	Exercise: No exercise-related adverse events Control: No exercise related adverse events

				87.4%		
CantareVillanueva 2012c;	66/95 eligible and consented 69%	Exercise: 97% Baseline: n=33 Completed: n=32 Control: 100% Baseline: n=33 Completed: n=33	Exercise: n=1 (breast cancer recurrence) Control: n=0	>85%	University medical centre outpatient clinic and swimming pool, supervised: Physical therapist	Exercise: N=3: transient increase of edema, N=4: increase in fatigue immediately after the beginning of the first session, which improved in the next few days. Control: None
CantareVillanueva 2013	68/163 eligible and consented 42%	Exercise: 94% Baseline: n=34 Completed: n=32 Control: 85% Baseline: n=34 Completed: n=29	Exercise: n=2 (did not commence n=1; too busy n=1) Control: n=5 (not contactable n=1; absent from test n=4)	84%	University medical centre outpatient clinic and swimming pool, supervised: Exercise specialist and physical therapists	Exercise N=3: discomfort or low-intensity pain/stiffness after an exercise session (nevertheless, they continued the program.) Control: None
Chandwani 2014	178/294 eligible and consented 61%	Exercise: 81% Baseline: n=53 Completed: n=43 Control (WL): 86% Baseline: n=54 Completed: n=46	Exercise: n=10 reasons not reported Control: n=8 reasons not reported	78%	Cancer treatment centre, supervised: certified yoga instructor	Exercise: Not reported. Control: None reported
Cormie 2013	62/135 eligible & consented 46%	High-load: 86% Baseline: n=22 Completed: n=19 Low-load: 100% Baseline: n=21 Completed: n=21 Control: 89% Baseline: n=19 Completed: n=17	High-load exercise (n=3): Unrelated medical condition n=1; time constraints n=2 Control (n=2): Unrelated medical condition n=1; time constraints n= 1	High-load exercise: 96% Low-load exercise: 96%	Hospital/health clinic, supervised: Accredited exercise physiologist	No exercise-related adverse events.
Cornette 2016	44/89 eligible and consented 49%	Exercise: 68% Baseline: n=22 Completed: n=15 Control: 68% Baseline: n=22 Completed: n=15	Exercise (n=7): N=2 excluded (n=1 did not complete baseline CTEP; n=1 using beta-blockers); n=5 no reason Control (n=7): n=7 no reason	88%	Home-based, unsupervised	No exercise-related adverse events.
Courneya 2003	53/370 eligible and consented 14%	Exercise: 96% Baseline: n=25 Completed: n=24 Control: 93% Baseline: n=28 Completed: n=26	Exercise: N=1 gastrointestinal complication Control: n=2 N=1 orthopaedic complication; n=1 Bronchitis	98%	Cancer institute and University, supervised: Accredited exercise physiologist	Five participants (20.8%) in the exercise group experienced an adverse event compared with two participants (7.1%) in the control group. The adverse events in the exercise group were lymphedema (n= 3), gynecologic complication (n=1), and influenza (n=1). Control: The control group's events were foot fracture (n =1) and bronchitis (n=1).
Courneya 2007	242/1468 eligible and	Aerobic: 95% Baseline: n=78	Aerobic n=4 Reasons not reported	Aerobic 72.0%	Cancer institute and University, supervised: Accredited exercise	Exercise N=2 after baseline maximal treadmill testing (n=1 light-

	consented 16%	Completed: n=74 Resistance: 94% Baseline: n=82 Completed: n=77 Control: 89% Baseline: n=82 Completed: n=73	Resistance n=5 Reasons not reported Control n=9 Reasons not reported	Resistance 68%	physiologist	headedness, hypotensive, and moderately nauseous; n=1dizziness, weakness, and mild diarrhoea). Control: none
Defelson 2016	214/1400 eligible and consented 15.2%	Exercise: 100% Baseline: n=37 Completed: n=37 Control: 100% Baseline: n=37 Completed: n=37	Unable to be determined.	66%	Hospital, supervised: not reported.	No exercise-related adverse events.
Danhauer 2009	44/299 responded, eligible and consented 15%	Exercise: 59% Baseline: n=22 Completed: n=13 Control: 64% Baseline: n=22 Completed: n=14	Exercise (n=9): N=9 did not return questionnaire (lost to follow up) Control (n=8): N=7 did not return questionnaire (lost to follow up); N=1 dropped out of study	60%.	Yoga studio, supervised: Certified yoga instructor	No exercise-related adverse events.
De Luca 2016	Not reported.	Exercise: 100% Baseline: n=10 Completed: n=10 Control: 100% Baseline: n=10 Completed: n=10	Exercise n=0 Control n=0	Not reported	University gymnasium, supervised: Fitness professional and physician	No exercise-related adverse events.
Dolan 2016	36/59 eligible and consented 61%	Interval: 100% Baseline: n=12 Completed: n=12 Continuous: 92% Baseline: n=12 Completed: n=11 Control: 83% Baseline: n=12 Completed: n=10	Interval: n=0 Continuous: n=1 Reason not reported Control: n=2 Reason not reported	Interval exercise: 98% Continuous exercise: 98%	Location not specified, supervised: Accredited exercise physiologist	No exercise-related adverse events.
Drouin 2005	23/39 eligible and consented 59%	Exercise: 100% Baseline: n=13 Completed: n=13 Control: 80% Baseline: n=10 Completed: n=8	Exercise: N=0 Control: N=2 personal commitments	Mean = 3.6 days/week that aerobic exercise was performed.	Home-based, unsupervised	Not reported.
Eakin 2012	143/383 eligible and consented 37%	Exercise: 93% Baseline: n=73 Completed: n=68 Control: 99%	Exercise (n=5): n=4 health concerns; n=1 no longer has cancer	88%	Home-based, telephone delivered: Accredited exercise physiologist	N=3: muscle soreness (n=2); musculoskeletal injury (n=1).

		Baseline: n=70 Completed: n=69	Control (n=1): n=1 health concerns			
Galiano-Castillo 2017	81/99 eligible and consented 82%	Exercise: 87.8% Baseline: n=41 Completed: n=36 Control: 87.8% Baseline: n=41 Completed: n=36	Exercise n=5 Busy n=1 Health problems n=3 Not reported n=1 Control n=5 Busy n=3 Personal problems n=1 Death n=1	93.9%	Home-based, internet-based (tele-rehabilitation): unsupervised	Exercise: no intervention-related adverse events. Control: no intervention-related adverse events.
Gokal 2015	63/164 eligible and consented 38%	Exercise: 84% Baseline: n=25 Completed: n=21 Control: 100% Baseline: n=25 Completed: n=25	Exercise: n=5: Hospitalisation n=4; Medical difficulties n=1 Control: n=0	80%	Home-based, unsupervised	Not reported
Guinan 2013	26/32 eligible & consented 81%	Exercise: 88% Baseline: n=16 Completed: n=14 Control: 80% Baseline: n=10 Completed: n=8	Exercise group: N=2: N=2 time constraints Control group: N=2: N=2 illness unrelated to their breast cancer.	Not reported	Location not specified, supervised: Physiotherapist and a research assistant + Home-based, unsupervised	Not reported.
Fernández-Lao 2013	98/132 eligible and consented 74%	Land-based exercise Baseline: n=31[CC] Water-based exercise Baseline: n=33[CC] Control Baseline: n=34[CC]	Not reported	Land-based: 85% Water-based: 92%	A gymnastic hall and heated swimming pool, supervised: Fitness specialist and physical therapists	Not reported.
Hatchett 2013	85/200 eligible & consented 42.5%	Exercise: 88% Baseline: n=43 Completed: n=38 Control: 86% Baseline: n=42 Completed: n=36	Exercise n=5: Discontinued participation (n=5) Control n=6: Discontinued participation (n=6)	Not reported	Home-based, unsupervised email delivered intervention: e-counselor exercise physiologist	Not reported
Hayes 2012	194/402 eligible & consented 48%	Exercise: 91% Baseline: n=67 Completed: n=61 Telephone: 94% Baseline: n=67 Completed: n=63 Control: 93% Baseline: n=60 Completed: n=56	N=14[LL99] (Reasons: too busy (n=4); unhappy with allocation (n=2); not coping with treatment (n=2); unknown (n=2); unable to contact/passive withdrawal (n=2); Reasons: no longer interested (n=2))	Exercise: 88% Telephone: 81%	Home-based, supervised and unsupervised: face-to-face or telephone contact with accredited exercise physiologist	No exercise-related adverse events.

Headley 2004	Not reported	84% Baseline: n=38 Completed: n=32	n= 6; disease progression.	75%	Cancer centre outpatient clinic, supervised: Oncology nurse	No exercise-related adverse events.
Herrero 2005	20/37 eligible & consented 54%	Exercise: 80% Baseline: n=10 Completed: n=8 Control: 80% Baseline: n=10 Completed: n=8	Exercise: N=2; Reasons not reported Control: n=2; Reasons not reported	91%	Community fitness centre, supervised: Exercise physiologists	No exercise-related adverse events.
Hornsby 2014	20/1445 eligible & consented 1%	Exercise: 90% Baseline: n=10 Completed: n=9 Control: 100% Baseline: n=10 Completed: n=10	Exercise: n=1; and DVT and PE Control: n=0	82%	Cancer institute, supervised: Accredited exercise physiologist	Exercise: n=1 (unexplained leg pain that quickly resolved following exercise cessation); n=3 during exercise testing (n=1 exercise-induced oxygen desaturation, SpO^2 84%), n=1 anxiety attack, n=1 dizziness). Exercise:N=7 events (persistent tachycardia n=1, diverticulosis n=1, urinary tract infection (UTI) n=1, diabetes mellitus n=1, upper respiration tract infection n=1, hemorrhoids n=1; and DVT and PE n=1 (more than one event was observed in the same patient) Control:N=1 shingles to secondary to varicella zoster infection
Husebø 2014	67/93 eligible & consented 72%	Exercise: 76% Baseline: n=33 Completed: n=25 Control: 85% Baseline: n=34 Completed: n=28	Exercise: n=8 (n=7 no reason reported; n=1 syncope due to a comorbid condition) Control: n=6 (no reason reported)	58%	Home-based, unsupervised	Exercise N=1 reported knee discomfort (remained in trial); n=1 syncope during the walking exercise (related to a secondary chronic condition, withdrew from trial). Control N=0
Hutnick 2005	Not reported.	Exercise: 75% Baseline: n=28 Completed: n=21 Control: 71% Baseline: n=21 Completed: n=15	Exercise: n=7 (reasons not reported) Control: n=6 (reasons not reported)	Overall: 79% Months 1-3: 82.2% Months 4-6: 75.9%	University clinical setting, supervised: exercise trainer And/or Home-based, unsupervised (periodic contact with exercise trainer)	Not reported.
Kilbreath 2012	160/457 eligible & consented 35%	Exercise: 95% Baseline: n=81 Completed: n=77 Control: 93% Baseline: n=79 Completed: n=74	Exercise: N=4 time constraints Control: N=5 (n=3 time constraints, n=1 developed metastases, n=1 unable to contact).	Overall: 84% Supervised: 78% Unsupervised: 90%	Location and supervision not specified + Home-based, supervision not specified	Not reported.
Kim 2006	Not reported.	Exercise: 59% Baseline: n=37 Completed: n=22 Control: 51% Baseline: n=37	Exercise: N=5 intervention withdrew Control: N=6 control withdrew Personal problems (n = 2), problems at home (n = 2),	78%	University exercise facility, supervised: Exercise physiologists	No exercise-related adverse events. Exercise: Not reported. Control: None Baseline testing: N=2 ECG abnormality or hypertensive episodes during baseline graded exercise testing.

		Completed: n=19	problems related to chemotherapy (n = 3), thrombophlebitis in the lower leg (n = 2), non-exercise-related injuries (n = 1), or death (n = 1). N=12 control missed either a pre- or post-intervention graded exercise test. N=10 intervention missed either a pre- or post-intervention graded exercise test.			
Ligibel 2008	101/199 eligible & consented 51%	Exercise: 78% Baseline: n=51 Completed: n=40 Control: 84% Baseline: n=49 Completed: n=42	Exercise: n=11 Lost to follow-up (n = 2)Family emergency (n=1); too much of a time commitment (n=3); too ill for final measurements (n=1); disease recurrence (n=1), developed unrelated cancer (n=1), withdrew consent (n=1), need for unrelated surgery (n=1) Control: n=7 Lost to follow-up (n = 3) Disease recurrence (n=2), withdrew upon assignment to control group (n=1), family problems (n=1)	73%	Location and supervision not specified + Home-based, unsupervised	Not reported.
Ligibel 2016	Not reported.	Exercise: 68% Baseline: n=48 Completed: n=33 Control Baseline: n=53 Completed: n=43 81%	Exercise group (n=15): n=4 stopped attending and unreachable by study team; n=4 time and travel reasons; n=3 disease progression; n=1 deceased due to disease; n=2 moved during intervention n=1 no reason Control group (n=10): n=5 unreachable by study team; n=2 disease progression; n=1 time and travel reasons; n=1 no reason; n=1 ineligible due to active brain metastases	Not reported	Home-based, supervised and unsupervised: Exercise physiologist	No exercise-related adverse events.
Loudon 2014	28/59 eligible & consented 47%	Exercise: 80% Baseline: n=15 Completed: n=12 Control: 85%	Exercise n=3 Surgery n=1; broken hip n=1; acute illness n=1 Control n=2	Overall: 92% Home-practice: 86% Group yoga	Location not specified, supervised: certified yoga instructor + Home-based, unsupervised	No exercise-related adverse events.

		Baseline: n=13 Completed: n=11	Family reasons n=1; acute illness n=1	sessions: 97%		
Macvicar 1989	Not reported	72% Baseline: n=62 Completed: n=45	n=9 disease progression; n=1 transportation problems; n=2 commenced cardio-toxic medications; n=2 extreme chemotherapy associated side effects; n=3 equipment failure.	Not reported.	Location not specified, supervision not specified	Not reported.
Maryam 2010	Not reported	Exercise: 100% Baseline: n=28 Completed: n=28 Control: 100% Baseline: n=28 Completed: n=28	Exercise: n=0 Control: n=0	Not reported.	Home-based, unsupervised	Not reported.
Milne 2008	58/131 eligible & consented 44%	Exercise: 100% Baseline: n=29 Completed: n=29 Control: 100% Baseline: n=29 Completed: n=29	Exercise: n=0 Control: n=0	60%	Rehabilitation clinic, supervised: Exercise physiologists	Not reported.
Moadel 2007	164/193 eligible & consented 85%	Exercise: 78% Baseline: n=108 Completed: n=84 Control: 73% Baseline: n=56 Completed: n=44	Exercise n=24 Loss to follow up: 16; Refused: 5; Change in health status: 3 Control; n=12 Loss to follow up: 8; Refused: 3; Change in health status: 1	58%	Cancer centre, supervised: Oncologist and certified yoga instructor	Not reported.
Mohan Rao 2015	Not reported	Exercise: 73% Baseline: n=45 Completed: n=33 Control: 68% Baseline: n=53 Completed: n=36	Exercise n=12 Reason not reported Control n=17 Reason not reported	Not reported.	Hospital, supervised: yoga instructor	Exercise: N=2 (infections, secondary suturing, seroma, discharge , uncontrollable pain) Control: N=8 (infections, secondary suturing, seroma, discharge, uncontrollable pain) *2008 Rao paper included:
Mulero Portela 2008	Not reported	Gym exercise: 75% Baseline: n=16 Completed: n=12 Home exercise: 68% Baseline: n=19 Completed: n=13 Control: 100% Baseline: n=9 Completed: n=9	Gym exercise: N=4; moved to the United States (n=1); developed eye cancer (n=1); developed headaches with referral or MRI(n=1); foot surgery (n=1) Home exercise: N=6; developed uterine cancer (n=1); no show with no reason given (n=1); asthma complications and non-clearance from	Gym exercise Overall: 55% Aerobic exercise: 47% Resistance exercise: 63% Home exercise Overall: 79% Aerobic exercise: 71% Resistance exercise: 86%	Gymnasium, supervised and unsupervised: physical therapists or Home-based, supervised and unsupervised: physical therapists	Gym exercise; n=1 hypoglycaemia while at the gym during an exercise; n=1 high blood pressure (>140/90 mmHg) during their participation in the exercise programs; n=1 severe headache at during post-intervention exercise testing; n=1 foot pain which worsening during the first exercise session leading to study withdrawal and surgery. Home exercise N=1 asthma episode during the 12-minute walk

			physician to continue (n=1); personal problems (n=1); high blood pressure with referral for stress test (n=1); discontent with schedule (n=1). Control: N=0			test at baseline (leading to withdrawal prior to commencing intervention); n=2 high blood pressure (>140/90 mm Hg) during their participation in the exercise programs
Musanti 2012	55/314 eligible & consented 18%	Overall 76% Baseline: n=55 Completed: n=42 Aerobic Baseline: ? Completed: n=12 Resistance Baseline: ? Completed: n=17	N=7 difficulty fitting the exercise into their lives because of work and/or family responsibilities; n=1 breast reconstruction surgery rescheduled; n=1 one did not give a reason; n=1 could not complete the initial fitness testing because of an elevated HR; n=1 wanted more supervised exercise;N=1 appendicitis	Aerobic exercise: 81% Resistance exercise: 91%	Home-based, unsupervised	Exercise: N=2 tendonitis (n=1 shoulder, n=1 foot) Control: none
Murtezani 2014	73/241 eligible & consented 30%	Exercise: 81% Baseline: n=37 Completed: n=30 Control: 89% Baseline: n=36 Completed: n=32	Exercise n=7 Transportation difficulties n=3; lymphoedema n=3; low back pain n=1 Control n=4 Gynaecologic problems n=1; unreachable n=2; personal reason n=1	85%	University clinical rehabilitation centre, supervised: not reported by whom	Not reported.
Naraphong 2015	26/177 eligible & consented 15%	Exercise: 81% Baseline: n=11 Completed: n=9 Control: 100% Baseline: n=12 Completed: n=12	Exercise n=2: Moved & withdrew from care at the site at week 7 (n=1); Too busy for exercising at week 10 (n = 1) Control n=0	Not reported	Home- and community-based, unsupervised (weekly contact with a nurse)	Not reported.
Naumann 2012	40/48 eligible & consented 83%	Exercise: 93% Baseline: n=15 Completed: n=14 Control: 83% Baseline: n=12 Completed: n=10	Group exercise: N=1 (n=1 unrelated injury) Control: N=2 (n=1 unrelated injury; failed to commence participation n=1)	74%	Gymnasium, supervised: Accredited exercise physiologist	No exercise-related adverse events.
Pinto 2005	86/424 eligible & consented 20%	Exercise: 90.7% Baseline: n=43 Completed: n=39 Control: 100% Baseline: n=43 Completed: n=43	Exercise (n=4): n=1; could not be contacted to determine reasons, n=2; and participation terminated, n=1; the study team terminated one woman's participation because of symptoms of chest pain during exercise and her refusal to have these symptoms	Not reported	Home-based, unsupervised: telephone support from research staff	Not reported

			evaluated by her physician). Control (n=0)			
Pinto 2013	192/351 eligible & consented 55%	Exercise: 79% Baseline: n=106 Completed: n=89 Control: 91% Baseline: n=86 Completed: n=84	Exercise (n=17): Lost contact=8, family issues=4, cancer=2, no interest=2, too busy=1 Control (n=2): Lost contact=2	Not reported	Home-based, unsupervised: telephone counselling: physical activity counsellors	N=1 sustained minor injuries related to falling off a treadmill, n=1 died during the trial for reasons unrelated to study participation.
Pinto 2015	76/595 eligible & consented 13%	Intervention: 92% Baseline: n=39 Completed: n=36 Control: 86% Baseline: n=37 Completed: n=32	Intervention (n=3): nonresponsive (n = 2), health issues (n = 1) Control (n=5): nonresponsive (n=2), too busy (n=2), physical health issues (n=1)	92%	Home-based, unsupervised: telephone counselling; physical activity counsellors	Intervention: chest pain and shortness of breath during exercise (n=6), vertigo (n=1), and ankle injury (n=4) Control: none
Raghavendra 2007	98/174 eligible & consented 56%	Exercise: 62% Baseline: n=45 Completed: n=28 Control: 64% Baseline: n=53 Completed: n=34	Intervention (n=17): Reason not reported Control (n=19): Reason not reported	Not reported.	Hospital, supervised: yoga instructor	Not reported.
Rao 2012	Not reported	100% Exercise: 100% Baseline: n=5 Completed: n=5 Control: 100% Baseline: n=5 Completed: n=5	Intervention (n=0): Control (n=0):	80%	Home- and community-based, supervised: personal trainer	Not reported.
Rogers 2009	41/119 eligible and consented 34%	Exercise: 95% Baseline: n=21 Completed: n=20 Control: 95% Baseline: n=20 Completed: n=19	Exercise: N=1 due to unrelated medical problems Control: N=1 due to travel distance	Overall: 99% Individual sessions: 100% Group sessions: 98%	Location not specified, supervised: ACSM exercise specialist and/or certified exercise physiologist + Home-based, unsupervised	No exercise-related adverse events; The following, non-exercise related events were recorded: wheezing requiring physician evaluation for asthma, cholinergic urticaria, herpes zoster, sinusitis, back pain related to falling, and elective cosmetic reconstructive surgery–not reported by group
Schmidt 2015	101/121 eligible & consented 83%	Exercise group: 98% Baseline: n=52 Completed: n=51[GG] Control group: 94% Baseline: n=49 Completed: n=46	Exercise group (n=1): N=1 psychological problems Control group (n=3): N=1 disliked intervention; n=1 time constraints; n=1 death	71%	Hospital, supervised: physical therapists	No exercise-related adverse events.

Schwartz 2007	72/75 eligible & consented 96%	Aerobic group: 92% Baseline: n=24 Completed: n=22 Resistance: 91% Baseline: n=23 Completed: n=21 Control: 92% Baseline: n=25 Completed: n=23	N=6 Too busy (n = 4) or the location was not convenient (n = 2). N=4 exercise N=2 control *Unable to determine whether withdrew prior or post-randominisation	Not reported.	Home-based, unsupervised	Not reported.
Short 2015	330/349 eligible 95%	Tailored-print: 89% Baseline: n=109 Completed: n=98 Targeted-booklet: 88% Baseline: n=110 Completed: n=97 Control group: 93% Baseline: n=111 Completed: n=104	Tailored-print (n=11): 1 poor health; 2 no reason given; 8 non responders Targeted-booklet (n=12): 8 non responders; 1 deceased; 9 non responders Control group (n=7): 7 non responders	NA	Home-based, unsupervised; tailored-physical activity print materials or targeted physical activity booklet	
Vallance 2007	377/1590 eligible & consented 24%	Pedometer group: 94% Baseline: n=94 Completed: n=88 Control group: 89% Baseline: n=96 Completed: n=85	Exercise (n=6): n=6 loss to follow-up Control (n=11): n=1 hadn't kept up with program; n=10 loss to follow-up.	Not reported	Home-based, unsupervised.	Not reported.
Vallance 2015	95/123 eligible & consented 77%	Intervention group: 83.67% Baseline: n=49 Completed: n=41 Control group: 80.4% Baseline: n=46 Completed: n=37	Intervention (n=8): No response (n=8) Control (n=9): No response (*n*=8); Passed away (n=1)	95%	Home-based, unsupervised: tailored print materials and pedometer	Not reported.
Van Waart 2016	230/536 eligible & consented 43%	High-intensity: 93% Baseline: n=76 Completed: n=71 Low-intensity: 89% Baseline: n=77 Completed: n=69 Control: 86%	High-intensity: n=5 n=2 felt to ill , n=1 physical accident unrelated to trial, n=1 physical accident related to trial, n=1 unwilling Low-intensity: n=8 N=1 neuropathy, n=1 emigrated, n=6 unwilling	High-intensity: 71%. Low-intensity Attendance of planned sessions: N/A.	Location not specified, supervised: supervised by specially trained physical therapists or Home-based, unsupervised	High-intensity exercise n=1 unspecified physical accident related to trial Low-intensity exercise Not reported Control Not reported

		Baseline: n=77 Completed: n=66	Control: n=11 n=2 felt to ill, n=7 unwilling, n=2 unknown.			
Wang 2011	72/160 eligible and consented 45%	Exercise: 86% Baseline: n=35 Completed: n=30 Control: 86% Baseline: n=37 Completed: n=32	Exercise n=5; Discomfort with exercise n=1; dizziness n=1; Dyspnoea n=1; Too busy n=1; No family support n=1 Control n=5: Anaemia n=1; Moved n=1; Prolonged treatment n=1; Progressed to metastatic disease n=1; Holiday n=1	93%	Home-based, unsupervised	Anemia n=1- control Dizziness with dyspnea n=1- exercise
Winters Stone 2011	106/359 eligible and consented 30%	Exercise: 69% Baseline: n=52 Completed: n=36 Control: 57% Baseline: n=54 Completed: n=31	Exercise: n=16 Lost to follow-up n=8; Too busy: n=5; Poor health: n=1; Dislike: n=1; Moved: n=1 Control: n=23 Lost to follow-up n=12; Too busy: n=4; Poor health: n=4; Dislike: n=3	57%	University setting, supervised: certified exercise instructors + Home-based, unsupervised	No exercise-related adverse events.
Winters-Stone 2013	71/258 eligible & consented 28%	Exercise: 66% Baseline: n=35 Completed: n=23 Control: 69% Baseline: n=36 Completed: n=25	Exercise: n=12 Reasons: Too busy (n=6); Poor health (n=1); Disinterested (n=1); Lost to follow-up (n=4) Control: n=11 Reasons: Too busy (n=5); Inconvenient (n=1); Cancer recurrence (1); Pregnancy (n=1); Lost to follow-up (n=3)	Overall: 44% Supervised sessions: 64% Home-based sessions: 26 %	University setting, supervised: certified exercise instructors	POWIR stopped increasing vest weight at month 6 due to back (N=2) or knee (N=1) pain, and one participant stopped lower body exercises at month 5 due to pain,
Yang 2010	Not reported	Intervention: 100% Baseline: n=19 Completed: n=19 Control: 100% Baseline: n=21 Completed: n=21	Intervention (n=0) Control (n=0)	77%	Home-based, unsupervised	No exercise-related adverse events.

Supplementary Content 5. Overview reasons for withdrawals across all trials (n=61).

	Withdrawals from intervention group n=311 (12% withdrawals out of total 2621 participants)		Withdrawals from usual care group n=256 (9% withdrawals out of 2579 participants)	
	≤12 week interventions n=167	>12 week interventions n=144	≤12 week interventions n=124	>12 week interventions n=132
Reason for withdrawals	**Health-related reasons n=33:** Unspecified health or medical problems or deterioration of health n=10 Hospitalisation n=4 Lymphoedema n=3 Unrelated medical condition n=2 Cancer n=2[1] Breast cancer recurrence n=1 Deep vein thrombosis with pulmonary embolism n=1 Surgery n=1 Broken hip n=1 Acute illness n=1 Low back pain n=1 Unrelated (unspecified) injury n=1 Psychological problems n=1 Symptoms of chest pain during exercise and refusal to have these symptoms evaluated by her physician n=1 Discomfort with exercise n=1 Dizziness n=1 Dyspnoea n=1 Death n=1 **Non-health-related reasons or other n=134:** Uncontactable or non-responder n=44 Did not return questionnaire (lost to follow up) N=31 No reason for withdrawal or reason not reported n=26 Time constraints n=8 Too busy n=7 Refused to continue for unspecified reason n=5 Family reasons n=5 Transportation difficulties n=3 Disinterested n=2 Moved & withdrew from care at the site n=1 No family support n=1	**Health-related reasons n=27:** Unspecified health or medical problems or deterioration of health n=9 Breast cancer progression n=3 Breast cancer recurrence n=2 No longer has cancer n=1 Syncope due to a comorbid condition n=1 Gastrointestinal complication n=1 Need for unrelated surgery n=1 Developed other cancer n=3[2] Developed headaches with referral for MRI n=1 Foot surgery n=1 Asthma complications and non-clearance from physician to continue n=1 High blood pressure with stress test referral n=1 Neuropathy n=1 Death n=1 **Non-health-related reasons or other n=117:** No reason for withdrawal or reason not reported n=62 Lost to follow-up n=14 Too busy n=11 Time and travel reasons n=7 Unwilling to continue for unspecified reason n=7 Moved during intervention n=5 Uncontactable or non-responder n=4 Family or personal reasons n=2 Discontent with schedule n=1 Unspecified physical accident n=2 Dislike or disinterested n=2	**Health-related reasons n=15:** Medical condition or illness unrelated to breast cancer n=3 Unspecified health or medical problems or deterioration of health n=1 Developed metastases n=2 Acute illness n=1 Unrelated (unspecified) injury n=1 Gynaecologic problems n=1 Physical health issues n=1 Anaemia n=1 Prolonged treatment n=1 Death n=3 **Non-health-related reasons or other n=109:** No reason for withdrawal or reason not reported n=32 Did not return questionnaire or lost to follow up n=25 Uncontactable or non-responder n=24 Absent from test n=8 Time constraints or too busy n=10 Family or personal reasons n=5 Failed to commence participation for unspecified reason n=1 Disliked intervention n=1 Hadn't kept up with program n=1 Moved n=1 Holiday n=1	**Health-related reasons n=17:** Unspecified health or medical problems or deterioration of health n=8 Disease recurrence n=4 Disease progression n=2 Orthopaedic complication n=1 Bronchitis n=1 Became ineligible due to active brain metastases n=1 **Non-health-related reasons or other n=115:** No reason for withdrawal or reason not reported n=65 Lost to follow-up n=18 Too busy n=9 Unwilling to continue n=7 Uncontactable or non-responder n=5 Dislike n=3 Time and travel reasons n=2 Did not complete baseline testing for unspecified reason n=1 Using beta-blockers n=1 Unhappy with group assignment n=1 Family problems n=1 Inconvenient n=1 Pregnancy n=1

[1] No further specification reported (i.e., unable to determine whether events were a cancer recurrence, cancer progression or development of new cancer)
[2] Other cancers were uterine (n=1); eye (n=1); and unspecified (n=1).

Supplementary Content 6. Overview of health outcomes and methods of assessment across all trials (n=61).

Outcome	Instrument/methods and number of studies
Quality of life (n=32)	FACT-B or FACT-B+4, n=14[1-14] EORTC QLRC30, n=8[15-22] Medical Outcomes Study 36-item short-form survey, n=3[23-25] FACIT-F, n=2[26, 27] Functional Living Index of Cancer, n=2[28, 29] FACT–Anemia scale, n=1[30] FACT-G, n=1[31] Lymphoedema QOL scale, n=1[32] QOL-BC, n=1[33]
Aerobic fitness (n=25)	VO_2peak testing using a modified Bruce treadmill protocol, n=4[19, 34-36] 6-minute walk test, n=3[1, 31, 37] 12-minute walk test, n=3[8, 10, 38] VO_2max or VO_2peak assessed using a cycle ergometer, n=8[2, 5, 15, 17, 26, 39-41] VO_2max or VO_2peak testing on a treadmill, n=3[30, 42, 43] Submaximal treadmill test using the Naughton protocol with the end point of 85% of predicted HRmax, n=1[11] Heart rate on completion of 3-minute step test, n=1[4] Steep Ramp Test: maximal short exercise capacity, n=1[21] Submaximal aerobic power cycle test, n=1[6] Rockport 1-mile test, n=1[44]
Fatigue (n=28)	FACT-F, n=12[3-5, 7, 12-14, 19, 26, 27, 31, 45] Piper Fatigue Scale, n=6[22, 34, 36, 46-48] Schwartz Cancer Fatigue Scale-6 (SCFS-6), n=2[6, 37] Profile of mood states fatigue scale, n=1[49] Brief Fatigue Inventory, n=1[23] Multidimensional fatigue inventory- MFI-20, n=1[15] 13-item Fatigue Scale, n=1[2] Functional Assessment of Cancer Therapy–Anemia fatigue scale, n=1[30] Medical Outcomes Survey Short Form (SF)–36 fatigue symptoms, n=1[50] Visual analogue scales, n=1[32] Fatigue Assessment Questionnaire (FAQ), n=1[20] Multidimensional Fatigue Inventory, n=1[21] MDASI-T, n=1[51]
Upper-body strength (n=17)	1RM chest press, n=4[24, 39, 52, 53] Handgrip dynamometer, n=2[10, 11, 22] 1RM bench press, n=1[54] Dynamometer elbow flexion, n=1[21] Overhead press 1RM, n=1[38] Bicep curl 1RM, n=1[42] 6RM chest press, n=1[36] Chest press – method or RM not specified, n=1[6] Shoulder muscle strength using hand-held dynamometer, n=1[18] Bench press dynamic muscle strength tests performing as many reps with 100–110%BW, n=1[17] Shoulder press – method or RM not specified, n=1[4] Shoulder press 1RM estimate based multiple repetition procedure, n=1[26] 8RM on the horizontal bench press, n=1[30]
Anxiety (n=16)	Profile of Mood States-Anxiety, n=6 [7, 34, 41, 47, 49, 51] Hospital Anxiety and Depression Scale, n=4[15, 36, 45, 55] State Trait Anxiety Inventory, n=2[12, 29] Functional Assessment of Cancer Therapy–Anemia scale Anxiety subscale, n=1[30] Greene Climacteric Scale, n=1[4] Spielberger State Anxiety Scale, n=1[43] Social Physique Anxiety Scale, n=1[6] Functional Living Index of Cancer, n=1[28]
Depression (n=16)	Profile of mood states-depression, n=5[34, 41, 47, 49, 51] The Hospital Anxiety and Depression Scale, n=4[15, 36, 45, 55] Centres for Epidemiological Studies-Depression (CES-D) measures, n=5[3, 20, 23, 30, 43] Greene Climacteric Scale, n=1[4] Beck Depression Inventory, n=1[29] Functional Living Index of Cancer, n=1[28]
Body fat (n=14)	Bioelectrical impedance analysis, n=5[16, 26, 36, 56, 57]

	Dual-energy X-ray absorptiometry, n=5[11, 30, 42, 52, 53] Sum of skinfolds measures, n=4[2, 17, 39, 44]
Body mass index (n=13)	n=14[2, 8, 10, 11, 15, 16, 39, 42-44, 46, 54, 57, 58]
Body weight (n=12)	n=13[2, 8, 16, 17, 30, 39, 40, 42, 43, 46, 52, 53, 57]
Waist circumference (n=7)	n=7[11, 16, 39, 40, 46, 57, 59]

EORTC QLRC30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
FACT: Functional Assessment of Cancer Therapy
FACT-B or FACT-B+4: Functional Assessment of Cancer Therapy Questionnaire for Breast Cancer
FACT-F: Functional Assessment of Cancer Therapy: Fatigue
FACIT: Functional Assessment of Chronic Illness Therapy
FACT-G: Functional Assessment of Cancer Therapy - General
HRmax: maximum heart rate
MDASI-T: MD Anderson Symptom Inventory
QOL-BC: Quality of Life Instrument - Breast Cancer Patient Version
RM: repetition maximum
VO_2max: maximal oxygen consumption
VO_2peak: peak oxygen consumption

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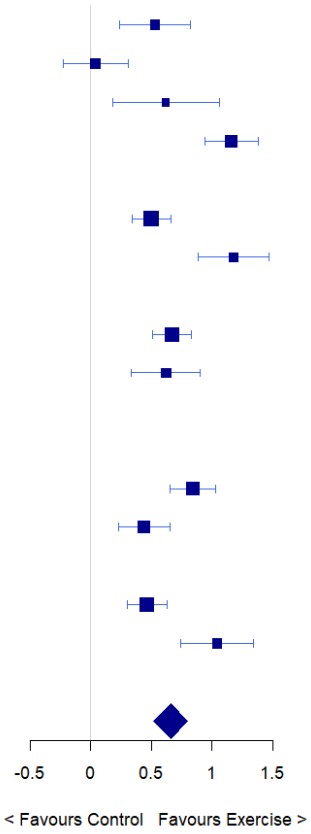
Supplementary Content 8. Meta-analyses results of depression with subgroup analyses for exercise mode, intervention supervision, timing and duration and sensitivity analyses (positive SMD values favour exercise).

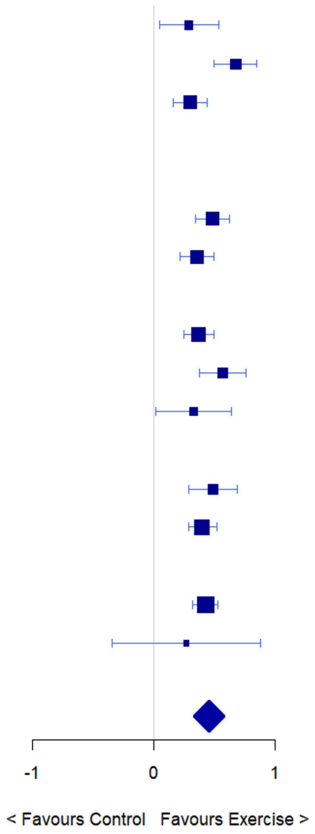
Subgroup	Studies (n=)	Participants (n=)	I^2 (%)	SMD (95% CI)	P-value
Exercise mode		Intervention vs. Control			
Aerobic exercise	4	83 vs. 128	81%	0.53 (0.24, 0.82)	<0.01
Resistance exercise	2	90 vs. 134	0%	0.04 (-0.23, 0.31)	0.79
Combined exercise	2	44 vs. 41	9%	0.62 (0.18, 1.06)	<0.01
Other exercise	6	203 vs. 205	93%	1.16 (0.94, 1.38)	<0.01
Supervision [1]					
Supervised interventions	9	308 vs. 398	93%	0.50 (0.34, 0.66)	<0.01
Unsupervised interventions	5	112 vs. 110	0%	1.18 (0.89, 1.47)	<0.01
Intervention timing					
During treatment	10	320 vs. 410	93%	0.67 (0.51, 0.83)	<0.01
Post-treatment	4	100 vs. 98	0%	0.62 (0.33, 0.90)	<0.01
Mixed	0	-	-	-	-
Duration					
<12 week interventions	8	250 vs. 268	93%	0.84 (0.65, 1.03)	<0.01
>12 week interventions	6	170 vs. 240	77%	0.44 (0.23, 0.65)	<0.01
Sensitivity analyses [2]					
High quality studies only	42	42	92%	0.46 (0.30, 0.63)	<0.01
Stage II+ only	10	10	21%	1.04 (0.74, 1.34)	<0.01
Overall	**14**	**420 vs. 508**	**90%**	**0.66 (0.52, 0.80)**	**<0.01**



[1] Supervised intervention were classed as interventions where ≥50% of prescribed exercise involved face-to-face supervision and unsupervised interventions involved <50% of prescribed exercise involving face-to-face supervision.
[2] Sensitivity analyses were performed only on i) high quality studies, and ii) studies with 100% of samples with stage II+ disease.

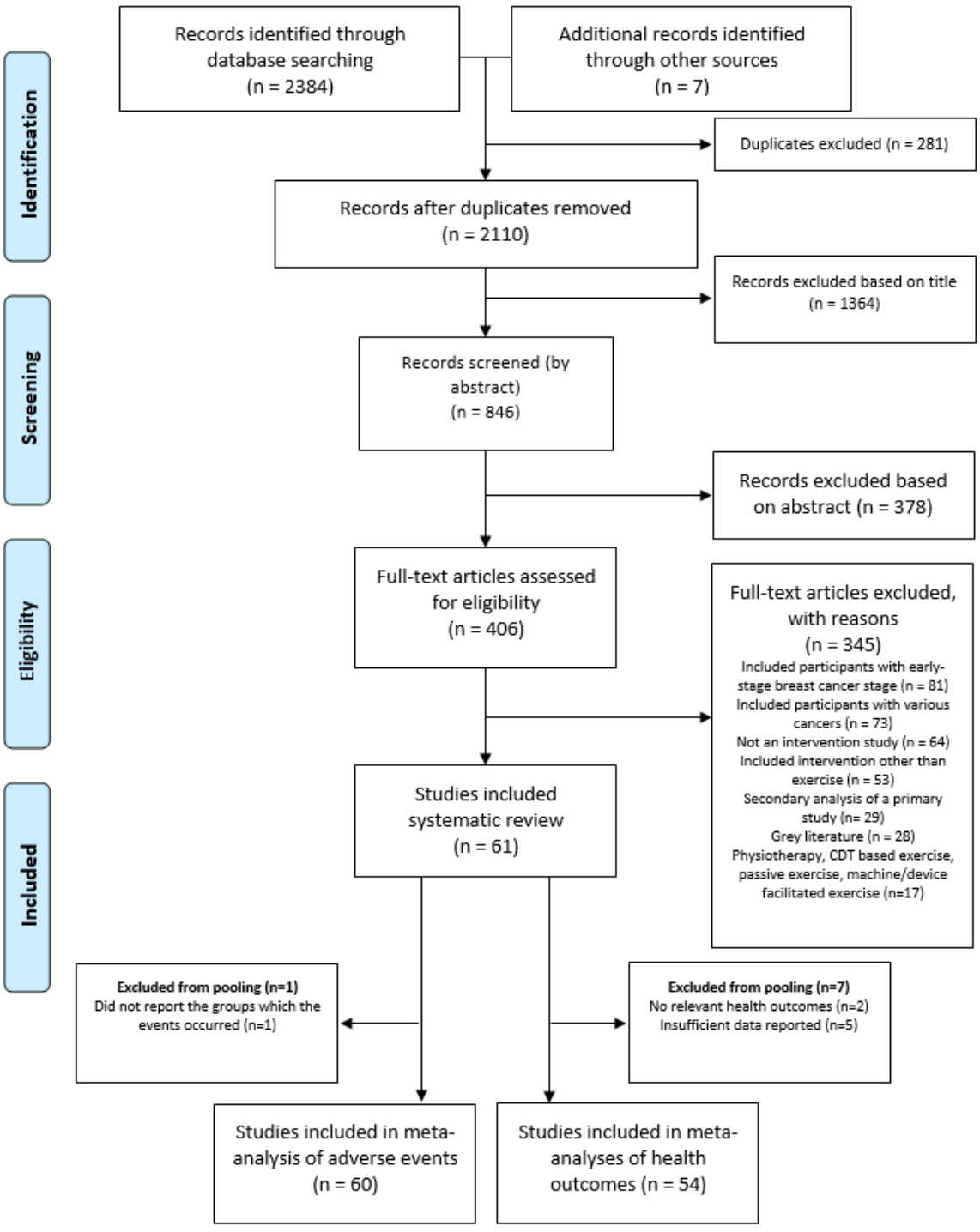
Supplementary Content 9. Meta-analyses results of upper-body strength with subgroup analyses for exercise mode, intervention supervision, timing and duration and sensitivity analyses (positive SMD values favour exercise).

Subgroup	Studies (n=)	Participants (n=)	I² (%)	SMD (95% CI)	P-value
Exercise mode		Intervention vs. Control			
Aerobic exercise	4	131 vs. 137	63%	0.29 (0.05, 0.54)	0.02
Resistance exercise	8	280 vs. 282	50%	0.68 (0.50, 0.85)	<0.01
Combined exercise	10	395 vs. 375	0%	0.30 (0.16, 0.44)	<0.01
Other exercise	0	-	-	-	-
Supervision [1]					
Supervised interventions	11	406 vs. 410	66%	0.49 (0.35, 0.63)	<0.01
Unsupervised interventions	11	400 vs. 384	3%	0.36 (0.22, 0.50)	<0.01
Intervention timing					
During treatment	8	490 vs. 484	65%	0.37 (0.25, 0.50)	<0.01
Post-treatment	13	235 vs. 231	34%	0.57 (0.38, 0.76)	<0.01
Mixed	1	81 vs. 79	-	0.33 (0.02, 0.64)	0.04
Duration					
<12 week interventions	8	198 vs. 197	29%	0.49 (0.29, 0.69)	<0.01
>12 week interventions	14	608 vs. 597	58%	0.40 (0.29, 0.52)	<0.01
Sensitivity analyses [2]					
High quality studies only	17	727 vs. 722	60%	0.43 (0.32, 0.53)	<0.01
Stage II+ only	2	25 vs. 18	0%	0.27 (-0.34, 0.88)	0.39
Overall	**22**	**806 vs. 794**	**49%**	**0.43 (0.33, 0.53)**	**<0.01**



[1] Supervised intervention were classed as interventions where ≥50% of prescribed exercise involved face-to-face supervision and unsupervised interventions involved <50% of prescribed exercise involving face-to-face supervision.
[2] Sensitivity analyses were performed only on i) high quality studies, and ii) studies with 100% of samples with stage II+ disease.

Supplementary Content 1: Systematic review flow diagram.



Supplementary Content 2: Ratings of all studies included in systematic review using the PEDro scale (n=61).

	PEDro Scale item number											
	1	2	3	4	5	6	7	8	9	10	11	Total score (Quality)
Ahmed 2006	1	1	0	1	0	0	1	1	0	1	1	6 (High)
Anderson 2012	1	1	1	1	0	0	1	0	0	1	1	6 (High)
Banerjee 2007	1	1	1	1	0	0	0	1	0	1	1	6 (High)
Campbell 2017	1	1	0	1	0	0	1	1	1	1	1	7 (High)
Cantarero-Villanueva 2012a	1	0	0	1	0	0	1	0	0	1	1	4 (Low)
Cantarero-Villanueva 2012b	1	1	1	1	0	0	1	1	1	1	1	8 (High)
Cantarero-Villanueva 2012c	1	1	1	1	0	0	1	1	1	1	1	8 (High)
Cantarero-Villanueva 2013	1	1	1	1	0	0	1	1	0	1	1	7 (High)
Chandwani 2014	1	1	0	1	0	0	0	0	0	1	1	4 (Low)
Cormie 2013	1	1	1	1	0	0	0	1	1	1	1	7 (High)
Cornette 2016	1	1	0	1	0	0	0	0	1	1	1	5 (Low)
Courneya 2003	1	1	1	1	0	0	1	1	1	1	1	8 (High)
Courneya 2007	1	1	1	1	0	0	0	1	1	1	1	7 (High)
Danhauer 2009	1	1	0	1	0	0	0	0	1	1	1	5 (Low)
De Luca 2016	1	1	0	0	0	0	0	1	0	1	1	4 (Low)
Dethlefsen 2016	1	1	0	1	0	0	0	0	0	1	1	4 (Low)
Dolan 2016	1	1	0	1	0	0	0	1	0	1	1	5 (Low)
Drouin 2005	1	1	0	1	0	0	0	0	0	0	1	3 (Low)
Eakin 2012	1	1	0	1	0	0	0	1	1	1	1	6 (High)
Fernández-Lao 2013	1	0	0	1	0	0	1	0	1	1	1	5 (Low)
Galiano-Castillo 2017	1	1	1	1	0	0	1	1	1	1	1	8 (High)
Gokal 2015	1	1	0	1	0	0	0	1	1	1	1	6 (High)
Guinan 2013	1	1	0	1	0	0	1	0	1	1	1	6 (High)
Hatchett 2013	1	1	0	1	0	0	0	1	0	1	1	5 (Low)
Hayes 2012	1	1	0	1	0	0	1	1	1	1	1	7 (High)
Headley 2004	1	1	0	1	0	0	0	0	0	1	1	4 (Low)
Herrero 2005	1	1	1	1	0	0	0	0	0	1	1	5 (Low)
Hornsby 2014	1	1	1	1	0	0	1	1	1	1	1	8 (High)
Husebø 2014	1	1	1	1	0	0	0	0	0	1	1	5 (Low)
Hutnick 2005	1	0	0	1	0	0	0	0	0	0	1	2 (Low)
Kilbreath 2012	1	1	1	1	0	0	1	1	1	1	1	8 (High)
Kim 2006	1	1	0	1	0	0	0	0	0	1	1	4 (Low)
Ligibel 2008	1	1	1	1	0	0	1	1	1	1	1	8 (High)
Ligibel 2016	1	1	0	1	0	0	1	0	0	1	1	5 (Low)
Loudon 2014	1	1	1	1	0	0	1	0	0	1	1	6 (High)
Macvicar 1989	0	1	0	1	0	0	0	0	0	1	0	3 (Low)
Maryam 2010	1	0	0	1	0	0	0	0	0	1	1	3 (Low)
Milne 2008	1	1	1	1	0	0	0	1	1	1	1	7 (High)
Moadel 2007	1	1	0	1	0	0	0	0	1	1	1	5 (Low)
Mohan Rao 2015	1	1	1	1	0	0	0	0	1	1	1	6 (High)
Mulero Portela 2008	1	1	0	1	0	0	1	0	0	1	1	5 (Low)
Murtezani 2014	1	1	1	1	0	0	1	1	0	1	1	7 (High)

Musanti 2012	1	1	1	1	0	0	1	0	1	1	1	7 (High)
Naraphong 2015	1	1	1	1	0	0	0	1	1	1	1	7 (High)
Naumann 2012	1	0	0	1	0	0	0	1	1	1	1	5 (Low)
Pinto 2005	1	1	0	1	0	0	0	1	1	1	1	6 (High)
Pinto 2013	1	1	1	1	0	1	1	0	1	1	1	8 (High)
Pinto 2015	1	1	1	1	0	0	1	1	0	1	1	7 (High)
Raghavendra 2007	1	1	1	1	0	0	0	0	0	1	1	5 (Low)
Rao 2012	1	1	1	1	0	0	1	1	1	1	1	8 (High)
Rogers 2009	1	1	1	1	0	0	0	1	1	1	1	7 (High)
Schmidt 2015	1	1	1	1	0	0	0	1	1	1	1	7 (High)
Schwartz 2007	1	1	0	1	0	0	0	1	1	1	1	6 (High)
Short 2015	1	1	1	0	0	0	0	1	1	1	1	6 (High)
Vallance 2007	1	1	1	1	0	0	0	1	1	1	1	7 (High)
Vallance 2015	1	1	1	1	0	0	0	0	1	1	1	6 (High)
Van Waart 2016	1	1	0	1	0	0	0	1	1	1	1	6 (High)
Wang 2011	1	1	0	1	0	0	0	1	0	1	1	5 (Low)
Winters Stone 2011	1	1	0	1	0	0	1	0	1	1	1	6 (High)
Winters-Stone 2013	1	1	1	1	0	0	1	0	1	1	1	7 (High)
Yang 2010	1	1	0	1	0	0	0	1	0	1	1	5 (Low)

Pedro scale items: 1. Eligibility criteria; 2. Subjects randomly allocated; 4. Groups similar at baseline; 5. Subject blinding; 6. Therapist blinding; 7. Assessor blinding; 8. Outcome obtained from >85% of subjects; 9. Intention to treat; 10. Results of between-group comparisons; 11. Point and variability measures