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Exercise interventions for people undergoing multimodal cancer treatment that includes surgery (Review)

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[Intervention Review]

Exercise interventions for people undergoing multimodal cancer treatment that includes surgery

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ABSTRACT

Background

People undergoing multimodal cancer treatment are at an increased risk of adverse events. Physical fitness significantly reduces following cancer treatment, which is related to poor postoperative outcome. Exercise training can stimulate skeletal muscle adaptations, such as increased mitochondrial content and improved oxygen uptake capacity may contribute to improved physical fitness.

Objectives

To determine the effects of exercise interventions for people undergoing multimodal treatment for cancer, including surgery, on physical fitness, safety, health-related quality of life (HRQoL), fatigue, and postoperative outcomes.

Search methods

We searched electronic databases of the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, SPORTDiscus, and trial registries up to October 2018.

Selection criteria

We included randomised controlled trials (RCTs) that compared the effects of exercise training with usual care, on physical fitness, safety, HRQoL, fatigue, and postoperative outcomes in people undergoing multimodal cancer treatment, including surgery.

Data collection and analysis

Two review authors independently selected studies, performed the data extraction, assessed the risk of bias, and rated the quality of the studies using Grading of Recommendation Assessment, Development, and Evaluation (GRADE) criteria. We pooled data for meta-analyses, where possible, and reported these as mean differences using the random-effects model.

Main results

Eleven RCTs were identified involving 1067 participants; 568 were randomly allocated to an exercise intervention and 499 to a usual care control group. The majority of participants received treatment for breast cancer (73%). Due to the nature of the intervention, it was not possible to blind the participants or personnel delivering the intervention. The risk of detection bias was either high or unclear in some cases, whilst most other domains were rated as low risk. The included studies were of moderate to very low-certainty evidence. Pooled data demonstrated that exercise training may have little or no difference on physical fitness (VO_2 max) compared to usual care (mean difference (MD) 0.05 L/min^{-1}, 95% confidence interval (CI) -0.03 to 0.13; I^2 = 0%; 2 studies, 381 participants; low-certainty evidence). Included studies also showed in terms of adverse effects (safety), that it may be of benefit to exercise (8 studies, 507 participants; low-certainty evidence). Furthermore, exercise training probably made little or no difference on HRQoL (EORTC global health status subscale) compared to usual care (MD 2.29, 95% CI -1.06 to 5.65; I^2 = 0%; 3 studies, 472 participants; moderate-certainty evidence). However, exercise training probably reduces fatigue (multidimensional fatigue inventory) compared to usual care (MD -1.05, 95% CI -1.83 to -0.28; I^2 = 0%; 3 studies, 449 participants moderate-certainty evidence). No studies reported postoperative outcomes.

Authors' conclusions

The findings should be interpreted with caution in view of the low number of studies, the overall low-certainty of the combined evidence, and the variation in included cancer types (mainly people with breast cancer), treatments, exercise interventions, and outcomes. Exercise training may, or may not, confer modest benefit on physical fitness and HRQoL. Limited evidence suggests that exercise training is probably not harmful and probably reduces fatigue. These findings highlight the need for more RCTs, particularly in the neoadjuvant setting.

PLAIN LANGUAGE SUMMARY

Exercise training interventions for people with cancer during cancer treatment before or after surgery

Background

People who are diagnosed with cancer will often undergo intensive treatment in the hope of achieving a cure. Such treatments may include surgery, chemotherapy, and chemoradiotherapy, frequently given in combination. These treatments can cause side effects (adverse effects), for example, making people feel less fit and more tired, and decreasing their quality of life. These adverse effects may be prevented, or at least reduced, if people with cancer undertake an exercise training programme during cancer treatment. In the past, people with cancer were told to rest, but current recommendations are to stay as active as possible.

Review question

In adult patients undergoing cancer surgery, what is the impact of exercise training versus usual care on fitness, safety, quality of life, fatigue (tiredness), and clinical outcomes?

Key results

We included 11 studies involving 1067 participants, published up until October 2018. The majority of people (73%) received treatment for breast cancer. Participants were randomly assigned to receive an exercise programme or usual care (no exercise training). The included studies suggested that exercise training may make little or no difference to physical fitness levels. The included studies also highlighted that it is probably safe to exercise, as the number of adverse events were low. The findings also showed that exercise training may make little or no difference to quality of life, but that it probably reduces fatigue (tiredness). We do not know whether it improves postoperative recovery, as no study reported this.

Quality of the evidence

The overall quality (certainty) of the evidence was moderate to very low for all of the outcomes, mainly because of the small number of studies and low number of participants, as well as study limitations.

Conclusion

The findings of this review should be interpreted with caution due to the overall low-certainty of the evidence, variation in cancer types and treatments, exercise interventions, and outcomes measured. We are moderately certain that exercise training during adjuvant treatment (chemotherapy or radiotherapy treatment after surgery) reduces fatigue.

This is a new area of research, and more information is needed to help us understand whether exercise benefits people undergoing cancer treatment. Future studies should also concentrate on people with a new diagnosis of cancer who have chemotherapy or radiotherapy prior to surgery (known as neoadjuvant treatment), to tell us whether exercise training prior to surgery is important.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

The effects of an exercise intervention compared to a usual care control group with people with cancer undergoing multimodal treatment?

Patient or population: People with cancer undergoing multimodal treatment including surgery
Setting: Hospital/community
Intervention: Exercise intervention
Comparison: Usual care

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with usual care control	Risk with Exercise			
Physical fitness assessed with: VO_2 max (L/min) follow up: range 6 weeks to 24 weeks	The mean post-intervention VO_2 max in the usual care control groups ranged from 1.5 to 1.88 L/min^{-1}.	The mean post-intervention VO_2 max in the intervention group ranged from 1.55 to 1.96 L/min^{-1}. MD 0.05, 95% CI -0.03 to 0.13	381 (2 studies)	⊕⊕◯◯ LOW [1]	
Safety follow up: range 5 weeks to 12 months		Seven studies reported no adverse events and one study reported that a participant with a brain tumour experiences a grade 3 seizure after exercise training	507 (8 studies)	⊕⊕◯◯ LOW [2]	
HRQoL assessed with: EORTC global health status subscale (higher is better) Scale from: 0 to 100 follow up: range 6 weeks to 24 weeks	The mean post-intervention HRQoL score in the usual care control group ranged from 63.3 to 74	The mean post-intervention HRQoL score in the intervention group ranged from 67.2 to 75.8 MD 2.29, 95% CI -1.06 to 5.65.	472 (3 studies)	⊕⊕⊕◯ MODERATE [4]	

Fatigue assessed with: Multidimensional fatigue inventory (lower is better) Scale from: 0 to 20 follow up: range 18 weeks to 24 weeks	The mean post-intervention fatigue score in the usual care control group ranged from 11.9 to 14.7	The mean post-intervention fatigue score in the intervention group ranged from 11.1 to 13.4, 1.05 lower then the usual care control group (95% CI -1.83 to -0.28)	449 (3 studies)	⊕⊕⊕○ MODERATE [5]
Postoperative outcome	No studies reported postoperative outcome		(0 studies)	

CI: Confidence interval; **MD**: Mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Downgraded 2 levels due to indirectness (the study by Adamsen included various cancer treatments and 52% of participants did not have cancer) and imprecision (small sample size).
[2] Downgraded 2 levels due to risk of bias (the study by Choi rated as high risk of allocation concealment bias and the study by Hwang was rated as unclear and the study by Husebo was rated as high risk for attrition bias) and indirectness (Adamsen study included various cancer treatments and 52% of participants did not have cancer which makes results difficult to interpret. Haines study included a sham intervention group).
[3] Downgraded 3 levels due to risk of bias (the study by Choi rated as high risk of allocation concealment bias and the study by Chandwani as unclear risk, whilst the study by Chandwani, Husebo and Reis were rated as high risk for attrition bias), inconsistency (large variation in results) and indirectness (different cancer types and treatment).
[4] Downgraded 1 level due to indirectness (Adamsen study included various cancer treatments were included and 52% of participants did not have cancer which makes results difficult to interpret. Haines study included a sham intervention group)
[5] Downgraded 1 level due to indirectness (Haines study included a sham intervention group)

BACKGROUND

Description of the condition

People with cancer are often faced with a multimodality treatment regimen that includes surgery in combination with other treatments, such as chemotherapy, radiotherapy, and immunotherapy. These treatments are of two kinds: adjuvant treatment is given after surgery to treat residual disease, in order to minimise the likelihood of tumour recurrence or spread (Papadimitriou 2015), whereas the aim of neoadjuvant treatment is to reduce tumour bulk prior to surgery, in order to improve the likelihood of optimal surgical resection of the cancer (Chau 2006). Major surgery is associated with significant morbidity and mortality, as recently highlighted in the European Surgical Outcome Study (International Surgical Outcomes Study group 2017), and morbidity has a major impact on postoperative recovery, quality of life, and survival (Khuri 2005; Moonesinghe 2014).

Cancer is frequently associated with cachexia (body weakness and wasting), which can worsen perioperative outcomes (Brown 1991). This condition can be exacerbated by chemotherapy, which is associated with muscle wasting and dysfunction. Furthermore, cancer treatment has been linked to decreased physical fitness, apparently related to the type of treatment, being worse in those receiving surgery and radiotherapy in combination with chemotherapy than in those receiving radiotherapy or surgery alone (Moros 2010). Moreover, this decrease in physical fitness may persist. In a series of studies, cardiorespiratory fitness was around 30% below that of age-matched sedentary healthy women up to three years following completion of adjuvant treatment for breast cancer (Jones 2007). Poor physical fitness reflects reduced physiological reserve, which predisposes people undergoing surgery to postoperative complications (Hennis 2012; Moran 2016; West 2011).

Description of the intervention

For the purposes of this review, we defined an exercise intervention as a prescribed period of aerobic physical activity, involving large muscle groups, with a minimum of three planned exercise sessions in total, each session lasting at least 10 minutes (O'Doherty 2013). The intervention may take place in any setting and be delivered to a group or to an individual participant. However, it must be supervised or delivered by a trainer or healthcare professional.

How the intervention might work

Higher physical fitness has been associated with improved prognosis in people with solid tumours (Jones 2013), longer cancer-specific survival, and lower cancer-related mortality (Brunelli 2014). Remaining physically active during and after cancer treatment could therefore be an important way of reducing associated adverse effects, improving overall survival, and reducing the rate of tumour recurrence (Thomas 2014). It has been shown that women with non-metastatic colorectal cancer who were physically active following diagnosis had a significantly lower risk of death than those who were not physically active (Meyerhardt 2006). Similarly, women with breast cancer who exercised at moderate intensity (i.e. at least 30 minutes per day on at least five days per week) were shown to have a reduced risk of death (Holmes 2005). Exercise has been shown to be safe for cancer survivors and significantly improves aerobic fitness (Turner 2018). Exercise training stimulates skeletal muscle adaptations such as increased mitochondrial (cell energy source) content and improved oxygen uptake capacity, both contributors to physical fitness (Holloszy 1984). In combination with chemotherapy, exercise training has been shown to slow tumour progression in solid tumours compared with chemotherapy alone (Betof 2015). Exercise may also reduce chronic inflammation, which has been associated with worse outcomes in people living with cancer (Proctor 2011).

Why it is important to do this review

Studies in people undergoing multimodal cancer treatment, in the form of neoadjuvant chemotherapy, chemoradiation, and surgery for upper and lower gastrointestinal cancer, suggest that the reduced physical fitness associated with these treatment modalities may be linked to higher in-hospital morbidity and mortality at one year post-treatment (Jack 2014; West 2014). The literature covering the effects of an exercise intervention to improve physical fitness in people with cancer undergoing single modality treatment has been synthesised in a number of systematic reviews. Two systematic reviews in people with non-small cell lung cancer (NSCLC) reported beneficial effects on physical fitness and other important clinical measures following participation in an exercise intervention in people who were treated surgically (Crandall 2014), and beneficial effects on physical fitness, symptoms and health-related quality of life (HRQoL) in people who were treated by surgery or a form of cancer treatment (Granger 2011). Two other systematic reviews in people with cancer (different cancer types) found evidence that exercise training in people who were surgically treated improved urinary continence (in prostate cancer), cardiorespiratory fitness, length of stay (Singh 2013), and HRQoL in people who received cancer treatment (Mishra 2012). However, to the best of our knowledge, there are no systematic reviews specifically addressing the effects of an exercise intervention on physical fitness and other important clinical outcomes in people with cancer undergoing multimodality treatment that includes surgery.

OBJECTIVES

To determine the effects of exercise interventions for people undergoing multimodal treatment for cancer, including surgery, on physical fitness, safety, health-related quality of life (HRQoL), fatigue, and postoperative outcomes.

METHODS

Criteria for considering studies for this review

Types of studies

We considered only randomised controlled trials (RCTs) for inclusion.

Types of participants

We included studies that evaluated the effects of an exercise intervention in adults (18 years and over) with a confirmed cancer diagnosis requiring multimodal cancer treatment that included surgery,regardless of gender, tumour type, tumour stage, and type of cancer treatment, and of any exercise/activity level.

Types of interventions

We included any exercise intervention that involved a prescribed period of aerobic physical activity, involving large muscle groups, with a minimum of three planned exercise sessions, each session lasting at least 10 minutes, delivered by trained personnel or a healthcare professional. The intervention could take place in any setting and be delivered to a group or to an individual participant. We included studies of exercise counselling interventions or prescribed exercise only, such as prescribed daily walking. We expected the interventions would vary to some extent with regard to the timing of initiation, duration, and content.

Types of outcome measures

Primary outcomes

- Physical fitness (aerobic fitness measured by: VO2 max, 6-minute walk distance test (MWD), 12 MWD, maximal short exercise capacity test, endurance time test, step test; strength (upper and lower body) measured by: grip strength test, chest press test, pull down test, elbow flexion test, 1-repetition max (1-RM), leg press test, 30-second chair-stand test, knee extension test and; physical activity (physical activity monitors or questionnaires).

Secondary outcomes

- Safety (number of adverse events).
- HRQoL (European Organisation for Research and Treatment of Cancer (EORTC QLQ-C30), EQ-5D, Short Form Health Survey (SF-36), World Health Organisation Quality of Life (WHOQOL) and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F).
- Fatigue (EORTC fatigue subscale, multidimensional fatigue inventory, Brief Fatigue Inventory (BFI), Schwartz Cancer Fatigue scale, Piper Fatigue Scale (PFS) and FACIT-F).
- Postoperative outcomes (morbidity, disease-free survival at 12 months, and overall survival at five years).

Search methods for identification of studies

Electronic searches

We searched the following electronic databases to obtain relevant studies for this review up until October 2018:

- the Cochrane Central Register of Controlled Trials (CENTRAL; 2018, Issue 10), in the Cochrane Library (Appendix 1);
- MEDLINE via Ovid (1946 to September week 3, 2018) (Appendix 2);
- Embase via Ovid (1980 to 2018 week 40) (Appendix 3);
- SPORTDiscus (1980 to October 2018) (Appendix 4).

We applied no language or date restrictions in the searches.

Searching other resources

We performed an expanded search for articles to identify 'grey literature', which included:

- Handsearching of reference lists of all articles, texts, and other review articles on exercise and cancer;
- PubMed: 'Related articles' feature;
- Web of Science: citation search of key authors;
- Clinical trials registers search: Clincaltrials.gov and the WHO International Clinical Trials Registry Platform (apps.who.int/trialsearch/) for ongoing trials and trial protocols;
- Unpublished literature through searches of conference proceedings;
- Attempts to contact study authors for missing data and information related to study methods.

Data collection and analysis

Selection of studies

Two authors (LL and MAW) imported all records retrieved from the searches into the reference management software package EndNote. We then removed duplicates and selected relevant articles for screening. We examined the remaining references independently and excluded those studies which did not clearly meet the inclusion criteria. We then obtained full-text copies of potentially relevant references and any disagreements were resolved through discussion or, if required, by a third review author (SJ). We linked together multiple records on the same study and documented the selection process in the Covidence web-based software platform. We excluded case reports and theses.

Data extraction and management

Two authors (LL and MAW) independently extracted study characteristics and outcome data, in accordance with predefined criteria, to a data collection form. We retrieved full texts of all studies in which the abstract referred to an exercise intervention in people with cancer, and studies for which there was no abstract but the title suggested relevance. We noted in the Characteristics of included studies table, if outcome data were not reported in a usable way. One review author (LL) transferred data into the Review Manager 2014 (RevMan) software and double-checked that the data were entered correctly by comparing the data entered into RevMan with the study reports. A second review author (MAW) did a spot-check of study characteristics for accuracy against the trial report. For included studies, the following data were extracted:

Study details

- study design, methodology;
- methods of recruitment of participants;
- study aim;
- study start and end date (study duration);
- author, country, and year of publication;
- sample size;
- duration of follow-up;
- study funding source;
- declarations of conflict of interest.

Participant characteristics

- inclusion criteria;
- exclusion criteria;
- baseline imbalances;
- total number randomised;
- number of participants in intervention group;
- number of participants in the control group;
- age;
- gender;
- race/ethnicity;
- cancer type;
- cancer treatment;
- attrition rate at specified follow-up time points;
- reasons for withdrawal.

Intervention details

- setting (in-hospital, community-based, home-based);
- exercise prescription components (frequency, intensity, time, type);
- monitoring during exercise;
- adherence;
- adverse events.

Comparison details

- description of usual care control groups;
- additional information, if appropriate.

Outcomes

- primary and secondary outcomes
    - method of outcome measurement and time point of outcome measurement.

Assessment of risk of bias in included studies

Two authors independently assessed and scored the methodological quality of each study in accordance with the Cochrane tool for assessing risk of bias (Higgins 2011). This tool includes the following seven domains:

- random sequence generation;
- allocation concealment;
- blinding of participants and personnel;
- blinding of outcome assessment;
- incomplete outcome data;
- selective reporting;
- other potential sources of bias.

Two authors (LL and MAW) independently applied the 'Risk of bias' tool , and resolved differences by discussion with a third review author (SJ). Results were summarised in both a 'Risk of bias' graph (Figure 1) and a 'Risk of bias' summary figure (Figure 2). We scored each item according to the criteria set out by Higgins 2011, and provided a quote from the study report and/or a statement of justification for the judgement for each item in the 'Risk of bias' table. When interpreting treatment effects, two authors took into account the risk of bias for the studies that contributed to that outcome.

Figure 1. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

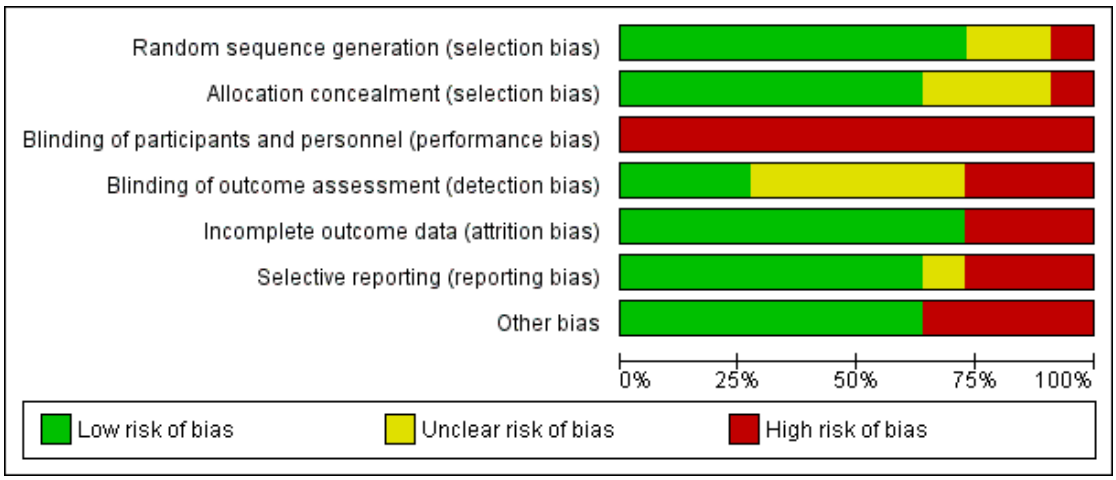
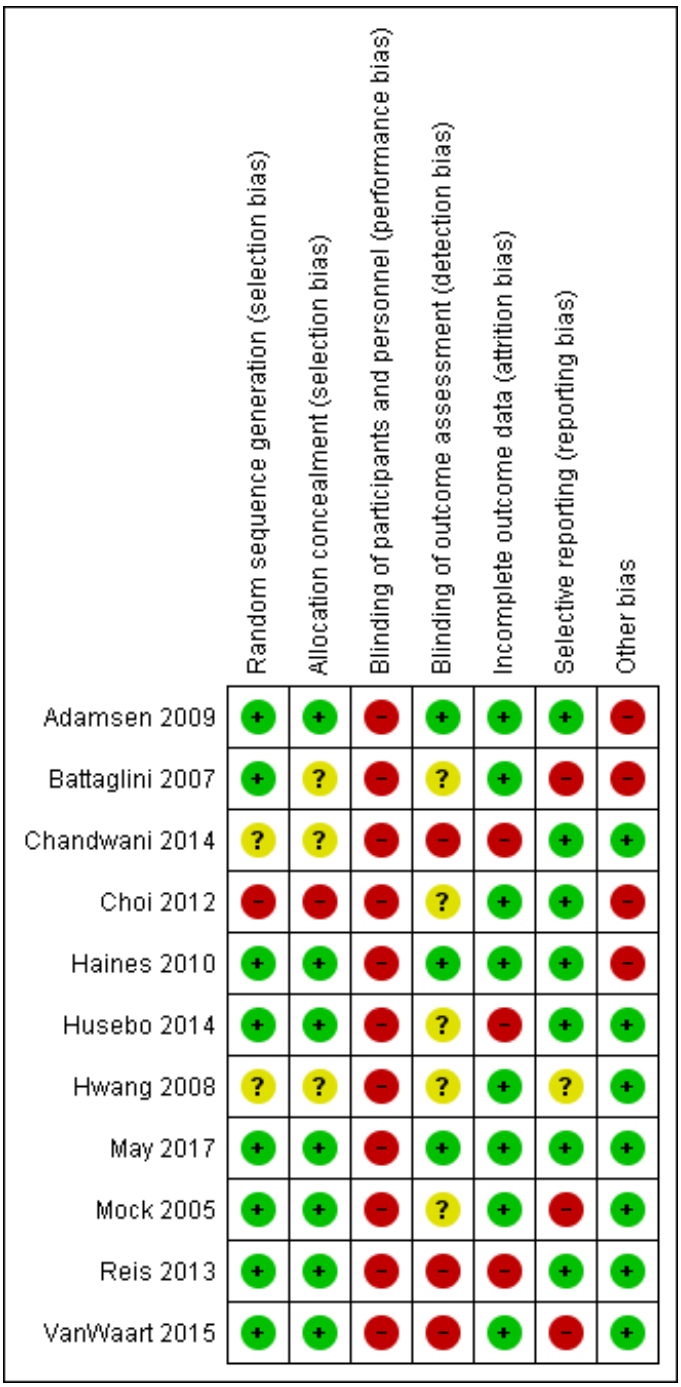


Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Measures of treatment effect

Both primary and secondary outcomes (e.g. physical fitness, HRQoL, fatigue) are continuous outcomes. For these, we recorded mean and standard deviation (SD) at baseline and post-intervention values of the outcome of interest and the number of participants assessed at stated follow-up in each treatment arm. For the other secondary outcome, safety, we reported it as number of adverse events.

Unit of analysis issues

All trials were two-armed except for two studies which were three-armed (Chandwani 2014; VanWaart 2015). However, the "stretching intervention" arm in the study by Chandwani 2014 was not reported as it was not classed as an exercise intervention. The study by VanWaart 2015 included two exercise intervention arms (home and supervised exercise groups). We extracted data from relevant arms, and compared the intervention arms versus the control group.

Dealing with missing data

When required, we made an attempt to contact study authors to obtain missing data (participants, intervention, outcome, or summary data).

Assessment of heterogeneity

Where we considered studies to be similar enough (based on consideration of participants, cancer treatment, exercise training characteristics, or outcome measures), we used clinical expertise to decide whether it was appropriate to combine trials in a meta-analysis. We assessed the degree of heterogeneity by visual inspection of forest plots, by estimation of the percentage of heterogeneity (I^2 measurement) between trials which could not be ascribed to sampling variation (Higgins 2003), by a formal statistical test of the significance of the heterogeneity (Chi^2) (Deeks 2001) and, where possible, by subgroup analyses. We regarded heterogeneity as substantial if I^2 was greater than 30% and either Tau^2 was greater than zero, or there was a low P value (< 0.10) in the Chi^2 test for heterogeneity.

Where we had concerns regarding clinical, methodological, or statistical heterogeneity across included studies, we did not report pooled results from meta-analysis and reported possible clinical or methodological reasons for this.

Assessment of reporting biases

If 10 or more studies investigated a particular outcome, we had planned to examine funnel plots corresponding to meta-analysis of the primary outcome to assess the potential for small-study effects such as publication bias.

Data synthesis

Mean differences (MDs) with 95% confidence intervals (CIs) were calculated by using a random-effects model. Where appropriate, we conducted statistical analysis using a random-effects model with inverse variance weighting for all meta-analyses (DerSimonian 1986). We considered the random-effects summary as the average range of possible treatment effects and discussed the clinical implications of treatment effects differing between studies. We entered the data of the included studies into RevMan version 5.3 software (Review Manager 2014). We used the GRADE criteria to assess the certainty of the evidence of the included studies. We presented results as the average treatment effect with its 95% CI and the estimates of I^2. Data from the following outcome measures were pooled for meta-analyses: aerobic fitness (VO_2 max (oxygen uptake at maximal capacity), 6-minute walk distance (6MWD), upper body strength (grip strength), HRQoL (EORTC QLQ-C30, EQ-5D, SF-36) and fatigue (multidimensional fatigue inventory and EORTC). Where meta-analyses were not possible, we reported all available effect information from the included studies in a narrative format.

Subgroup analysis and investigation of heterogeneity

We did not conduct subgroup analyses according to: cancer type, exercise intervention characteristics, or participant characteristics due to the small number of studies measuring the same outcomes.

Sensitivity analysis

Where appropriate, we performed sensitivity analyses on the basis of trial quality by repeating our analysis including only trials that were of high quality (i.e. we did not include low quality trials identified using the Cochrane's tool for assessing risk of bias).

Summary of findings table

Two authors independently rated the certainty of the evidence for each outcome using GRADE (GRADE Working Group 2004). A 'Summary of findings' table was created in GRADEpro GDT. For assessments of the overall certainty of evidence for each outcome that included pooled data from RCTs only, we downgraded the evidence from 'high certainty' by one level for serious (or by

two for very serious) study limitations (risk of bias), indirectness of evidence, serious inconsistency, imprecision of effect estimates, or potential publication bias. We included the following outcomes in the Summary of findings for the main comparison:

- physical fitness;
- safety;
- HRQoL;
- fatigue;
- postoperative outcomes (morbidity and survival).

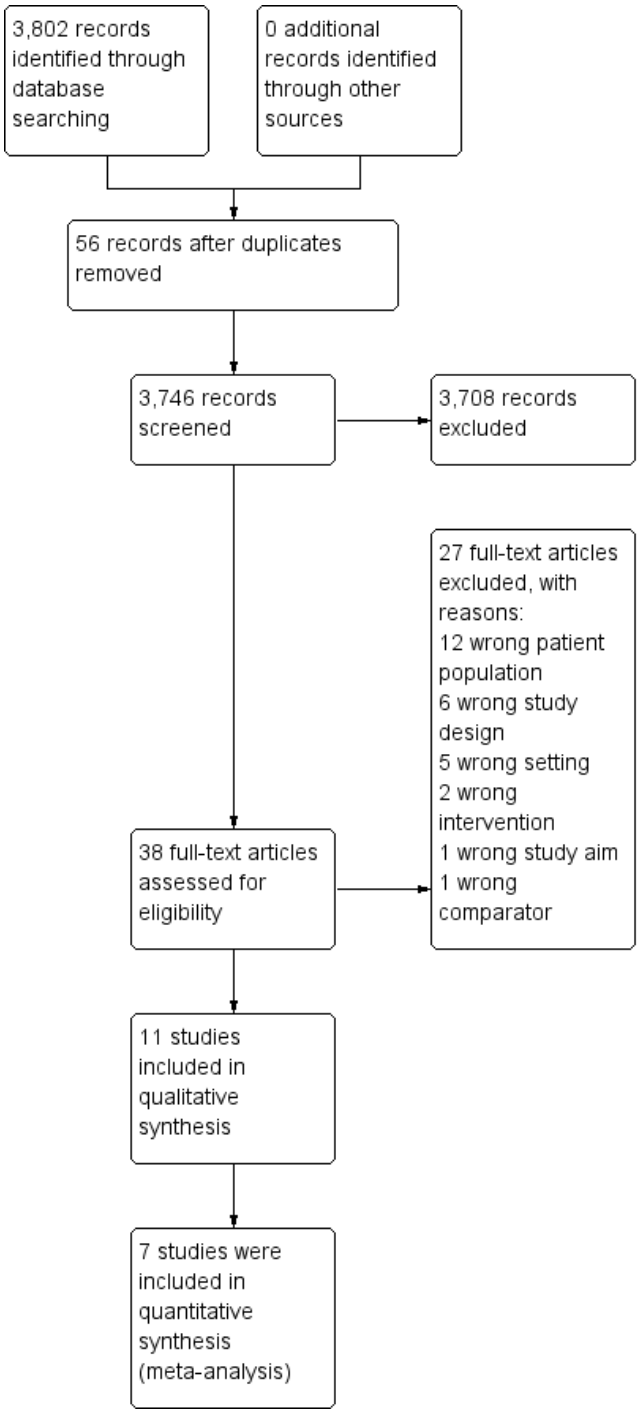
RESULTS

Description of studies

Results of the search

Our database search yielded 3802 candidate abstracts, including 56 duplicates. We therefore reviewed 3746 abstracts for potential inclusion. We excluded 3708 abstracts during the initial title and abstract screening and assessed 38 studies on the basis of full-text review. Of these, we excluded 27 studies and 11 studies met the inclusion criteria. The study flow diagram is shown as Figure 3.

Figure 3. Study flow diagram.



Nine ongoing studies were identified through searching other resources such as clinicaltrials.gov and the WHO International Clinical Trials Registry Platform (Loughney 2016; Morielli 2018; NCT02159157; NCT02454777; NCT02802826; NCT02999074; NCT03102866; NCT03280836; NCT03509428). Characteristics describing the primary author, methodology, outcomes of interest, intervention, study start date, and expected end date as well as country of study conduct are reported in (Characteristics of ongoing studies). Of the nine ongoing studies, six were breast cancer studies, two colorectal cancer, and one included all major cancers. Eight studies were either not yet recruiting or recruiting, whilst one colorectal cancer study had closed (results were being prepared for publication in 2018) (Loughney 2017).

Included studies

We included 11 studies in this review, the majority of which were studies of women with breast cancer undergoing surgery and adjuvant cancer treatment. The studies involved 1067 participants (73% in breast cancer studies), 568 of whom were randomly allocated to a form of an exercise intervention for a minimum of five weeks, while 499 were randomly assigned to a control group. The individual studies are described in Characteristics of included studies and further details are given below. All authors of the included studies, except two, were contacted about missing data (Adamsen 2009; Haines 2010), five of which responded to provide us with additional study information (Chandwani 2014; Husebo 2014; May 2017; Reis 2013; VanWaart 2015).

Study details

The included studies were conducted in different countries. Four were undertaken in the United States (Battaglini 2007; Chandwani 2014; Mock 2005; Reis 2013), two studies in Korea (Choi 2012; Hwang 2008) and Netherlands (May 2017; VanWaart 2015), while the remaining studies were conducted in Australia (Haines 2010), Denmark (Adamsen 2009), and Norway (Husebo 2014).The sample size ranged from 20 to 269: six studies had sample sizes with fewer than 100 participants (Battaglini 2007; Choi 2012; Haines 2010; Husebo 2014; Hwang 2008; Reis 2013), three studies had sample sizes between 100 to 200 (Chandwani 2014; May 2017; Mock 2005), while the remaining two had sample sizes of more than 200 (Adamsen 2009; VanWaart 2015). All studies were two-arm RCTs that assigned participants to an exercise and usual care control group except for two studies that were three-arm RCTs comprising two intervention arms and one control arm (Chandwani 2014; VanWaart 2015). The "stretching intervention" arm in the study by Chandwani 2014 was not reported as it was not classed as an exercise intervention. For the purposes of this review, the two intervention arms in the VanWaart 2015 study were referred to as Intervention 1 (On-Track), which was a supervised hospital-based exercise programme, and Intervention 2 (Onco-Move), which was an unsupervised home-based programme.

Participants

Cancer types varied across studies: one included 21 different cancer types (52% were reported not to have any cancer) (Adamsen 2009), seven included breast cancer (Battaglini 2007; Chandwani 2014; Haines 2010; Husebo 2014; Hwang 2008; Mock 2005; Reis 2013), one stomach cancer (Choi 2012), and two included a combination of breast and colon cancer (May 2017; VanWaart 2015). Cancer treatments were mainly delivered in the adjuvant setting but varied across studies. Half of the included studies reported one type of cancer treatment such as radiotherapy (Hwang 2008; Reis 2013), or chemotherapy (Battaglini 2007; Choi 2012; VanWaart 2015), while the remaining five reported a mix of cancer treatments: for example, one study reported 59 different chemotherapy regimens (Adamsen 2009), another study reported adjuvant treatment but type of cancer treatment was not provided (Haines 2010), while the remaining studies reported chemotherapy, other systemic treatment, and radiotherapy (Husebo 2014), chemotherapy and radiotherapy (May 2017), or adjuvant cytotoxic chemotherapy/radiation therapy (Mock 2005). The study by Chandwani 2014 reported that participants would be randomised according to chemotherapy (neoadjuvant or adjuvant) among other variables but details of numbers undergoing either treatment were not reported. The study by May 2017 reported that fewer than 5% underwent neoadjuvant treatment. The age of participants in the included studies ranged from 40 to 70 years. There was substantial gender imbalance, with 73% of the included studies being breast cancer studies.

Intervention details

Supervised programmes

Six studies included a supervised exercise intervention (Adamsen 2009; Battaglini 2007; Chandwani 2014; Hwang 2008; May 2017; VanWaart 2015), of which three were hospital-based (Adamsen 2009; Chandwani 2014; May 2017), one based in a rehabilitation centre (Battaglini 2007), one based in the community (VanWaart 2015) and one did not report the setting (Hwang 2008). The exercise intervention was delivered to a group in one study (Adamsen 2009), on a one-to one basis in three other studies (Battaglini 2007; Chandwani 2014; VanWaart 2015), while the remaining two studies did not report this information (Hwang 2008; May 2017).

The duration of the exercise intervention varied: a 5-week (Hwang 2008), 6-week (Adamsen 2009; Chandwani 2014), 15-week Battaglini 2007) or 18-week period (May 2017); in one study, the duration was not clearly reported ("Started with the first cycle of chemotherapy and continued until 3 weeks after the last cycle") (VanWaart 2015). The exercise intervention components also varied across studies and included a combination of aerobic, strength, balance, coordination, and relaxation (Adamsen 2009), yoga (Chandwani 2014), aerobic, strength, and stretching (Hwang 2008), or aerobic and strength (Battaglini 2007; May 2017; VanWaart 2015). Exercise was prescribed for two sessions per week (Battaglini 2007; May 2017; VanWaart 2015) or three sessions per week (Adamsen 2009; Chandwani 2014; Hwang 2008).

Description of the intensity of aerobic exercise also varied: high and low intensities (Adamsen 2009), 50% to 70% age-adjusted heart rate maximum (Hwang 2008), interval intensities (May 2017), 50% to 80% maximal workload (steep ramp test) and by the BORG scale (rating of perceived exertion) (less than 12 for increase and more than 16 for a decrease) (VanWaart 2015); while in two studies the intensity was not clearly reported (Battaglini 2007; Chandwani 2014). Description of the intensity of strength exercise varied: 70% to 100% 1-repetition maximum (RM) (Adamsen 2009), 65% 1-RM gradually increasing to reach 1 x 10 repetitions (75% 1-RM), 20 x repetitions (45% 1-RM) by the end of the programme (May 2017), 80% 1-RM (VanWaart 2015), and in one study, the intensity was not clearly reported (Battaglini 2007).

The duration of the exercise programmes varied: 30 to 90 minutes (min) (Adamsen 2009), 50 min (Hwang 2008; VanWaart 2015), 60 min (Chandwani 2014), or no more than 60 min (Battaglini 2007); the duration was not reported in one study (May 2017).

The type of exercises varied across studies and included cycle ergometer, strength exercises on machines (Adamsen 2009; Battaglini 2007), as well as body awareness and restoring training and massage (Adamsen 2009), yoga exercises (Chandwani 2014), treadmill and bicycling (Hwang 2008), and the type of exercise was not reported in two studies (May 2017; VanWaart 2015). Adherence to the supervised programmes was 71% (Adamsen 2009; VanWaart 2015), 83% (May 2017), 87% (Chandwani 2014), 100% (Battaglini 2007), and one study did not report adherence (Hwang 2008).

Home-based programmes

Six studies included home-based exercise interventions (Choi 2012; Haines 2010; Husebo 2014; Mock 2005; Reis 2013; VanWaart 2015). The exercise intervention was delivered over eight weeks (Choi 2012), 12 weeks (Reis 2013) or 12 months (Haines 2010), where only data for EQ-5D were collected at 12 months (over the telephone), and for other outcome measures, follow-up assessment was conducted at six months. However, it must be noted that, in some cases, it was unclear. One study reported that the duration of the programme was for the period from initiation to cessation of adjuvant therapy: six weeks of radiotherapy or three to six months of chemotherapy (Mock 2005). In the study by Husebo 2014, the exercise intervention was delivered for the duration of chemotherapy (18 to 24 weeks), however, not all participants received chemotherapy. One study reported that the exercise programme "Started with the first cycle of chemotherapy and continued until 3 weeks after the last cycle" (VanWaart 2015).

The exercise intervention components were also varied, and included aerobics (Choi 2012; Mock 2005; VanWaart 2015), aerobics, strength, balance, and shoulder mobility (Haines 2010), aerobics and strength (Husebo 2014) or aerobics, strength, balance, yoga, stretching (known as the Nia programme) (Reis 2013).

Exercise was prescribed for three sessions per week (Husebo 2014; Reis 2013), more than three sessions per week (Choi 2012), five sessions per week (VanWaart 2015), and five to six times per week (Mock 2005); in two studies, the frequency of exercise was not clear (Haines 2010), or not reported (Husebo 2014).

The intensity of the aerobic component was moderate intensity (Choi 2012; Husebo 2014), with moderate intensity described as approximately 50% to 70% of maximum heart rate (Mock 2005) or as a score of 12 to 14 on the BORG scale (VanWaart 2015). In the study by Reis 2013, intensity was not clear: "The practice of Nia can be gentle for individuals with a sedentary lifestyle or challenging for those with an active lifestyle".

The duration of the exercise intervention varied between 15 to 30 min (Mock 2005), 20 to 60 min (Reis 2013), 30 min (Husebo 2014; VanWaart 2015), 36 min (Haines 2010) or 60 min (Choi 2012). The type of exercise was mainly walking or a combination: walking (Choi 2012; Mock 2005; VanWaart 2015), walking and home-based exercises for strength balance and mobility (Haines 2010), or walking and strength-resistant exercises (Mock 2005). One study did not report the exercise type fully (Reis 2013).

Adherence to home-based programmes was reported by the number of sessions/percentage and, in some cases, for each exercise component: 3.8 sessions per week (Choi 2012), or at the three months median interquartile range (IQR) sessions per patient with 32 sessions for strength or balance and 22 sessions for endurance; while at the six months median (IQR), there were 12 sessions for strength or balance and 13 sessions for endurance (however this was a 12-month programme and overall adherence was not reported) (Haines 2010). One study reported adherence to the aerobic component at 17% and 15% to the strength component (Husebo 2014), while other studies reported 55% (VanWaart 2015) and 72% (Mock 2005) to aerobic exercise programmes or two days per week of the Nia programme plus two sessions per week of other aerobic exercise (Reis 2013).

Participants assigned to the home-based programmes received support from research staff throughout the study period. In one study, a weekly 5 to 10 min telephone conversation was conducted, and a weekly short (less than 40 characters) message for exercise reinforcement was sent to the participant for eight weeks (Choi 2012).

Two studies reported that a member of the research team telephoned participants, but the timing was not documented (Haines 2010; Husebo 2014). One study reported that the research team contacted participants every two weeks to evaluate the prescription and participant progress; furthermore, the exercise programme was detailed in a booklet and video to ensure standardisation (Mock 2005). One other study provided participants with an activity diary that was discussed at each chemotherapy cycle, where specially trained nurses encouraged participants to engage in exercise (VanWaart 2015). In one study, participants received encouragement from a nurse in the chemotherapy unit to be physical active at least 30 minutes per day. This encouragement was provided each time the nurse saw the participant (VanWaart 2015).

Usual care control group details

The usual care control groups generally received no formal exercise training, except in one study, and some other studies provided participants with exercise advice. In the study by Haines 2010, the usual care control group was an active sham group which included a home-based flexibility and relaxation programme. Participants received a phone call from a member of the research team weekly. In the study by Hwang 2008, the usual care control group was shown how to perform a shoulder range of motion exercises and were encouraged to continue normal activities. In studies by May 2017 and Mock 2005, the usual care control groups were asked to maintain their current physical activity levels but no formal exercise programme was provided. Similar advice was provided to the usual care control group in the study by Reis 2013, except the control group participants also met individually with the principal investigator. Participants were instructed to record their activities in an exercise log. At six-week and 12-week time points, participants met individually with the principal investigator to discuss topics such as physical, emotional, mental, and spiritual well-being.

Excluded studies

Twenty-seven full-text articles were excluded from the review due to the following reasons:

- wrong patient population (n = 12) (Ahmed 2006; Bloomquist 2014; Cadmus 2009; Coleman 2003; Courneya 2009; Devoogdt 2011; Dimeo 1997; McNeely 2008; Mina 2014; Pehlivan 2011; Saxton 2014; Villanueva 2011);
- wrong study design (n = 6) (Cho 2008; Coleman 2003; Jones 2010; McNeely 2010; Salhi 2014; So 2006);
- wrong setting (n = 5) (Duijts 2012; Harder 2015; Kilbreath 2012; Salhi 2015; Thorsen 2005);
- wrong intervention (n = 2) (Song 2013; Xu 2015);
- wrong study aim (n = 1) Courneya 2008);
- wrong comparator (n = 1) (Courneya 2014).

See characteristics of Excluded studies for an overview.

Risk of bias in included studies

Due to the nature of the intervention, it was expected that blinding of participants and personnel delivering the interventions would not be possible. Consequently, risk of performance bias in all studies was high. Risk of bias for other bias domains varied across the included studies, and in some studies, insufficient detail was provided to inform judgement. Where insufficient detail was provided, all authors were contacted by email. See Figure 1, 'Risk of bias' graph, and Figure 2, 'Risk of bias' summary table, for an overview.

Allocation

We judged nine studies as being at low risk for random sequence generation (Adamsen 2009; Battaglini 2007; Haines 2010; Husebo 2014; May 2017; Mock 2005; Reis 2013; VanWaart 2015) and one study as high risk (Choi 2012), while the remaining two studies provided insufficient information to inform judgement (Chandwani 2014; Hwang 2008). We judged seven studies as being at low risk for allocation concealment (Adamsen 2009; Haines 2010; Husebo 2014; May 2017; Mock 2005; Reis 2013; VanWaart 2015), one as high risk (Choi 2012), and the remaining three provided insufficient information to inform judgement (Battaglini 2007; Chandwani 2014; Hwang 2008).

Blinding

Performance bias

Due to the nature of the intervention, risk of performance bias was high in all studies.

Detection bias

We could only assess six studies for detection bias; three were rated as low risk (Adamsen 2009; Haines 2010; May 2017), three as high risk (VanWaart 2015; Reis 2013; Chandwani 2014), while the remaining five studies provided insufficient information to inform judgement (Battaglini 2007; Choi 2012; Husebo 2014; Hwang 2008; Mock 2005).

Incomplete outcome data

We judged eight studies as being at low risk for attrition bias (Adamsen 2009; Battaglini 2007; Choi 2012; Haines 2010; Hwang 2008; May 2017; Mock 2005; VanWaart 2015), and three as high risk of bias (Chandwani 2014; Husebo 2014; Reis 2013).

Selective reporting

We judged three studies as being at high risk for reporting bias (Battaglini 2007; Mock 2005; VanWaart 2015), and seven as low risk (Adamsen 2009; Chandwani 2014; Choi 2012; Haines 2010; Husebo 2014; May 2017; Reis 2013), while the remaining study provided insufficient information to inform judgment (Hwang 2008).

Other potential sources of bias

We judged four studies as being at high risk for other sources of bias. Adamsen 2009 included various cancer types, however, 52% of the study population were reported not to have cancer. The measure of HRQoL reported by Choi 2012 was not clearly stated. Although reference was made within the study to two other studies, the references were an unpublished doctoral dissertation and a master's thesis. In Haines 2010, the control group was a sham intervention group. Furthermore, the exercise intervention was reported as a 12-month intervention. However, all measures, except EQ-5D, were reported at six months while EQ-5D was reported at 12 months over the telephone. The study by Battaglini 2007 reported data pre-surgery and post-cancer treatment. No data were collected following surgery or before cancer treatment, therefore, these data were not included in the review.

Effects of interventions

See: **Summary of findings for the main comparison** The effects of an exercise intervention compared to a usual care control group with people with cancer undergoing multimodal treatment?
See: Summary of findings for the main comparison for the main comparisons between the exercise intervention and usual care control groups.
All outcome results for meta-analyses were based on the earliest follow-up time point following completion of the exercise intervention. All other outcome results that were not appropriate for meta-analyses were reported comparing the exercise intervention and usual care control groups using baseline and earliest follow-up time point following completion of the exercise intervention.

Primary outcomes

Physical fitness

In this review, physical fitness included any measure of aerobic fitness and strength, as well as physical activity.

Aerobic fitness

A total of eight studies reported aerobic fitness using a variety of different outcome measures assessed by: VO_2 max test (Adamsen 2009; Battaglini 2007; May 2017); six-minute walk distance test (6MWD) (Haines 2010; Husebo 2014; Reis 2013); maximal short exercise capacity test (VanWaart 2015); endurance time test (VanWaart 2015); step test (Haines 2010); and 12-minute walk distance test (12MWD) (Mock 2005). Meta-analyses were conducted for VO_2 max test and 6MWD.
A meta-analysis was conducted using data from two studies that reported the VO_2 max test using a cycle ergometer (Adamsen 2009; May 2017). In the study by Battaglini 2007, data for VO_2 max were not reported. Findings showed that there may be no difference between the intervention group compared to usual care, given here as mean difference (MD) 0.05 L/min^{-1}, 95% CI -0.03 to 0.13, I^2 = 0% ; 2 studies, 381 participants; low-certainty evidence (Analysis 1.1).
A meta-analysis was also conducted using data from studies that reported the 6MWD (Haines 2010; Husebo 2014; Reis 2013). Findings showed that there was probably no difference between the intervention group compared to the usual care group (MD 16.79 metres, 95% CI -7.39 to 40.96, I^2 = 0%; 3 studies, 146 participants; moderate-certainty evidence) (Analysis 1.2).

Aerobic fitness data from individual studies

A narrative description of all other outcome results, reported below, are presented in Table 1.
In the study by VanWaart 2015, there was a significant difference in the maximal short exercise capacity test from baseline to post-intervention (end of chemotherapy, duration of which varied for each participant) between the intervention group 1 OnTrack group (a supervised programme) (n = 71) compared to the usual care control group (n = 66). However there were no significant differences between the usual care control group and the intervention 2 group Onco-Move (home-based programme) (n = 69). Additionally, in the same study, the endurance timed test showed significant effects favouring the intervention 1 OnTrack group and the intervention 2 Onco-Move group compared to the usual care control group.
In the study by Haines 2010, the step test showed no significant difference from baseline to post-intervention (six weeks) between the intervention group (n = 32) and to the usual care control group (n = 31). Data for the 12MWD (Mock 2005) were not reported.

Upper body strength

A total of five studies reported upper body strength assessed by grip strength (Haines 2010; May 2017; VanWaart 2015), chest press (Adamsen 2009), pull down (Adamsen 2009), elbow flexion (VanWaart 2015), and 1-repetition max (1-RM) (Battaglini 2007).

Meta-analyses were conducted for grip strength (Haines 2010; May 2017; VanWaart 2015), findings of which showed that there was probably no difference between the intervention group compared to the usual care control group (MD 0.73 kg, 95% CI -0.86 to 2.32, I^2 = 42%; 3 studies, 419 participants; moderate-certainty evidence) (Analysis 1.3). Findings from a sensitivity analysis including only studies with a low risk of bias (Haines 2010; May 2017) also indicated no difference (MD 0.21 kg, 95% CI -1.85 to 1.43, I^2 = 0%, 2 studies).

Upper body strength data from individual studies

A narrative description of all other outcome results, reported below, are presented in Table 1.

Adamsen 2009 reported significant improvements in the chest press test and the pull-down test from baseline to post-intervention (six weeks) favouring the intervention group (n = 118) compared to the usual care group (n = 117).

VanWaart 2015 reported a significant effect favouring the intervention 1 OnTrack group (supervised programme) on the elbow flexion test from baseline to post-intervention (duration of which varied, dependent on each participants chemotherapy regimen) (n = 71) compared to the usual care control group (n = 66), with no significant effect between the intervention 2 Onco-Move group (home-based programme) (n = 77) and the usual care control group.

In the study by Battaglini 2007, data for 1-RM were only reported at pre-surgery and end of adjuvant cancer treatment time points. No data were collected following surgery/before cancer treatment, therefore, these data were not included in the review.

Lower body strength

A total of four studies reported lower body strength, assessed by leg press (Adamsen 2009; Haines 2010), 30-second chair-stand test (VanWaart 2015), knee extension (VanWaart 2015) and a cybex dynamometer at angular velocities of 60°/s and 180°/s (right/left knee extensor and flexor peak torque) (May 2017). Meta-analyses were precluded for leg press due to substantial heterogeneity (85%) which may be explained by the variation between both studies for the duration of exercise intervention (six weeks versus six months), different cancer types (several cancer groups versus breast) as well as the wide variation in values reported (Adamsen 2009; Haines 2010).

Lower body strength data from individual studies

A narrative description of all other outcome results, reported below, are presented in Table 1

For the leg press test, Adamsen 2009 reported a significant improvement from baseline to post-intervention (six weeks) favouring the intervention group (n = 118) compared to the usual care group (n = 117). Haines 2010 reported no significant differences from baseline to post-intervention (six months) in the same test between the intervention group (n = 30) and the usual care control group (n = 29).

For the 30-second chair stand test, VanWaart 2015 reported no significant between group effects. From baseline and post-intervention (the duration of which varied, dependent on each participant's chemotherapy regimen), there were no significant differences between the intervention 1 OnTrack group (supervised programme) (n = 71) compared to the usual care control group (n = 66) and, similarly, for the intervention 2 Onco-Move group (n = 69) when compared to the usual care control group. In the same study, the knee extension test showed a significant effect favouring the intervention 1 OnTrack group compared to a reduction in the usual care control group. However, no significant differences were reported between the intervention group 2 Onco-Move group (home-based programme) when compared to the usual care control group.

In the study by May 2017, lower body muscle strength for flexion and extension of both right and left legs were significantly higher than the usual care control groups at 60°/s, but not for 180°/s (P values were not provided). From baseline to post-intervention (18 weeks), right knee extensor peak toque at 60°/s increased in the intervention group (n = 63) compared to a reduction in the usual care control group (n = 51). A similar change was reported for right knee flexor peak torque at 60°/s; left knee extensor peak torque at 60°/s; and left knee flexor peak torque at 60°/s. For the right knee extensor peak torque at 180°/s, between baseline to post-intervention, the intervention group showed an increase compared to a reduction in the usual care control group whilst for the right knee flexor peak torque at 180°/s, the intervention and usual care control group had increased values. For the left knee extensor peak torque at 180°/s, the intervention group increased and the usual care control group decreased and for left knee flexor peak torque at 180°/s, both the intervention and usual care control group had increased values.

Physical activity

Physical activity was reported in five studies, all of which also used different outcome measures: leisure time physical activity questionnaire (Adamsen 2009), international physical activity questionnaire (short-form) (Husebo 2014), physical activity for the elderly (VanWaart 2015), physical activity questionnaire (Mock 2005) and physical activity (Short QUestionnaire to ASess Health enhancing physical activity) (May 2017). This variation in outcome measures precluded meta-analyses. Adamsen 2009 reported pre-illness and baseline physical activity levels but no follow-up data. Husebo 2014 reported no significant differences from baseline to post-intervention (18 to 24 weeks) in the intervention group (n = 29) 1333.66 (1367.67) metabolic equivalent of task

(MET) minutes/week to 1621.12 (1734.42) compared to the usual care control group (n = 31) 1138 (1148.81) to 1018.97 (1396.25), P = 0.398. VanWaart 2015 reported no significant findings and raw data for physical activity in the elderly were not reported. Mock 2005 reported non-significant findings for physical activity with no raw data reported. However, on dividing the data into high and low exercises, findings were significant. These data were not reported in this review, as the subgroup analyses were not clearly stated in the methods and this was judged as a possible source of bias. Physical activity data in the study by May 2017 were not reported in the study and data were not provided.

Secondary outcomes

Safety

Eight of the 11 included studies reported safety (adverse events), while the remaining studies did not (Battaglini 2007; Chandwani 2014; Reis 2013). Of these, seven reported that no significant adverse events were related to the exercise programme. Adamsen 2009 reported that one participant with a brain tumour experienced a grade three seizure after exercise training: this participant was admitted to hospital, recovered within three hours, and was discharged the same day. The participant was subsequently excluded from the intervention. The included studies showed low-certainty evidence that exercise may be of benefit (8 studies, 638 participants).

Health-Related Quality of Life (HRQoL)

HRQoL was reported in seven studies measured using: European Organisation for Research and Treatment of Cancer (EORTC QLQ-C30) subscales (Adamsen 2009; Haines 2010; May 2017; VanWaart 2015); EQ-5D (utility) (Haines 2010; May 2017), EQ-5D (visual analogue scale (VAS)) (Haines 2010), Short Form Health Survey (SF-36) (Adamsen 2009; Chandwani 2014; May 2017); World Health Organisation quality of life (WHOQOL) (Hwang 2008) and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) (Reis 2013). In the study by Choi 2012, the type of HRQoL outcome measure was not reported. Meta-analyses were conducted for EQ-5D (utility) and EORTC subscales for: global health status, cognitive functioning, and social functioning. However, meta-analyses for other EORTC subscales, such as role functioning, were not possible due to substantial heterogeneity (76%) and similarly for emotional functioning (82%), which may be due to the variation between the studies in duration of exercise intervention (six weeks versus six months), and also to the different cancer types (several cancer groups versus breast), as well as the wide variation in values reported (Adamsen 2009; Haines 2010).

A meta-analysis was conducted using data from studies that reported the EORTC global health state subscale (Adamsen 2009; Haines 2010; May 2017). Findings showed that exercise may have no difference on this subscale between the intervention group compared to the usual care control group (MD 2.29, 95% CI -1.06 to 5.65, I^2 = 0%; 3 studies, 472 participants; low-certainty evidence) (Analysis 1.4). A meta-analysis was also conducted using data from studies that reported the EORTC cognitive functioning subscale (Adamsen 2009; Haines 2010; VanWaart 2015). Similarly, there was probably no difference between the intervention group compared to the usual care control group (MD 3.13, 95% CI -0.55 to 6.80, I^2 = 0%, 3 studies, 505 participants; moderate-certainty evidence) (Analysis 1.5). The meta-analysis from studies that reported social functioning (Adamsen 2009; Haines 2010; VanWaart 2015) showed that there was probably no difference between the intervention group compared to the usual care control group (MD 3.62, 95% CI -0.33 to 7.58, I^2 = 0%, 3 studies. 505 participants; moderate-certainty evidence) (Analysis 1.6). A meta-analysis was precluded for the EORTC physical functioning subscale due to substantial heterogeneity (91%) (Adamsen 2009; Haines 2010; VanWaart 2015). A narrative description from individual studies that reported EORTC results, reported here, are presented below in Table 2. In the study by Adamsen 2009, from baseline to post-intervention (six weeks), the physical functioning subscale score was significantly greater in the intervention group (n = 118) compared to the usual care control group (n = 117). In contrast, Haines 2010 reported a reduction in the intervention group (n = 33) and in the usual care control group (n = 32). The study by VanWaart 2015 showed varied responses: intervention group 1 demonstrated a reduction compared to an even greater reduction in the usual care control group. Furthermore, they reported a reduction in intervention group 2 which was significantly different to the usual care control group. For the EORTC subscale for role functioning, in the study by Adamsen 2009, there was no significant difference in the role functioning subscale scores between the intervention group (n = 118) compared to the usual care control group (n = 117). Similarly, in the study by Haines 2010, from baseline to post-intervention (six months), there were no significant differences between the intervention group (n = 33) and usual care control group (n = 32). For the emotional functioning subscale, in the study by Adamsen 2009, there were no significant differences between the intervention group compared to the usual care control group. Similarly, Haines 2010 reported no significant difference between the intervention group compared to the usual care control group.

A meta-analysis was conducted using data from studies that reported EQ-5D (utility) (Haines 2010; May 2017). Findings showed that there may be no difference between the intervention group compared to the usual care control group (MD 0.01, 95% CI -0.05 to 0.07, I^2 = 9%, 2 studies, 263 participants; low-certainty evidence) (Analysis 1.7). Haines 2010 reported no significant differences from baseline to post-intervention (12 months) for EQ-5D (VAS) between the intervention group (n = 33) compared to the control group.

Pooled data from studies that reported SF-36 (general health perceptions subscale) (Adamsen 2009; Chandwani 2014) showed that we are uncertain whether there are differences between the intervention group compared to the usual care control group (MD 0.67, 95% CI -3.24 to 4.57, I^2 = 33%, 2 studies, 317 participants; very low-certainty evidence) (Analysis 1.8). A meta-analysis was conducted using studies that reported the SF-36 subscale mental health component (Adamsen 2009; Chandwani 2014). Findings showed that we are uncertain whether there are differences between the intervention group compared to the usual care control group (MD 2.58, 95% CI 0.16 to 5.01, I^2 = 6%, 2 studies, 317 participants; very low-certainty evidence) (Analysis 1.9). Additionally, pooled data from studies that reported the bodily pain subscale (Adamsen 2009; Chandwani 2014) showed that we are uncertain whether there are differences between the intervention group compared to the usual care control group for this subscale also (MD 0.06, 95% CI -3.03 to 3.15, I^2 = 0%, 2 studies, 317 participants; very low-certainty evidence) (Analysis 1.10). Due to substantial heterogeneity, meta-analyses were precluded for the following subscales: physical component scale (71%), physical functioning (71%), and role physical (88%) (Adamsen 2009; Chandwani 2014).

HRQoL data from individual studies

A narrative description of all other outcome results, reported below, are presented in Table 2.

Adamsen 2009 reported that physical functioning reduced, with a significant difference between the intervention group (n = 118) compared to the usual care control group (n = 117). Chandwani 2014 reported no significant difference from baseline to post-intervention between the intervention group (n = 39) compared to the usual care control group (n = 43). Adamsen 2009 reported a significant improvement in the physical component scale between the intervention group (n = 118) compared to the usual care control group (n = 117). Chandwani 2014 reported no significant difference between the intervention group and the usual care control group. For the role physical subscale, Adamsen 2009 reported a significant improvement in the intervention group compared to the usual care control group. Chandwani 2014 reported no significant differences between the intervention group (n = 39) compared to the usual care control group (n = 43). The study by Adamsen 2009 reported other general well-being SF-36 subscales. Between baseline and post-intervention (six weeks), there were significant favourable effects reported for the intervention group (n = 118) compared to the usual care control group (n = 117) for the following subscales: (i) role physical; (ii) vitality; (iii) role emotional; and (iv) mental health. For social functioning, there were no statistical significant differences between the intervention group compared to the usual care control group,

Hwang 2008 reported the subscales of the WHOWOL-BREF score such as overall quality of life; overall health, physical, psychological and social scores significantly increased from baseline to post-intervention (five weeks) in the intervention group (n = 17) compared to the usual care control group (n = 20). From baseline to post-intervention, significant improvements were reported for the intervention group compared to the usual care control group for overall health; the physical subscale; the psychological subscale; and for the social subscale. There was no significant differences for the environmental subscale between the intervention group compared to the usual care control group.

Reis 2013 reported several subscales of the FACIT-F questionnaire. From baseline to post-intervention (12 weeks), there were no significant differences between the intervention group (n = 12) and the usual care control group (n = 17) for physical well-being, social/family well-being, emotional well-being, functional well-being or FACT-G (no P values were reported).

The study by Choi 2012 reported significant differences between the intervention group (n = 11) compared to the usual care control group (n = 13) (however the tool used was not clearly reported).

Fatigue

Fatigue was reported in ten studies, measured using: EORTC fatigue subscale (Adamsen 2009; VanWaart 2015); multidimensional fatigue inventory (Haines 2010; May 2017; VanWaart 2015); brief fatigue inventory (BFI) (Chandwani 2014; Hwang 2008); Schwartz cancer fatigue scale (Choi 2012; Husebo 2014); the Piper fatigue scale (PFS) (Mock 2005); and functional assessment of chronic illness therapy-fatigue (FACIT-F) (Reis 2013). Meta-analyses were conducted for the EORTC fatigue subscale and multidimensional fatigue inventory. Meta-analyses were not conducted for BFI as Hwang 2008 did not report data. Meta-analyses were also precluded for the Schwartz cancer fatigue scale (Choi 2012; Husebo 2014), due to substantial heterogeneity (77%) which may be explained due to both studies having contrasting directions of effect.

A meta-analysis was conducted using data from studies that reported the multidimensional fatigue inventory (Adamsen 2009; May 2017; VanWaart 2015). Findings showed that exercise probably reduces fatigue (MD -1.05, 95% CI -1.83 to -0.28, I^2 = 0%, 3 studies, 449 participants; moderate-certainty evidence) (Analysis 1.11). Pooled data from studies that reported the EORTC fatigue subscale (Adamsen 2009; Haines 2010; VanWaart 2015) showed that exercise probably reduces fatigue (MD -5.91, 95% CI -10.15 to -1.68, I^2 = 0%, 3 studies, 506 participants; moderate-certainty evidence) (Analysis 1.12).

Fatigue data from individual studies

A narrative description of all other outcome results, reported below, are presented in Table 3.

For BFI, in the study by Hwang 2008, the authors reported that "the mean BFI decreased in the intervention group (n = 17) and

increased in the usual care control group (n = 20) between baseline and post-intervention (five weeks) and there was a significant difference in the change in BFI between groups favouring the intervention group". Data were only presented graphically, and raw data were not available to be included in this review. For BFI, Chandwani 2014 reported a significant effect favouring the intervention group (n = 49) from baseline to post-intervention compared to the usual care control group (n = 48).

For the Schwartz cancer fatigue scale, the study by Choi 2012 reported statistical differences favouring the intervention group (n = 11) following a 8-week exercise programme compared to the usual care control group (n = 13). The study by Husebo 2014 reported increases in fatigue scores using the same scale in both the intervention group (n = 33) and the usual care control group (n = 34), but P values were only reported for the whole sample.

For the FACIT-F score, the study by Reis 2013 reported a statistical significant improvement between baseline and post-intervention (12 weeks) favouring the intervention group (n = 12) compared to the usual care control group (n = 17).

For the Piper fatigue scale, in the study by Mock 2005, findings were reported for high exercisers, low exercisers, and the entire sample, however, no data were reported for the exercise intervention or usual care control groups. Their findings showed that for the PFS, there was a statistical significant difference favouring the low exercisers mean (SD) 2.42 (2.63) to 4.28 (2.70) compared to the high exercisers 2.44 (2.27) to 2.92 (2.00) ($P < 0.01$). For the whole sample, from baseline to post-intervention, findings were 2.43 (2.46) to 3.64 (2.48) (P values were not presented).

Postoperative outcomes

No included studies reported postoperative outcomes.

Sensitivity analysis

Sensitivity analyses were conducted for grip strength and included only studies of high quality (studies for which both allocation concealment and incomplete outcome data were rated as low risk). Findings were consistent with the overall summary effect estimates.

- Overall summary (MD 0.73 kg, 95% CI -0.86 to 2.31, I^2 = 42%, 3 studies, 419 participants) (Haines 2010; VanWaart 2015; May 2017);
- Sensitivity analyses (MD 0.21 kg, -1.85 to 1.43, I^2 = 0%, 2 studies, 213 participants) (Haines 2010; May 2017).

DISCUSSION

Summary of main results

This is the first systematic review of reports of exercise training interventions in people undergoing multimodal cancer treatment including surgery. This review summarised 11 studies published between 2005 and 2017, including 1067 participants (73% of whom had breast cancer) and all studies were conducted in the adjuvant setting. Pooled analyses demonstrated that exercise training in this context may have made little or no difference to physical fitness. The included studies demonstrated that exercise training is probably safe, makes little or no difference to HRQoL, but probably reduces fatigue. No studies reported postoperative outcomes such as morbidity and survival. Our findings should be viewed with caution, as overall we rated the certainty of evidence between very low to moderate. Further higher quality trials are required to confirm the efficacy of exercise interventions, particularly in the neoadjuvant setting.

Overall completeness and applicability of evidence

Findings from this review should be viewed with caution due to the small sample sizes, the variety of cancer treatments, with many different exercise interventions (supervised or home), and outcome measures.

An objective measure of physical fitness is the gold standard. Objective physical fitness levels of people with breast cancer, even before initiating adjuvant treatment, have been reported to be 17% lower than healthy volunteer controls (Peel 2014); thus, the physical fitness of a 50-year old woman with breast cancer is comparable to that of a sedentary 60-year old woman (Peel 2014). This decline in physical fitness has been reported to be sustained for seven years after treatment (Lakoski 2013). Cancer treatment (in the neoadjuvant setting) has been shown to reduce whole body fitness, and this reduction is related to poor surgical outcome (Jack 2014; West 2014). Furthermore, cancer treatment reduces objective physical activity levels in people with colorectal cancer (Loughney 2017). Two of the included studies reported objectively measured physical fitness (Adamsen 2009; May 2017). However, pooled analysis demonstrated that there was probably no difference in physical fitness levels (VO_2 max) following an exercise intervention compared to usual care. Furthermore, no studies assessed physical activity levels objectively but assessed physical activity using self-reported measures. However, it has been recently documented that people with cancer self-report their physical activity levels to be nearly four-fold higher when compared to objective physical activity monitoring data (Vassbakk-Brovold 2016).

Eight of the 10 included studies reported on safety (adverse events), of which seven reported no adverse events related to treatment. In this relatively new area of research, future exercise studies should incorporate safety as an outcome measure.

HRQoL was reported in almost half of the included studies but varied in the type of outcome measure used. It has been reported that chemotherapy negatively effects HRQoL (Vrettos 2012).

Pooled analysis demonstrated that exercise training probably made no difference to HRQoL (EORTC global health status subscale) compared to usual care.

Fatigue was also a commonly reported outcome measure among the included studies. Fatigue is one of the commonest side effects of cancer and cancer treatment, manifesting in the clinic as weakness and exercise intolerance, which can affect quality of life and physical activity. Pooled analysis demonstrated that exercise training probably reduces fatigue (multidimensional fatigue inventory).

We do not know whether an exercise intervention improves postoperative outcomes, such as survival, as no study reported these.

Quality of the evidence

The overall quality (certainty) of the evidence for each of the important outcomes in the review are reported in the Summary of findings for the main comparison.

The aim of this review was to identify studies that included an exercise intervention for people with cancer undergoing multimodal treatment. However, no studies were identified in the neoadjuvant setting. Due to the nature of the intervention, it was not possible to blind the participants or personnel delivering the intervention. The risk of detection bias was high or unclear in some cases whilst most other domains were rated as low risk. The certainty of the evidence was graded between moderate to very low. The included studies varied greatly in the type of cancer treatments (radiation, chemotherapy, hormonal therapy, and other systemic treatment), the duration of the exercise training (between five weeks to 12 months, and, in some cases, the precise duration was unclear, the setting (supervised or home-based), the frequency (two to three times per week), the intensity (varied in method of prescription), time (25 min to 90 min) and type (home-based exercises or machine-based exercise) of the intervention. Time points of assessments and outcome measures also varied considerably. Only three studies had roughly the same duration of exercise intervention (+/- one week), but in these, the outcome measures differed (Adamsen 2009; Chandwani 2014; Hwang 2008).

Potential biases in the review process

This systematic review included search strategies for the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase and SPORTDiscus, which were formulated by the Cochrane Gynaecological, Neuro-oncology and Orphan Cancers Group. The search strategies were first conducted in January 2017, August 2017, and October 2018. Two authors independently screened candidate articles using predefined search terms, and undertook data extraction, and risk of bias judgment independently. Although we emailed all authors for missing data, some did not reply. Therefore, exclusion of these results may be a potential source of bias. The sample population consisted largely of breast cancer patients (73%), therefore findings may not be generalisable to other cancer types. Conclusions drawn from this review are limited by the low number of included studies, as well as the lack of eligible studies in the neoadjuvant setting.

Agreements and disagreements with other studies or reviews

Consistent with findings presented in a recent review Jones 2013, we found that the majority of work conducted in the adjuvant setting includes people with breast cancer. This review is in agreement that there are few studies in this area, limiting our understanding of the most effective exercise training programme (Crandall 2014; Granger 2011; Jones 2007; West 2011).

AUTHORS' CONCLUSIONS

Implications for practice

The included studies demonstrated low-certainty evidence that exercise training may make little or no difference to physical fitness. The included studies also showed that it is probably safe to exercise. Moderate-certainty evidence suggests that exercise training probably makes little or no difference to HRQoL, but that exercise probably reduces fatigue. The current evidence is based on a small number of studies which greatly varied by cancer treatment, exercise intervention, and outcomes. The characteristics and setting (supervised or home) of an exercise programme are not known, therefore, more research is required to inform implications for practice.

Implications for research

This review makes it clear that a more focused approach is required in future studies to include similar outcome measures and similar duration of exercise interventions for better inter-study comparisons. Furthermore, blinding of outcome assessors is required. Additionally, most of this work included people with breast cancer (73%), therefore, more research is required with other cancer patient groups. Future work should include those undergoing more major surgery, such as bowel surgery. For example, it has been shown that, in people with colorectal and oesophageal cancer, neoadjuvant cancer treatments significantly reduce physical fitness before surgery and this reduction is linked to poor postoperative outcomes (Jack 2014; West 2014). Although it is encouraging that five of the ongoing studies identified are investigating exercise interventions in the neoadjuvant setting, there is an urgent requirement for adequately powered RCTs and to investigate effects on postoperative outcomes. A cancer diagnosis may lead individuals to make positive changes to their health behaviours,

a concept sometimes called the 'teachable moment'. Future work should investigate the effectiveness of exercise training, initiated at cancer diagnosis, throughout the entire cancer care journey. Better understanding of the optimal training duration, pattern, intensity, and composition of such interventions will be needed to maximise efficacy. The included studies in this review demonstrated that the countries currently leading this area of research are the USA with four studies, Korea and the Netherlands with two studies each, and Norway, Australia, and Denmark with one study each. Perhaps international collaboration to advance generalisable research in this area is required to answer these important research questions. Furthermore, addressing the substantial heterogeneity in both interventions and outcome measurements should also be a priority for researchers. Efforts to harmonise or standardise reporting of characteristics of exercise interventions and outcome measures to quantify physical exercise outcomes within such studies would be of value in improving opportunities to compare, contrast, and combine such data in order to better understand the impact of interventions for people with cancer (Myles 2016). We suggest answering the following specified research questions in future studies:

- What is the optimal time to initiate an exercise programme and what kind of programme is the most effective in improving clinically important outcome measures?
- What is the optimal prescribable dose of exercise and in what format will this most benefit cancer patients?
- Does combining aerobic and resistance exercise programmes improve the response and provide greater outcome benefits?
- Is a home-based exercise training intervention as effective as supervised training in-hospital intervention? Although home programmes may be cheaper and more convenient for the patient, to date, the evidence suggests that they may not be as effective with low adherence rates. Also, what are the social benefits of exercising in groups compared to home programmes?

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Adamsen 2009

Methods	**Study design:** two-arm randomised controlled trial **Methods of participant recruitment:** Quote: "The patients were approached and enrolled by research nurses or by physicians and nurses from eight treatment departments" **Aim of study:** Quote: "To investigate the effect of a six week supervised structured group intervention comprising high intensity physical training and low intensity training in an intervention group compared with a control group" **Start date of study:** March 2004 **End date of study:** March 2007 **Total study duration:** 3 years **Country:** Denmark **Sample size:** 270 **Duration of follow-up:** 6 weeks **Study funding source:** Quote: "This research was supported by grants from The Lundbeck Foundation, The Novo Nordic Foundation, The Egmont Foundation, The Danish Cancer Society, The Svend Andersen Foundation, The Aase and Ejnar Danielsen Foundation, The Beckett Foundation, The Wedell-Wedellsborg Foundation, The Hede Nielsen Family Foundation, The Gangsted Foundation, Copenhagen University Hospital. The authors' work was independent from the funders" **Declaration of conflict of interest:** none declared
Participants	**Included criteria:** Quote: "Participants were eligible if they had a diagnosis of cancer, had received at least one cycle of chemotherapy for advanced disease or as adjuvant treatment, had a WHO performance status of 0 or 1, and were aged 18-65 years" **Excluded criteria:** Quote: "Exclusion criteria were brain or bone metastases, thrombocytopenia (50×109/L), myocardial infarction within the past three months, or uncontrolled hypertension (diastolic pressure > 95 mm Hg)" **Total no randomised:** 269 **No. intervention group:** 135 **No. control group:** 134 **Baseline imbalances:** Quote: "the control and intervention groups were matched at baseline for demographic and medical characteristics" **Age (years):** Intervention: 47.2 ± 10.7; Control: 47.2 ± 10.6 **Gender:** 73 male and 196 female **Race/ethnicity:** not reported **Cancer type:** 21 different cancer diagnoses: 17 with solid tumours and 4 with malignant haematological diseases. Forty-eight per cent had evidence of disease **Cancer treatment:** Quote: "59 different chemotherapy regimens. The most frequent chemotherapy regimen included cyclophosphamide, epirubicin, and 5-fluorouracil and was administered to 49 patients in each group. Also frequent were 5-fluorouracil based regimens in patients with colorectal cancer (12 in the control group and 14 in the intervention group) and platinum based regimens in women with ovarian cancer (10 v 15) and in men with testicular cancer (eight v six). All other regimens were given to

	fewer than five patients and regimens were balanced between groups" **Attrition rate:** 12.7% No. intervention group assessed at follow-up time point: 6 weeks (118); No. control group assessed at follow-up time point: 6 weeks (117) **Reasons for withdrawal:** No. intervention group at week 6 (n = 17): never started (2), infections (7), bone marrow suppression (4), excluded (1), other health problems (3); No. control group at week 6 (n = 17): non-contactable (3), absent from test (8), infections (2), bone marrow suppression (4)
Interventions	**Intervention characteristics** Intervention • *Setting:* hospital-based • *Group/non-group based*: group-based • *Components of programme*: aerobic, strength, balance and coordination, relaxation • *Frequency*: 3 sessions/week x 6 weeks • *Intensity*: high and low intensity sessions High intensity: aerobic: 85%-95% maximum heart rate. Estimated intensity of 15 METs (3.75 MET hours per training session) Strength: 70%-100% 1RM, estimated intensity of 5.5 METs (4 MET hours per training session) Low intensity: (relaxation training and massage), estimated to have an intensity of 1 MET (total of 3 MET hours per week), while body awareness and restorative training were estimated to have an intensity of 2.5 METs (3.25 MET hours per week) • *Time*: High intensity: 90 mins Low intensity: 30 mins • *Type*: High intensity: aerobic: cycle ergometer; strength: 6 machines: leg press, chest press, pull-down, abdominal crunch, lower back, knee extension Low intensity: relaxation, body awareness and restorative training, and massage • *Monitoring during exercise*: heart rate (wireless heart rate transmitter). Quote: "The inclusion and exclusion criteria, the daily screening procedures, the presence of the clinical nurse specialist during training, and training phygmomanometer ensured the required level of safety". • *Support source*: Quote: "the participants could contact the project team directly; information was accessible on posters and pamphlets in the hospitals inpatient and outpatient departments". • *Adherence*: 70.8% • *Adverse events*: Quote: "Five participants with breast cancer had lymphoedema at baseline; none experienced exacerbations during the intervention. One participant with a brain tumour experienced a grade 3 seizure after cardiovascular training. This participant was admitted to the hospital, recovered within 3 hours, and was discharged the same day. The participant was subsequently excluded from the intervention".
Outcomes	*Aerobic fitness (VO_2 max)* • **Outcome type**: continuous • U**nit of measure**: L/min • **Direction**: higher is better

	Upper body muscle strength (chest press) • **Outcome type**: continuous • **Unit of measure**: kg • **Direction**: higher is better *Upper body muscle strength (pull-down)* • **Outcome type**: continuous • **Unit of measure**: kg • **Direction**: higher is better *Lower body muscle strength (leg press)* • **Outcome type**: continuous • **Unit of measure**: kg • **Direction**: higher is better *Physical activity (leisure time physical activity questionnaire)* • **Outcome type**: continuous • **Direction**: higher is better *HRQoL (EORTC QLQ-C30 subscales)* • **Outcome type**: continuous • **Scale:** 0-100 • **Direction**: higher is better *HRQoL (Medical Outcome Study (MOS) SF-36 subscales)* • **Outcome type**: continuous • **Scale:** 0-100 • **Direction**: higher is better *Fatigue (EORTC QLQ-C30)* • **Outcome type**: continuous • **Scale:** 0-100 • **Direction**: lower is better
Identification	**Setting:** Rigshospitalet and Herlev Hospital (Copenhagen University Hospitals) **Authors name:** Adamsen L **Institution:** University Hospitals Centre for Nursing and Care Research, Copenhagen University Hospital **Email:** la@ucsf.dk **Address:** University Hospitals Centre for Nursing and Care Research, Copenhagen University Hospital, DK-2100 Copenhagen, Denmark
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: Quote: "Randomisation was done by computer (Clinical Internet Trial Management System: CITMAS). The allocation sequence was executed by the clinical research unit and concealed from the project team"

Adamsen 2009 (*Continued*)

Allocation concealment (selection bias)	Low risk	Judgement comment: Quote: "The allocation sequence was executed by the clinical research unit and concealed from the project team"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: Quote: "The data were collected by a physiotherapist and a trained nurse specialist, who also conducted the daily training sessions. Data were anonymised by use of an identification code; administrative data were kept in a separate database. Blinding the participants to group assignment was not possible"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: Quote: "Outcome measures were keyed in and analysed by research assistants who were not involved with the participants"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: consented: 269, completed: 235. Consort provided (attrition 12.7%)
Selective reporting (reporting bias)	Low risk	Judgement comment: All outcomes listed in methods were reported sequentially in the results section
Other bias	High risk	Judgement comment: Various cancer treatments were included and 52% of participants did not have cancer which makes results difficult to interpret

Battaglini 2007

Methods	**Study design:** two-arm randomised controlled trial **Methods of participant recruitment:** Quote: "All the subjects were recruited from the northern Colorado region through oncology practices between January 2001 and April 2003. Patients were screened for participation based upon a physician's review of the patient's medical history and a physical examination" **Aim of study:** Quote: "The main purpose of this study was to assess the effects of an individualized exercise intervention emphasizing resistance training, on changes in body composition and muscle strength in breast cancer patients during treatment" **Start date of study:** January 2001 **End date of study:** April 2003 **Total study duration:** 27 months **Country:** United States **Sample size**: 20 **Duration of follow-up:** 15 weeks **Study funding source:** Quote: "University of Northern Colorado, Sponsored Programs and Academic Research Center" **Declaration of conflict of interest:** none declared
Participants	**Included criteria:** Quote: "recently been diagnosed with breast cancer, and designated for surgery and chemotherapy treatment" **Excluded criteria:** Quote: "The criteria for non-participation in the study included the presence of cardiovascular disease; acute or chronic respiratory disease; acute or chronic bone, joint or muscle abnormalities (unless these diseases would not compromise the patient's ability to participate in the exercise rehabilitation program); metastatic disease; and immune deficiency" **Baseline imbalances:** not reported **No. recruited:** 20 **Total no. intervention group:** 10 **Total no. control group:** 10 **Age (years):** Intervention: 57.5 ± 23 Control: 56.6 ± 16 **Gender:** female **Race/ethnicity:** not reported **Cancer type:** breast cancer **Cancer treatment:** adjuvant chemotherapy **Attrition rate:** 100% No. intervention group assessed at follow-up time point: 15 weeks (10); No. control group assessed at follow-up time point: 15 weeks (10) **Reasons for withdrawal:** N/A
Interventions	**Intervention characteristics** • *Setting:* rehabilitation centre • *Group/non-group based*: not reported • *Frequency*: 2 sessions/week x 15 weeks • *Intensity:* Aerobic: not clear. Quote: "Each of the individualized exercise prescriptions was based on the results from the fitness assessment administered at the beginning of the study". Resistance: not clear. Quote: "For the resistance exercise portion of the exercise protocol, the intensities of the exercises were determined according to the results obtained in the first fitness assessment".

	• *Time*: warm-up: approximately 6-12 minutes, whole-body stretching sessions (5-10 minutes), resistance training (15-30 minutes), cool-down: approximately 8 minutes. • *Type*: aerobic: treadmill/cycle ergometer/elliptical equipment; resistance training: Quote: "eight to twelve different types of resistance exercises emphasizing all the major muscle groups were utilized. All the resistance exercises were performed using weight training machines, free weights (hand dumbbells), elastic bands, and/or therapeutic balls. The resistance exercises that were assigned to the exercise group included: lateral and frontal raises, horizontal chest press, lateral pull down, alternating biceps curls with dumbbells, triceps extension, leg press, leg extension, leg curl, standing calf raises and three different types of abdominal exercises (forward crunches, oblique crunches, and lower abdominal crunches)". • *Monitoring during exercise*: Heart rate. Quote: "Each patient wore an A3 Polar heart rate monitor (Lake Success, New York) to determine resting heart rate and to monitor heart rate responses during cardiovascular assessments, as well as for controlling intensities during exercise sessions". • *Support source*: not reported (may not be applicable due to the nature of the supervised programme) • *Adherence*: 100% • *Adverse events*: safety was not reported
Outcomes	*Aerobic fitness (VO_2 max)* • **Outcome type**: continuous • **Unit of measure**: L/min • **Direction**: higher is better *Upper body muscle strength (1 repetition maximum)* • **Outcome type**: continuous • **Unit of measure**: kg • **Direction**: higher is better
Identification	**Setting:** Campus Recreation Centre and Rocky Mountain Cancer Rehabilitation Institute of the University of Northern Colorado, and the North Colorado Medical Centre (Northern Colorado region) **Authors name:** Battaglio C **Institution:** Rocky Mountain Cancer Rehabilitation Institute of the University of Northern Colorado, in Greeley, Colorado **Email:** claudio@email.unc.edu **Address:** Department of Exercise and Sport Science, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment:: "The randomization procedure involved the drawing of numbers by the patients, which ranged from 1 to 20. Subjects who drew even

Battaglini 2007 (*Continued*)

		numbers were placed into the experimental group while subjects who drew odd numbers were placed into the control group"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: not possible due to nature on intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment:: "the adherence rate among all the subjects was 100%"
Selective reporting (reporting bias)	High risk	Judgement comment: Data for cardiovascular endurance were not reported
Other bias	High risk	Judgement comment: Time points of assessments included pre-surgery and post adjuvant cancer treatment only (start of adjuvant cancer treatment was not reported) therefore interpretation of findings are difficult

Chandwani 2014

Methods	**Study design:** three-arm randomised controlled trial (only 1 intervention and control arm were reported in this systematic review) **Methods of participant recruitment:** Quote: "Eligible patients were identified through an institutional database or by referring physicians and were approached at their simulation appointment" **Aim of study:** Quote: "To investigate the effects of yoga on quality of life in people with breast cancer" **Start date of study:** Sept 2006 **End date of study:** August 2009 **Total study duration:** 35 months **Country:** United States **Sample size:** 150 **Duration of follow-up:** 6 weeks **Study funding source:** not reported **Declaration of conflict of interest:** none declared
Participants	**Included criteria:** Quote: "Inclusion criteria were 18 years old or older; ability to read, write, and speak English; and scheduled to undergo daily adjuvant XRT for 6 weeks at MD Anderson Cancer Center" **Excluded criteria:** Quote: "Patients with lymphedema; metastatic bone disease; deep

	vein thrombosis; documented diagnosis of a formal thought disorder (e.g. schizophrenia) ; extreme mobility problems; or who had practiced YG in the year before diagnosis were excluded" **Baseline imbalances:** Quote: "All groups were similar in baseline demographic, medical, self-report measures (except for SF-36 GH), and cortisol slopes" **Total no. randomised:** 178 **No. intervention group:** 53 **No. control group:** 54 **Age (years):** Intervention group: 52.4 ± 1.4 Control group: 52.1 ± 1.3 **Gender:** female **Cancer type:** breast cancer stage 0-III **Cancer treatment:** adjuvant radiotherapy **Race/ethnicity:** Intervention group 1: black/African American (9); white (32); Latino/Hispanic/Mexican (4); Asian/Pacific Islander (2); other (0); Control group: black/African American (7); white (37); Latino/Hispanic/Mexican (5); Asian/Pacific Islander (1); other (2) **Attrition rate:** 30.9% No. intervention group assessed at follow-up time point: post-treatment (39) No. control group assessed at follow-up time point: post-treatment (43) **Reasons for withdrawal:** 13 dropped out before and 15 after randomisation in Intervention groups (reasons not provided)
Interventions	**Intervention characteristics** Intervention • *Setting:* hospital-based (large conference style rooms near the radiation treatment) • *Group/non-group based*: one-to-one (given before or after radiotherapy to accommodate participants' schedules) • *Frequency*: 3 sessions/week • *Intensity*: light intensity (restorative yoga) • *Time*: 60 mins • *Type*: (1) preparatory warm-up synchronized with breathing; (2) selected postures, or asana (forward-, backward-, and side-bending in sitting and standing position, cobra posture, crocodile, and half-shoulder-stand with support); (3) deep relaxation (supine posture); (4) alternate-nostril breathing, or pranayama; and (5) meditation • *Monitoring during exercise*: not reported • *Support source*: not reported • *Adherence*: 87% • *Adverse events*: not reported
Outcomes	*HRQoL (SF-36)* • **Outcome type**: continuous • **Scale:** 0-100 • **Direction**: higher is better *Fatigue (Brief fatigue inventory (BFI)* • **Outcome type**: continuous • **Scale:** 0-10

	• **Direction**: lower is better
Identification	**Setting:** MD Anderson Cancer Centre. **Authors name:** Lorenzo Cohen **Institution:** Integrative Medicine Program, The University of Texas MD Anderson Cancer Center, Department of Integrative Medicine **Email:** lcohen@mdanderson.org **Address:** Integrative Medicine Program, The University of Texas MD Anderson Cancer Center, Department of Integrative Medicine, 1515 Holcombe Blvd,Unit 460, Houston, TX 77030
Notes	Note: Stretching group was not included into this review as it did not meet the inclusion criteria as an exercise intervention Quote: "Participants were given a gift certificate ($20 value) after each assessment completion" Some data were taken from a separate publication linked to this study: reference: Ratcliff CG, Milbury K, Chandwani KD, Chaoul A, Perkins G, Nagarathna et al. Examining mediators and moderators of yoga for women with breast cancer undergoing radiotherapy. Research Articles, 2016: 1-13

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Judgement comment: unclear. Quote: "Participants were then randomly assigned to one of three groups: 1) YG; 2) ST; or WL control by using a form of adaptive randomization,according to age, stage of disease, time since diagnosis, type of surgery, and chemotherapy (neoadjuvant or adjuvant)"
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: not possible due to the nature of the intervention
Blinding of outcome assessment (detection bias) All outcomes	High risk	Judgement comment: author email correspondence: "for questionnaires, patients would sometimes reveal their group"
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: consented 191; completed 132. Consort provided (attrition 30.9%)
Selective reporting (reporting bias)	Low risk	Judgement comment: all prespecified outcomes were reported accordingly

Chandwani 2014 (*Continued*)

Other bias	Low risk	Judgement comment: none identified

Choi 2012

Methods	**Study design:** two-arm randomised controlled trial **Methods of recruitment of participants:** not reported in translated script **Aim of study:** to evaluate the effect of a home-based exercise program for randomly-assigned stomach cancer patients receiving oral chemotherapy after surgery **Start date of study:** September 2007 **End date of study:** June 2008 **Total study duration:** 10 months **Country:** Korea **Sample size:** 28 **Duration of follow-up:** 8 weeks **Study funding source:** not reported **Declaration of conflict of interest:** not reported
Participants	**Included criteria:** Quote: "1. Patients diagnosed with gastric cancer (Ib, II, III) receiving oral chemotherapy following surgery; 2. ECOG (Eastern Cooperative Oncology Group) Performance score ranging from 0-23.The following detected through complete blood count (CBC): haemoglobin count of more than 10g/dL, leukocyte count more than 2000/mm; 3 (Absolute Neutrophil Count (ANC) > 1000), platelet count of more than 100,000m^3; 4. Patients aged over 20 years capable of filling out a questionnaire; 5. Patients capable of understanding the purpose of the study and able to give written consent" **Excluded criteria:** Quote: "Patients who do not consume drugs that affect the immune system; Patients who do not have acute or chronic pain that could interfere with physical activity" **Baseline imbalances:** not reported **Total no. randomised:** 28 **No. intervention group:** 14 **No. control group:** 14 **Age (years):** Intervention: < 50 (n = 3); 51-60 (n = 4); > 61 (n = 4) Control: < 50 (n = 0); 51-60 (n = 4); > 61 (n = 9) **Gender:** male and female Intervention: male (n = 5); women (n = 6) Control: male (n = 9); women (n = 4) **Race/ethnicity:** not reported **Cancer type:** stomach cancer **Cancer treatment:** oral chemotherapy **Attrition rate:** 14.8% Intervention: 11/14 Control: 12/14 **Reason for withdrawal:** Intervention (n = 3): rejected the treatment (1), rejected the intervention (1), cancer metastasis (1) Control (n = 1) (cancer metastasis)

Interventions	**Intervention characteristics** • *Setting*: home-based • *Group/non group-based*: non-group based • *Components of programme*: aerobic • *Frequency*: more than 3 times/week x 8 weeks • *Intensity*: moderate intensity • *Time*: 60 minutes: 5 minutes of warming up, 45 minutes of exercise, and 10 minutes of cool down • *Type*: walking • *Monitoring during exercise*: self-monitoring diary and pedometer. Patients were provided a pedometer to use for the self-monitored diary records and were instructed to wear it on one's waistband while exercising. • *Source of support*: Quote: "A telephone conversation was conducted once a week for approximately 5 to 10 minutes for 8 weeks. A short message service (SMS) message for exercise reinforcement was sent once every week to each patients' cell phone for a total of 8 weeks, which consisted of a text message of less than 40 characters. • *Adherence*: Quote: "3.8 exercises per week, the average number of steps measured by the pedometer was 6050." • *Adverse events*: not reported
Outcomes	*Health related quality of life (tool not described)* • **Outcome type**: continuous • **Scale:** 14-70 • **Direction**: higher is better *Fatigue (Schwarts Cancer Fatigue Scale (SCFS-6)* • **Outcome type**: continuous • **Scale:** 6-30 • **Direction**: lower is better
Identification	**Setting:** Medical Centre, Seoul City **Comments:** this article was translated by Heather Swan **Authors name:** Jin Yi Choi **Institution:** College of Nursing Science, Kyung Hee University, Seoul, Korea **Email:** hyunsuk@khu.ac.kr **Address:** College of Nursing Science, Kyung Hee University, Seoul, Korea
Notes	Quote: "The exercise program was developed based on the research of Winningham, Glass and MacVicar (1990) and the walking information of the Korea Athletic Promotion Association (2007). The program was modified and supplemented according to the advice of exercise experts. In order to improve the validity of the home exercise programs developed by the researchers, the opinions of three cancer rehabilitation and exercise experts were obtained and confirmed following each exercise, patients were instructed to record the number of steps, exercise duration and how they felt in the self-monitored diary, in addition to the date and time and self-reported fatigue. The outpatient clinic provided a home exercise program booklet prepared for participants in the experimental group. Participants were also individually educated for 20 to 30 minutes"
Risk of bias	

Choi 2012 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Judgement comment: Quote: "Due to the ease of data collection, participants were selected on the basis of accessibility through convenient sampling"
Allocation concealment (selection bias)	High risk	Judgement comment: Quote: Patients were randomly assigned to the experiment or control group by the researcher picking up one of two folded papers with either the number '1' or '2' printed on it. As a result, the number 1 was assigned to the experimental group, and the number 2 was assigned to the control group. The number of subjects was not the same for the purposes of this study and so it was not possible to calculate the magnitude of effects. Additionally, due to the nature of the cancer, there is a limit to the accessibility, unlike with more common illnesses"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: not possible due to the nature of the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: consented 27; completed 23 (attrition (14.8%) Judgement comment: There was no consort provided but data were provided. Quote: "During the 10-month data collection period, 3 of the 14 participants in the experiment group were excluded (1 rejected the treatment, 1 rejected the intervention, and 1 had cancer metastasis) and 1 of the participants from the control group was excluded (cancer metastasis). Ultimately, the experimental group had 11 participants, and the control groups had 13"
Selective reporting (reporting bias)	Low risk	Judgement comment: All outcome measures were clearly described and reported

Choi 2012 (*Continued*)

Other bias	High risk	Judgement comment: The measure of HRQoL reported was not clearly stated. Although reference was made about the measure within the study to two other studies, the references are an unpublished doctoral dissertation and a master's thesis

Haines 2010

Methods	**Study design:** two-arm randomised controlled trial **Methods of recruitment of participants:** Quote: "Potential participants were identified at their 2-week post surgery Breast Clinic appointments or when booked in for radiation therapy 'planning'" **Aim of study:** Quote: "aimed to evaluate the efficacy and economic efficiency of a multimedia, multimodal exercise program for the enhancement of health related quality of life amongst women with breast cancer undergoing adjuvant therapy following surgery for breast cancer" **Start date of study:** May 2006 **End date of study:** September 2007 **Total study duration:** 16 months **Country:** Australia **Sample size:** 89 **Duation of follow-up:** 12 months **Study funding source:** Quote: "This study was funded by a project grant from the Princess Alexandra Hospital Cancer Collaborative Group. Associate Professor Terry P Haines is supported by a National Health and Medical" **Declaration of conflict of interest:** none declared
Participants	**Included criteria:** Quote: "Participants in this study were women with newly diagnosed breast cancer undergoing adjuvant therapy (radiation therapy, chemotherapy and hormonal therapy) following surgery" **Excluded criteria:** Quote: "Exclusion criteria were severe cardiac disease, uncontrolled hypertension or orthopaedic injury precluding participation in an exercise program" **Baseline imbalances:** yes, as presented in baseline characteristics table **Total no. randomised:** 89 **No. intervention group:** 46 **No. control group:** 43 **Age (years):** Intervention group: 55.9 ± 10.5 Control group: 54.2 ± 11.5 **Gender:** female **Race/ethnicity:** not reported **Cancer type:** breast cancer (staging not provided) **Cancer treatment:** adjuvant treatment (prescription not provided) **Attrition rate:** 18% No. intervention group assessed at follow-up time point: 12 months (37) No. control group assessed at follow-up time point: 12 months (36) **Reasons for withdrawal:** not reported

Interventions	**Intervention characteristics** • *Setting*: home-based • *Group/non-group based*: alone • *Duration of programme*: 12 months • *Frequency*: Number of sessions per week were not described. • *Intensity*: not clear. Quote: "Strategies of progression were recommended to make exercises harder every 2-4 weeks particularly if muscles were not feeling tired after completing the second set of exercises (for strength exercises), If the minimum number of repetitions within a set could not be completed, then the participants were recommended to try an easier version of that exercise. Participants were recommended to complete one set of each exercise, then complete a second set so that specific muscle groups could rest between sets". • *Time*: Aerobic (20 min); balance/strength/mobility (36 min) varied between: 5-15 repetitions x 2/3 sets. • *Type*: Aerobic (walking) and balance/strength/mobility (lunges, bicep curls, wall push-ups, standing hip abduction, seated rows with resistance tubing, sit to stand with emphasis on eccentric control of stand to sit, overhead press, heel raises, shoulder mobility/rolling orange in large circles on kitchen tables, four quadrant step test) • *Monitoring during exercise*: not reported • *Support source*: phone call from member of research team • *Adherence*: Adherence was reported as number of sessions. At 3 months: median (IQR) sessions: strength and balance 32 (19, 39) and endurance 22 (16.5, 34); at 6 months median (IQR) strength/balance 12 (6.25, 37) and endurance 13 (2.75, 27.25). • *Adverse events*: Quote: "There were nine participants who reported musculoskeletal pain in their adverse event logs (three control, six intervention: odds ratio (95% CI): 2.39 (0.58, 89.92), P = 0.23), three of which reported pain whilst performing exercises as a part of the intervention program and one as a part of the control program. Participants ceased performing the provoking exercise in each case. There were eight fallers (one fall each) during the study period (five control, three intervention: odds ratio (95% CI): 0.58 (0.14, 2.42), P = 0.48), one of which resulted from an intervention group participant tripping on a tree stump whilst undertaking the walking program". Usual care control group • *Setting*: home-based • *Supervision*: unsupervised • *Group/non-group based*: alone • *Components of programme*: flexibility and relaxation • *Frequency*: number of sessions in 12-month period not clear • *Intensity*: not clear • *Time*: flexibility: 30s x 3 repetitions, relaxation: 10 min • *Type*: flexibility: static stretching, quadriceps, gastrocnemius, biceps, triceps, trapezius, pectoralis major; relaxation: supine relaxation program following the Feldenkrais method • *Monitoring during exercise*: not reported • *Support source*: phone call from member of research team • *Adherence*: Adherence was reported as number of sessions. At 3-months: median (IQR) sessions: flexibility 30.5 (18.75, 36) and relaxation 28.5 (13.25, 36). At 6-

	months median (IQR) flexibility 22.5 (7, 36.5) and relaxation 18 (1.5, 33.5). • *Adverse events*: There were nine participants who reported musculoskeletal pain in their adverse event logs (three control, six intervention: odds ratio (95% CI): 2.39 (0. 58, 89.92), P = 0.23), three of which reported pain whilst performing.
Outcomes	*Aerobic fitness (step test - steps in 15 secs)* • **Outcome type**: continuous • **Direction**: higher is better *Aerobic fitness (6-minute walk test)* • **Outcome type**: continuous • **Unit of measure**: metres • **Direction**: higher is better *Upper body muscle strength (grip strength)* • **Outcome type**: continuous • **Unit of measure**: kg • **Direction**: higher is better *Upper body muscle strength (leg press)* • **Outcome type**: continuous • **Unit of measure**: kg • **Direction**: higher is better *HRQoL (EQ-5D visual analogue scale (VAS)* • **Outcome type**: continuous • **Scale**: 0-100 • **Direction**: higher is better *HRQoL (EQ-5D Utility)* • **Outcome type**: continuous • **Scale:** 0.59-1 • **Direction**: higher is better HRQoL (EORTC subscales) • **Outcome type**: continuous • **Scale:** 0-100 • **Direction**: higher is better *Fatigue (multidimensional fatigue inventory (MFI)* • **Outcome type**: continuous • **Scale**: 0-20 • **Direction**: lower is better *Fatigue (EORTC*) • **Outcome type**: continuous • **Scale**: 0-100 • **Direction**: lower is better
Identification	**Setting:** Quote: "The Princess Alexandra Hospital: provides cancer services to residents on the south side of Brisbane extending down to the Gold Coast region in Queensland, Australia" **Authors name:** T. P. Haines **Institution:** Allied Health Clinical Research Unit, Kingston Centre **Email:** terrence.haines@med.monash.edu.au **Address:** Allied Health Clinical Research Unit, Kingston Centre,Southern Health, Cheltenham, Victoria 3192, Australia

Notes	Interventional notes as follows: Quote: "Participants allocated to the home-based strength, balance, shoulder mobility and cardiovascular endurance program received a multimedia instructional package along with equipment to facilitate the completion of the program. Participants were provided with pedometers and water weights (3 kg capacity) 6 pieces of rubber band (2 pieces x 3 resistance grades) and 2 re-usable shopping bags (one of which acted as the program materials bag" Quote: "The DVD included general safety precautions related to exercise, health advice related to the post-surgical period, a description of how to use the materials that had been provided with the program, a description of how to perform and progress each exercise in the program and a description of how to record data in log books related to adherence, adverse events and use of health care resources" Usual care control note as follows: Quote: "An active (sham intervention) control condition was employed consisting of flexibility and relaxation activities. Previous studies have highlighted problems of increased activity levels amongst women with breast cancer allocated to 'usual activity' control groups. This potential bias was addressed by providing patients in the control group with what looked like an exercise program with an equivalent amount of supporting material. The video material was of similar content to that in the intervention program (though the actual exercises described differed). There was no progression of activities performed in this condition"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: Quote: "Participants were randomised to intervention or control groups using a computer-generated randomization sequence that was entered into numbered, opaque, sealed envelopes by a study investigator (TH)"
Allocation concealment (selection bias)	Low risk	Judgement comment: Quote: "Participants were randomised to intervention or control groups using a computer-generated randomization sequence that was entered into numbered, opaque, sealed envelopes by a study investigator (TH)"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: not possible due to nature of intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: Quote: "A 12-month telephone follow-up assessment was also completed by researchers blinded to participant group allocation using a tele-

		phone version of the EQ-5D with VAS instrument, whilst also enquiring of sustained adherence to the allocated intervention"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: recruited: 89; follow-up: 73. Consort provided (attrition 18%)
Selective reporting (reporting bias)	Low risk	Judgement comment: All outcome measures were reported.
Other bias	High risk	Judgement comment: 1. This exercise intervention was reported as a 12-month intervention. However all measures except EQ-5D were reported at 6 months while EQ-5D was reported at 12 months over the telephone. Quote: "Face-to-face follow-up assessments coincided with follow-up appointments at the Breast Clinic at 3 and 6 months. A 12-month telephone follow-up assessment was also completed by researchers blinded to participant group allocation using a telephone version of the EQ-5D with VAS instrument, whilst also enquiring of sustained adherence to the allocated intervention" 2. The control group was a sham group. Quote: "The final limitation was that the sham intervention may have had some beneficial effects. This combined with the previous limitation would lead the authors to consider that the estimates of intervention efficacy established through this trial are likely to be conservative"

Husebo 2014

Methods	**Study design:** two-arm randomised controlled trial **Methods of participant recruitment:** not reported **Aim of study:** Quote: "To investigate the effects of a scheduled home-based exercise intervention in breast cancer patients during adjuvant chemotherapy, on cancer-related fatigue, physical fitness, and activity level" **Start date of study:** 2010 **End date of study:** 2012 **Total study duration:** 2 years **Country:** Norway **Sample size:** 60 **Duration of follow-up:** 18 to 24 weeks **Study funding source:** A PhD scholarship was funded by governmental funds allocated to the University of Stavanger **Declarations of conflict of interest:** none declared
Participants	**Included criteria:** Quote: "Eligible breast cancer patients were between 18 and 70 years of age, surgically treated for early stage breast cancer (mastectomy or lumpectomy), and allocated to adjuvant chemotherapy according to the national treatment guidelines of the Norwegian Breast Cancer Group. The included patients had to be able to read, write, and speak Norwegian, and they were approved for participation in this study by a clinical oncologist" **Excluded criteria:** not reported **Baseline imbalances:** no differences reported on demographics and characteristics of study population table **Total no. randomised:** 67 **No. intervention group:** 33 **No. control group:** 34 **Age (years):** Intervention: 50.8 ± 9.7 Control: 53.6 ± 8.8 **Gender:** female **Race/ethnicity:** intervention: Norwegian: 27; other: 5; missing: 1; control: Norwegian: 30; Other: 4; Missing: 0 **Cancer type:** breast cancer stage I or II **Cancer treatment:** chemotherapy (n = 33), other systemic treatment (n = 56) and radiotherapy (n = 48) **Attrition rate:** 29.9% No. intervention group assessed at follow-up time point: completion of chemotherapy (18-24 weeks) (29) No. control group assessed at follow-up time point: completion of chemotherapy (18-24 weeks) (31) **Reasons for withdrawal:** Due to Norwegian Research Ethics Legislation, study participants were not obligated to give a reason for withdrawal, and the researchers were not allowed to ask
Interventions	**Intervention characteristics** • *Setting*: home-based • *Group/non-group based*: alone • *Frequency*: aerobic: daily, strength: 3 sessions/week • *Intensity*: aerobic: moderate, strength: 1-3 sets for 20 repetitions

	• *Time*: aerobic: 30 mins (could be split into 10 mins periods), strength: not reported • *Type*: aerobic: walking, strength: resistance bands for arms and legs/strength training for the upper body • *Monitoring during exercise*: Quote: "The women in the intervention group were supported and encouraged in their exercise by motivational telephone calls from the research team every second week. The telephone calls were also used to monitor adverse events. The women in the control group were encouraged to remain on their regular activity level and received one follow-up call during the intervention time period". • *Support source*: phone call from member of research team • *Adherence*: aerobic: 17% to the trial prescription; resistance: 15% • *Adverse events*: Quote: "One participant in the intervention group reported knee discomfort and was referred to her primary physician for further evaluation. The patient stayed in the trial and completed the exercise prescription. Another participant in the intervention group experienced syncope during the walking exercise. This was related to a secondary chronic condition, and the patient was advised by her oncologist to withdraw from the trial".
Outcomes	*Aerobic fitness (6-minute walk test)* • **Outcome type**: continuous • **Unit of measure**: metres • **Direction**: higher is better *Physical activity (International physical activity questionnaire)* • **Outcome type**: continuous • **Unit of measure**: met-minute/week • **Direction**: higher is better *Fatigue (Schwarts Cancer Fatigue Scale (SCFS-6)* • **Outcome type**: continuous • **Scale:** 6-30 • **Direction**: lower is better
Identification	**Setting:** University Hospital Norway **Authors name:** Husebo AL **Institution:** University of Stavanger **Email:** anne-marie.l.husebo@uis.no **Address:** Department of Health Studies, Univeristy of Stavanger, 4036 Stavanger, Norway
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: Quote: "The random assignment of subjects to the intervention group or to the control group was carried out by the use of concealed envelopes, drawn by the research assistant prior to the

Husebo 2014 (*Continued*)

		first data collection"
Allocation concealment (selection bias)	Low risk	Judgement comment: Quote: "The random assignment of subjects to the intervention group or to the control group was carried out by the use of concealed envelopes"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: not possible due to the nature of the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: consented 67, completed 53. Consort provided (attrition 29.9%)
Selective reporting (reporting bias)	Low risk	Judgement comment: All outcome measures were reported.
Other bias	Low risk	Judgement comment: none identified

Hwang 2008

Methods	**Study design:** randomised controlled trial **Methods of participant recruitment:** Quote: "consecutive unselected women on the outpatient waiting list for radiotherapy for breast cancer approached at their first planned visit" **Aim of study:** Quote: "to determine whether supervised and structured moderate-intensity exercise during radiotherapy would offer some benefit to breast cancer patients by improving QOL and shoulder mobility and reduce levels of fatigue and pain" **Start date of study:** not reported **End date of study:** not reported **Total study duration:** not reported **Country:** Korea **Sample size:** 40 **Duration of follow-up:** 5 weeks **Study funding source:** not reported **Declaration of conflict of interest:** not reported
Participants	**Included criteria:** Quote: "consecutive unselected women on the outpatient waiting list for radiotherapy for breast cancer" **Excluded criteria:** Quote: "The exclusion criteria included concurrent major health problems that could affect their participation in an exercise program, including uncontrolled hypertension, cardiovascular disease, acute or chronic respiratory disease, and cognitive dysfunction" **Baseline imbalances:** Quote: "There were no significant differences in all of the outcome

	measures at the baseline between groups" **Total no. randomised:** 40 **No. intervention group:** 17 **No. control group:** 20 **Age (years):** Intervention: 46.3 ± 7.5; Control: 46.3 ± 9.5 **Gender:** female **Race/ethnicity:** not reported **Cancer type:** breast cancer **Cancer treatment:** adjuvant radiotherapy. Quote: "Patients were irradiated with a dose of 50 Gy during 5 weeks with a dose per fraction of 2 Gy" **Attrition rate:** 7.5% No. intervention group assessed at follow-up time point: 5 weeks (17) No. control group assessed at follow-up time point: 5 weeks (20) **Reasons for withdrawal:** Intervention (n = 0) Control (n = 3) as they did not want to participate in follow-up assessment
Interventions	**Intervention characteristics** • *Setting*: not clear (supervised) • *Group/non-group based*: not reported • *Frequency*: 3 sessions/week • *Intensity*: aerobic: 50%-70% age-adjusted heart rate maximum • *Time*: 50 min (10-min warm up, 30-min exercise (including stretching exercises focused on shoulders, aerobic exercise such as treadmill walking and bicycling, and strengthening exercise) and 10-min cool down (relaxation period) • *Type*: aerobic: treadmill and bicycling, strength: not reported • *Monitoring during exercise*: not reported • *Support source*: not reported • *Adherence*: not reported • *Adverse events*: Quote: "No significant exercise-related adverse events such as lymphedema were reported".
Outcomes	*HRQoL (World Health Organisation quality of life (WHOQOL) overall quality of life subscale)* • **Outcome type**: continuous • **Scale:** 1-5 • **Direction**: higher is better *HRQoL (WHOQOL overall health subscale)* • **Outcome type**: continuous • **Scale:** 1-5 • **Direction**: higher is better *HRQoL (World Health Organisation quality of life (WHOQOL) physical subscale)* • **Outcome type**: continuous • **Scale:** 4-20 • **Direction**: higher is better *HRQoL (WHOQOL psychological subscale)* • **Outcome type**: continuous

	• **Scale:** 4-20 • **Direction**: higher is better *HRQoL (WHOQOL social subscale)* • **Outcome type**: continuous • **Scale:** 4-20 • **Direction**: higher is better *HRQoL (WHOQOL environmental subscale)* • **Outcome type**: continuous • **Scale:** 4-20 • **Direction**: higher is better *Fatigue (Brief fatigue inventory (BFI))* • **Outcome type**: continuous • Scale: 0-10 • **Direction**: lower is better
Identification	**Setting:** not reported **Authors name:** Dr. Hyun Jung Chang **Institution:** Department of Physical Medicine Rehabilitation, Samsung Medical Center **Email:** reh.chj@gmail.com **Address:** Department of Physical Medicine Rehabilitation, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Ilwon-dong,Gangnam-gu, Seoul 135-710, Korea
Notes	Control group were shown how to perform shoulder ROM exercises and were encouraged to continue normal activities

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement comment: not reported
Allocation concealment (selection bias)	Unclear risk	Judgement comment: not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: not possible due to nature of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: consented 40, complete 37 (attrition 7.5%) Consort not provided, but numbers were clearly stated. Quote: "Forty participants were recruited and randomly assigned to either an exercise or control group. Three

Hwang 2008 (*Continued*)

		patients in the control group were lost during follow-up because they did not want to participate in follow-up measurements. Finally, 37 patients completed the follow-up assessment (17 in the exercise group, 20 in the control group)"
Selective reporting (reporting bias)	Unclear risk	Judgement comment: results are not clearly described according to primary/secondary
Other bias	Low risk	Judgement comment: none identified

May 2017

Methods	**Study design:** two-arm randomised controlled trial **Methods of participant recruitment:** Participants were invited by their clinician or oncological nurse during a regular outpatient clinic visit. Quote: "Breast cancer patients willing to participate were asked to visit the study centre to confirm eligibility and sign informed consent" **Aim of study:** Quote: "To assess the cost-effectiveness of the 18 week physical activity during cancer treatment (PACT) intervention for patients with breast and colon cancer. The PACT trial showed beneficial effects for fatigue and physical fitness" **Start date of study:** 2010 **End date of study:** 2013 **Total duration of study:** 3 years **Country:** Netherlands **Sample size:** 150 **Duration of follow-up:** 18 weeks **Study funding source:** Quote: This work was supported by The Netherlands Organisation for Health Research and Development (ZonMw, project number: 171 002 202), the Dutch Cancer Society (KWF Kankerbestrijding, project number: UU 2009-4473) and the Dutch Pink Ribbon Foundation (2011.WO02.C100). All grants are unrestricted" **Declarations of conflict of interest:** none declared Reference of a separate article published on this trial (data of which are reported here) . Reference: Travier N, Velthuis MJ, Steins Bisschop, Van den Buijis B, Monninkhof EM, Backx F, et al. Effects of an 18-week exercise programme started early during breast cancer treatment: a randomised controlled trial. BMC Medicine 2015; 13: 121
Participants	**Included criteria:** Quote: "The inclusion criteria were a definitive full histological breast cancer diagnosis < 6 weeks before recruitment; stage M0 (i.e., no distant metastasis); scheduled for chemotherapy (as part of the treatment regimen); aged 25 to 75 years; not treated for any cancer in the preceding 5 years (except basal skin cancer); able to read and understand the Dutch language; Karnovsky Performance Status of ≥ 60; and no contraindications for physical activity. Inclusion was irrespective of the patients' current physical activity level" **Excluded criteria:** not reported **Total no. randomised:** 204 **Total no. intervention group:** 102

	Total no. control group: 102 **Age (years):** Intervention: breast: 50.0 ± 7.9, colon: 49.4 ± 7.6; Control: breast: 49.4 ± 7.6, colon 59.1 ± 8.9 **Gender:** intervention (breast: 87 female; colon: 7 male and 7 female); control (breast: 78 female; colon: 11 male and 4 female) **Race/ethnicity:** not reported **Cancer type:** breast and colon **Cancer treatment:** adjuvant chemotherapy and radiotherapy. Quote: "Neo-adjuvant chemotherapy was still rare, and was used in less than 5% of PACT participants" Intervention: breast (60 radiotherapy and 54 chemotherapy); colon (1 radiotherapy and 14 chemotherapy) Control: breast (52 radiotherapy and 53 chemotherapy); colon (1 radiotherapy and 15 chemotherapy) **Attrition rate:** 19.6% No. intervention group assessed at follow-up time point: 20 weeks (101) No. control group assessed at follow-up time point: 20 weeks (93) **Reasons for withdrawal:** Intervention (n = 13): logistic reasons 1, disappointment because of randomisation 2, mental burden 4, unknown 6 Control (n = 9): medical reasons 3, mental burden 3, problems with travelling 1, died 1, unknown reason 1
Interventions	**Intervention characteristics** • *Setting*: hospital-based • *Group/non-group based*: one-to-one • *Components of programme*: aerobic and strength (upper/lower) • *Frequency*: 2/week • *Intensity*: Aerobic: interval (alternating intensity performed with heart rate at (3x2 min increasing to 2x7 min) or below (3x4 min decreasing to 1x7min) ventilatory threshold. Strength: 2x10 (65% one-repetition maximum) and gradually increased to reach 1x10 repetitions (75 one-repetition maximum) and 1x20 repetitions (45% one-repetition maximum) by end of programme. • *Time*: 60 min (5 min warm-up, 25 min each of aerobic and muscle strength training, 5 min cool down) • *Type*: patient preference (types not reported) • *Monitoring during exercise*: heart rate (method not reported) and RPE scale • *Support source:* Quote: "The Netherlands Organisation for Health Research and Development (ZonMw, project number: 171002202), the Dutch Cancer Society (KWF Kankerbestrijding, Project number: UU 2009-4473), and the Dutch Pink Ribbon Foundation (2011.WO02.C100). The contribution of N Travier was supported by the Spanish Ministry of Health (Instituto de Salud Carlos III RTICC RD06/0020/0091 and RD12/0036/0018)". • *Adherence*: 83% • *Adverse events*: No serious adverse events related to exercise were observed during the study period.
Outcomes	Aerobic fitness (cardiopulmonary exercise test (CPET) on a cycle ergometer) • **Outcome type**: continuous

	• **Unit of measure:** L/min • **Direction**: higher is better Upper body strength: handgrip (right/left) (note right and left arm data were averaged for the purpose of the meta-analyses as all other studies did not report which arm the test was conducted on) • **Outcome type**: continuous • **Unit of measure:** kg • **Direction**: higher is better Lower body muscle strength (mechanical handgrip dynamometer): right/left knee extensor/flexor peak torque at 60^o/s • **Outcome type**: continuous • **Unit of measure:** Nm • **Direction**: higher is better Lower body muscle strength (mechanical handgrip dynamometer): right/left knee extensor/flexor peak torque at 180^o/s • **Outcome type**: continuous • **Unit of measure:** Nm • **Direction**: higher is better Physical activity levels (Short QUestionnaire to ASess Health enhancing physical activity (SQUASH) • **Unit of measure:** minutes per week of moderated to high total physical activity and leisure and sport activity • **Direction:** higher is better *HRQoL (EQ-5D utility)* • **Outcome type**: continuous • **Scale**: 0.59-1 • **Direction**: higher is better HRQoL (EORTC QLQ-C30 subscales) • **Outcome type**: continuous • **Scale:** 0-100 • **Direction**: higher is better *HRQoL (SF-36)* • **Outcome type**: continuous • **Scale:** 0-100 • **Direction**: higher is better *Fatigue (multidimensional fatigue inventory (MFI)* • **Outcome type**: continuous • **Scale**: 4-20 • **Direction**: lower is better
Identification	**Setting:** outpatient clinics of 7 hospitals in the Netherlands (1 academic and 6 general hospitals) **Authors name:** Dr Anne M. May **Institution:** UMC Utrecht **Email:** A.M.May@umcutrecht.nl **Address:** not reported
Notes	Some data were taken from a separate publication linked to this study. Reference: Travier N, Velthuis MJ, Bisschop CNS, Van der Buijs B, Monninkhof EM, Backx F, et al. Effects of an 18-week exercise programme started early during breast cancer treatment:

	a randomised controlled trial. BMC Medicine 2015; 13 (121) Interventional notes were as follows: Quote: "Training intensity was re-evaluated every 4 weeks by submax cardiopulmonary exercise testing (CPET) and 1-repition maximum (RM)" Quote: "Participants in the intervention group were encouraged to be physically active for at least 30 min on at least three other days as recommended by Dutch guidelines" Quote: "Heart rate and the Borg scale of perceived exertion were monitored during the aerobic training" Quote: "Participants randomised to control received usual care and were asked to maintain their habitual physical activity pattern up to week 18"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A concealed computer-generated randomisation, following a 1:1 ratio, stratified per age, adjuvant treatment (radiotherapy yes/no before chemotherapy), use of tissue expander, and hospital by sequential balancing, was used to allocate participants to study groups"
Allocation concealment (selection bias)	Low risk	Judgement comment: as above: Quote: "Concealed randomisation of patients..."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: Quote: "Blinding of participants was not possible due to the nature of the study"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Judgement comment: Quote: "outcome measures were assessed by researchers not involved with the participants"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: consented 204; completed 164. Consort not provided in this article but it is in other related article (attrition 19.6%)
Selective reporting (reporting bias)	Low risk	Judgement comment: All outcome measures were reported according to methods
Other bias	Low risk	Judgement comment: none identified

Mock 2005

Methods	**Study design:** two-arm randomised controlled trial **Methods of participant recruitment:** Quote: "Potential participants were identified from new patient appointment lists at the site clinics between 1998 and 2001 and approached by investigators during their consultation visits prior to initiating adjuvant therapy" **Aim of study:** Quote: "To conduct a randomised controlled trial to determine the effects of a home-based walking exercise program on levels of fatigue in women with breast cancer receiving adjuvant cytotoxic chemotherapy or radiation therapy" **Start date of study:** 1998 **End date of study:** 2001 **Total study duration:** 3 years **Country:** United States **Sample size:** 120 **Duration of follow-up:** The exercise programme was implemented to span the period of time from initiation to cessation of adjuvant therapy: 6 weeks of radiotherapy or 3-6 months of chemotherapy **Study funding source:** Quote: "This study was funded by a competitive FIRE1 (Fatigue Initiative in Research and Education) multi-institutional award from the Oncology Nursing Society Foundation to Dr Mock under the aegis of the Johns Hopkins University" **Declaration of conflict of interest:** not reported
Participants	**Included criteria:** Quote: "Women aged 18-70 years of age, treated for Stage 0-III breast cancer by definitive surgery and scheduled to receive outpatient radiation therapy or adjuvant chemotherapy were eligible for the study" **Excluded criteria:** Quote: "Exclusion criteria included concurrent major health problems that could affect participation in an exercise program, including obesity (body mass index > 35 kg/m^2), cardiovascular disease, acute or chronic respiratory disease, and cognitive dysfunction. Also ineligible for study participation were patients already engaged in active exercise, defined as exercising more than 45 min per week" **Baseline imbalances:** Yes: Quote: "The baseline covariates were balanced between the randomised groups except for the 12-min walk performance" **Aim of study:** Quote: "To conduct a randomised controlled trial to determine the effects of a home-based walking exercise program on levels of fatigue in women with breast cancer receiving adjuvant cytotoxic chemotherapy or radiation therapy" **Total no. randomised:** 119 **No. intervention group:** 60 **No. control group:** 59 **Age (years):** Intervention: 51.3 ± 8.9 Control: 51.6 ± 9.7 **Gender:** female **Race/ethnicity:** Quote: "Caucasian (intervention: 85%, control: 79.3%)" **Cancer type:** breast cancer stage O-III **Cancer treatment:** adjuvant cytotoxic chemotherapy/radiation therapy: Intervention: chemotherapy (41.7%), radiotherapy (58%) Control: chemotherapy (42.4%) ,radiotherapy (57.6%) **Attrition rate:** 9.3% No. intervention group assessed at follow-up time point: not clearly stated (dependent

	on treatment type) (n = 54) No. control group assessed at follow-up time point: not clearly stated (dependent on treatment type) (n = 54) **Reasons for withdrawal:** Intervention (n = 6): radiotherapy: patient request (1); chemotherapy: moved and withdrew from care at site (1), withdrew from chemotherapy (2), allergic reaction to chemotherapy (1), patient request (1) Control (n = 5): radiotherapy: patient request (1); chemotherapy: patient request (1) and did not complete post-test (3)
Interventions	**Intervention characteristics** • *Setting*: home-based • *Group/non-group based*: alone • *Frequency*: 5-6 times/week • *Intensity*: moderate pace in target heart range (approx. 50%-70% of MHR) • *Time*: 15 mins walk increasing to 30 mins as training progressed • *Type*: walking • *Monitoring during exercise*: heart rate. Quote: "all exercise participants kept daily diaries of exercise periods including pulse rates, perceived exertion rates and fatigue levels". Note: method of measuring pulse rate not clear • *Support source*: phone call from member of research team: Quote: "Contacted every 2 weeks by research team to evaluate the prescription and participant progress". • *Adherence*: participants on chemotherapy (75%) and on radiotherapy (71%) • *Adverse events*: No adverse events attributable to the walking exercise program were reported or observed in the study. • *Withdrawals*: Intervention: radiotherapy: patient request (1); chemotherapy: moved and withdrew from care at site (1), withdrew from chemotherapy (2), allergic reaction to chemotherapy (1), patient request (1), Control: 5: radiotherapy: patient request (1); chemotherapy: patient request (1) and did not complete post-test (3)
Outcomes	*Aerobic fitness (12-min walk test)* • **Outcome type**: continuous • **Direction**: higher is better *Physical activity levels (physical activity questionnaire)* • **Outcome type**: continuous • **Unit of measure:** metabolic equivalents and kilocalories • **Direction**: higher is better *Fatigue (Total score of the Piper Fatigue scale (PFS)* • **Outcome type**: continuous • **Scale:** 0-10 • **Direction**: lower is better
Identification	**Sponsorship source:** not reported **Country:** United States **Setting:** 4 university teaching hospitals for National Cancer Institute designated cancer centres and 4 community cancer centres in eastern United States **Authors name:** Mock, V **Institution:** Center for Nursing Research, Johns Hopkins University **Email:** vmock@son.jhmi.edu

	Address: Center for Nursing Research, Johns Hopkins University, P.O. Box 50250, Baltimore, MD 21211- 4250, USA
Notes	1. Programme was detailed in a booklet and video provided to patients in the exercise group to ensure standardisation across subjects and across 8 clinical sites 2. Patients in the control group were encouraged to maintain current PA levels but no exercise prescription or formal programs were offered 3. All participants in the intervention group kept exercise diaries detailing pulse rates, RPE, and fatigue levels. These diaries were sent to the data coordinating centre each week 4. Exercising participants were contacted by the research team every two weeks to evaluate their prescription and progress

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement comment: Quote: "Consecutively numbered sealed opaque envelopes containing the computer-generated randomization assignments were prepared at the coordinating center and opened at the site following baseline pre-testing for each participant"
Allocation concealment (selection bias)	Low risk	Judgement comment: Quote: "Consecutively numbered sealed opaque envelopes containing the computer-generated randomization assignments were prepared at the coordinating center and opened at the site following baseline pre-testing for each participant"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: Quote: "It is a limitation of the study that members of the research staff were not blind to participants' group assignment"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Judgement comment: not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: consented 119, completed 108. Consort provided (attrition 9.3%)
Selective reporting (reporting bias)	High risk	Judgement comment: Outcome measures were clearly defined however within the results section following reporting of non-

Mock 2005 (*Continued*)

		significant findings, the authors allocated the exercise group into high and low walkers (this was not stated within the methods)
Other bias	Low risk	Judgement comment: none identified

Reis 2013

Methods	**Study design:** two-arm randomised controlled trial **Aim of study:** Quote: "to compare the effects of a 12-week Nia program to usual care in women with breast cancer undergoing radiation therapy to further test Nia in cancer and cancer treatment rehabilitation" **Methods of recruitment of participants:** not reported **Study start date:** Nov 2008 **Study end date:** Jan 2010 **Total study duration:** 14 months **Country:** United States **Sample size:** 41 **Duration of follow-up:** 12 weeks **Study funding source:** Oncology Nursing Foundation **Declaration of conflict of interest:** none
Participants	**Included criteria:** Quote: "All women aged 18 years and older receiving radiation therapy for stage I, II, or III breast cancer" **Excluded criteria:** Under 18 years old, non-English speaking, breast cancer stage 0 or stage 4 **Baseline imbalances:** no **Total randomised:** 41 **No. intervention group:** 22 **No. control group:** 19 **Age (years):** Intervention: 54 ± 11.1 Control: 59 ± 10.7 **Gender:** female **Race/ethnicity:** Intervention: Caucasian (20); African American (1); other (1) Control: Caucasian (17); African American (2); other (-) **Cancer type:** breast (stage I, II, III) **Cancer treatment:** radiation **Attrition rate:** 29.3% Quote: "Note. For the Nia intervention group, n = 12; for the control group, n = 17. Total participant count for this analysis is 29" **Reasons for withdrawal:** illness and loss of strength (numbers not provided)
Interventions	**Intervention characteristics** • *Setting*: home-based • *Group/non-group based*: alone • *Frequency*: 3 sessions/week • *Intensity*: not reported. Quote: "The practice of Nia can be gentle for individuals

	with a sedentary lifestyle or challenging for those with an active lifestyle (Rosas Rosas, 2004). Therefore, the adaptive nature of Nia may be of enhanced benefit to individuals with cancer". • *Time*: 20-60 mins • *Type*: not reported • *Monitoring during exercise:* The PI met participants at week 6 and week 12 to review their ability and how to modify movements to enhance their Nia practice. The PI met with control group to instruct them to maintain current exercise regimen. Both groups kept exercise logs during the 12-week study period. • *Support source*: as per above • *Adherence*: intervention: 2 days/week Nia + 2/sessions/week of other aerobic exercise • *Adverse events*: none reported
Outcomes	*Aerobic fitness (6-minute walk test)* • **Outcome type**: continuous • **Unit of measure:** metres • **Direction**: higher is better *HRQoL (Functional assessment of cancer therapy-General (FACT-G)* • **Outcome type**: continuous • **Scale:** 0-108 • **Direction**: higher is better *HRQoL (FACT-G subscale physical well-being)* • **Outcome type**: continuous • **Scale:** 0-28 • **Direction**: higher is better *HRQoL (FACT-G subscale social or family)* • **Outcome type**: continuous • **Scale:** 0-28 • **Direction**: higher is better *HRQoL (FACT-G subscale functional well-being)* • **Outcome type**: continuous • **Scale:** 0-28 • **Direction**: higher is better *Fatigue (FACT-G subscale fatigue)* • **Outcome type**: continuous • **Scale:** 0-52 • **Direction**: higher is better *Fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale* • **Outcome type**: continuous • **Scale**: 0-160 • **Direction**: higher is better
Identification	**Setting:** Flower Hospital, community-based hospital in north-west Ohio **Authors name:** Reis, D **Institution:** not reported **Email:** deb.reis@promedica.org **Address:** not reported

Reis 2013 (*Continued*)

Notes	Interventional notes are as follows: Quote: "Nia, which focuses on the body, mind, and spirit. Nia is a cardiovascular and whole-body conditioning program that integrates five sensations: strength, flexibility, mobility, agility, and stability (Rosas Rosas, 2004). Nia is based in nine movement forms: three martial arts (TaiChi, Tae Kwon Do, and Aikido), three dance arts (jazz dance, modern dance, and Duncan dance), and three healing arts (yoga, the teachings of Moshe Feldenkrais, and the Alexander Technique)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Judgement comment: Randomisation was stratified by stage of disease (I, II, III) and age (59 or younger, 60 and older) in an attempt to ensure equal representation of these groups in both interventions
Allocation concealment (selection bias)	Low risk	Judgement comment: Envelopes were sealed with group assignment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: not possible in this type of intervention
Blinding of outcome assessment (detection bias) All outcomes	High risk	Judgement comment: Outcome assessors were not blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	Judgement comment: consented 41, completed 29 (attrition 29.3%) Quote: "For the Nia intervention group, n = 12; for the control group, n = 17. Total participant count for this analysis is 29"
Selective reporting (reporting bias)	Low risk	Judgement comment: All outcomes were reported clearly.
Other bias	Low risk	Judgement comment: none identified

VanWaart 2015

Methods	**Study design:** three-armed randomised controlled trial **Methods of recruitment of participants:** Quote: "Potentially eligible patients with breast cancer were identified through hospital records, whereas patients with colon cancer were identified by their treating physicians" **Aim of study:** Quote: "to evaluate the effectiveness of a home-based, low-intensity physical activity program (Onco-Move) and a supervised, moderate- to high-intensity, combined resistance and aerobic exercise program (OnTrack) in maintaining or enhancing physical fitness and minimizing fatigue in patients undergoing adjuvant chemotherapy" **Start date of study:** March 2010 **End date of study:** December 2012 **Total study duration:** 33 months **Country:** Netherlands **Sample size:** 192 **Duration of follow-up:** end of cancer treatment (estimated between 117 and 119 days (17 weeks) **Study funding source:** Quote: "Supported by Alpe d'Huzes/Dutch Cancer Society Grant No. ALPE-2009-4299, the CZ Fund, Zilveren Kruis Achmea, and the Comprehensive Cancer Centre of the Netherlands" **Declarations of conflict of interest:** none declared
Participants	**Included criteria:** Quote: "Patients were eligible for the trial if they had histologically confirmed primary breast or colon cancer and were scheduled to undergo adjuvant chemotherapy at one of 12 hospitals in the Amsterdam region of the Netherlands" **Excluded criteria:** Quote: "Patients were excluded if they had serious orthopedic, cardiovascular, or cardiopulmonary conditions, were suffering from malnutrition, had serious psychiatric or cognitive problems, or did not have basic fluency in Dutch. There was no upper age limit" **Baseline imbalances:** Quote: "Baseline characteristics were balanced across groups" **Gender:** female and male **Population:** breast and colon cancer (however data for the breast cancer participants were only reported due to small sample) **Total no. randomised:** 230 **Total no. intervention group 1:** 76 **Total no. intervention group 2:** 77 **Total no. control group:** 77 **Race/ethnicity:** not reported **Cancer type:** breast and colon cancer (however analysis only focused on breast cancer due to the low number with colon cancer) **Cancer treatment:** adjuvant chemotherapy **Age (years):** Intervention 1 (OnTrack): 49.9 ± 8.4 Intervention 2 (Onco-Move): 50.5 ± 10.1 Control: 51.6 ± 8.8 **Attrition rate:** 14.4% No. intervention group 1 assessed at follow-up: end of chemotherapy (71) No. intervention group 2 assessed at follow-up: end of chemotherapy (69) No. control group assessed at follow-up: end of chemotherapy (66) **Reasons for withdrawal:** Intervention 1: too ill (2), physical accident unrelated to trial (1), physical accident

	related to trial (1), unwilling (1) Intervention 2: neuropathy (1); emigrated (1); unwilling (6) Control: too ill (2), unwilling (7), unknown (2)
Interventions	**Intervention characteristics** Intervention 1 (On Track) • *Setting*: community (supervised by community-based physiotherapists who had received training in the intervention and were part of an oncology-physiotherapy network. Every attempt was made for patients to avail of a physiotherapist located close to their home). • *Group/non-group based*: alone • *Frequency*: 2 sessions/week • *Intensity*: aerobic: 50%-80% maximal workload (steep ramp test) and BORG scale (less than 12 for increase and more than 16 for a decrease), strength: 80% 1 rep max • *Time*: aerobic: 30 mins, strength: 20 mins • *Type*: aerobic and strength (upper and lower limb): not reported • *Source of support*: not reported if any • *Adherence*: 71% • *Monitoring during exercise*: not reported if any • *Adverse events*: none Intervention 2 (Onco-Move) • *Setting*: home-based • *Supervision*: unsupervised • *Group/non-group based*: alone • *Duration of exercise programme*: started with the first cycle of chemotherapy and continued until 3 weeks after the last cycle (varied per patient) • *Components of the exercise programme*: aerobic • *Frequency*: 5 days/week • *Intensity*: 12-14 BORG scale • *Time*: 30 mins • *Type*: walking • *Source of support*: Participants received encouragement from a nurse in the chemotherapy unit to be physical active at least 30 minutes per day. This encouragement was provided each time the nurse saw the patient. • *Adherence*: 55% • *Monitoring during exercise*: not reported if any • *Adverse events*: none
Outcomes	*Aerobic (steep ramp test: maximal short exercise capacity)* • **Outcome type**: continuous • **Unit of measure:** minutes • **Direction**: higher is better *Aerobic fitness (endurance time)* • **Outcome type**: continuous • **Unit of measure:** watts • **Direction**: higher is better *Upper body muscle strength (elbow flexion)* • **Outcome type**: continuous] • **Unit of measure:** Newton meters (Nm)

	• **Direction**: higher is better *Upper body muscle strength (grip strength dynamometer)* • **Outcome type**: continuous • **Unit of measure:** kg • **Direction**: higher is better *Lower body muscle strength (knee extension)* • **Outcome type**: continuous • **Unit of measure:** Nm • **Direction**: higher is better *Lower body muscle strength (30-sec chair stand)* • **Outcome type**: continuous • **Unit of measure**: seconds • **Direction**: higher is better Physical activity levels (Physical Activity Scale for the Elderly) • **Outcome type**: continuous • **Direction**: higher is better HRQoL (EORTC QLQ-C30 subscales) • **Outcome type**: continuous • **Scale:** 0-100 • **Direction**: higher is better Fatigue (EORTC QLQ-C30 subscale) • **Outcome type**: continuous • **Scale:** 0-100 • **Direction**: lower is better *Fatigue (multidimensional fatigue inventory (MFI)* • **Outcome type**: continuous • **Scale**: 4-20 • **Direction**: lower is better
Identification	**Setting:** 12 hospitals in the Amsterdam region of the Netherlands **Authors name:** Neil K. Aaronson **Institution:** Division of Psychosocial Research and Epidemiology, Netherlands Cancer Institute **Email:** n.aaronson@nki.nl **Address:** Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, the Netherlands
Notes	1. Participants in the OnTrack group were also encouraged to be physically active 5 days each week for 30 minutes per session and to keep an activity diary 2. Each participant in the OncoMove group had an activity diary that was discussed at each chemotherapy cycle. Specially trained nurses encouraged participants to engage in exercise

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Judgement comment: email reply from main author: "We used a computer pro-

		gram specifically designed to carry out a minimisation process for assigning patients to one of the three trial groups. The study staff that carried out the randomisation used that program"
Allocation concealment (selection bias)	Low risk	Judgement comment: email reply from main author: "We used a computer program specifically designed to carry out a minimisation process for assigning patients to one of the three trial groups. The study staff that carried out the randomisation used that program"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Judgement comment: due to the nature of the intervention, blinding of participants and personnel not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Judgement comment: Author email replied to email to say that the outcome assessors were not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judgement comment: consented 230, completed 197. Consort provided (attrition 14.4%)
Selective reporting (reporting bias)	High risk	Judgement comment: data not reported. Quote: "There were no other significant group differences at T1 or T2 for the remaining EORTC QLQC30 scales or the measures of psychological distress (Hospital Anxiety and Depression Scale), functioning in daily life (Impact on Participation and Autonomy instrument), or self-reported activity level (Physical Activity Scale for the Elderly; data not shown)"
Other bias	Low risk	Judgement comment: none identified

ANC:Absoluteneutrophilcount

BFI: Brief fatigue inventory questionnaire
BORG: Borg rating of perceived exertion
CBC: Complete blood count
CPET: Cardiopulmonary exercise test
ECOG: European cooperative oncology group
EORTC QLQ-C30: European organisation for research and treatment of cancer questionnaire
EQ-5D: standardised instrument for measuring general health status
FACIT-F: Functional assessment of chronic illness therapy - Fatigue

FACT-G: Functional assessment of chronic illness therapy - General
GH: General health perception
HRQoL: Health related quality of life
IQR: Interquartile range
MET: Metabolic equivalent threshold
MFI: Multidimensional fatigue inventory
MHR: Maximal heart rate
MOS: Medical outcome study NA: Not applicable
PA: Physical activity
PACT:Physcial activity during cancer intervention trial
PFS: Piper fatigue scale
PI: Principle investigator
ROM: Range of motion
RPE: Rating of perceived exertion
SCFS-6: Shwartz cancer fatigue scale
SF-36: Short form health survey
SMS: Short message service
SQUASH: Short questionnaire to assess health enhancing physical activity
VAS: Visual analogue scale
VO2 max: Oxygen uptake at maximal capacity
WHOQOL: World health organisation quality of life
YG: Yoga group
1RM: 1-repeition maximum

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ahmed 2006	Wrong patient population
Bloomquist 2014	Wrong patient population
Cadmus 2009	Wrong patient population
Cho 2008	Wrong study design
Coleman 2003	Wrong study design
Coleman 2008	Wrong patient population
Courneya 2008	Wrong study aim
Courneya 2009	Wrong patient population
Courneya 2014	Wrong comparator
Devoogdt 2011	Wrong patient population

(*Continued*)

Dimeo 1997	Wrong patient population
Duijts 2012	Wrong setting
Harder 2015	Wrong setting
Jones 2010	Wrong study design
Kilbreath 2012	Wrong setting
McNeely 2008	Wrong patient population
McNeely 2010	Wrong study design
Mina 2014	Wrong patient population
Pehlivan 2011	Wrong patient population
Salhi 2014	Wrong study design
Salhi 2015	Wrong setting
Saxton 2014	Wrong patient population
So 2006	Wrong study design
Song 2013	Wrong intervention
Thorsen 2005	Wrong setting
Villanueva 2011	Wrong patient population
Xu 2015	Wrong intervention

Characteristics of ongoing studies *[ordered by study ID]*

Loughney 2016

Trial name or title	The EMPOWER trial: The effects of neoadjuvant chemoradiotherapy and an in-hospital exercise training programme on physical fitness and quality of life in locally advanced rectal cancer patients: study protocol for a randomised controlled trial
Methods	2-arm RCT (target sample 46)
Participants	Colorectal cancer (neoadjuvant treatment)

Loughney 2016 (*Continued*)

Interventions	In-hospital supervised exercise training Quote: "Patients are requested to attend three in-hospital exercise training sessions per week for 6 to 9 weeks (dependent on the time interval between neoadjuvant CRT and surgery at each hospital). The exercise training is an aerobic interval exercise training programme incorporating moderate and severe intensities"
Outcomes	Physical fitness (cardiopulmonary exercise test) Physical activity (sense wear activity monitoring)
Starting date	October 2013 (end date: Dec 2017) results being prepared for publication (2018)
Contact information	Dr Sandy Jack, PhD, s.jack@soton.ac.uk
Notes	ClinicalTrials.gov identifier: NCT01914068 Country: United Kingdom

Morielli 2018

Trial name or title	Exercise during and after neoadjuvant rectal cancer treatment (the EXERT trial): study protocol for a randomised controlled trial
Methods	2-arm RCT (target sample 60)
Participants	Rectal cancer (neoadjuvant treatment)
Interventions	Supervised & non-supervised exercise training "Participants in the exercise training group will be asked to complete three supervised, high-intensity interval training sessions/week during NACRT and ≥ 150 min/week of unsupervised, moderate-to-vigorous-intensity, continuous exercise training after NACRT prior to surgery"
Outcomes	Cardiorespiratory fitness (VO2 peak) Quality of life (European Organisation of Research and Treatment of Cancer, and symptom management assessed by the M.D. Anderson Symptom Inventory)
Starting date	June 2017 (proposed end date: June 2019).
Contact information	Andria R. Morielli, ac.atreblau@illeirom
Notes	ClinicalTrials.gov identifier: NCT03082495 Country: Canada

NCT02159157

Trial name or title	A randomised, controlled trial to determine the effects of an exercise intervention on physical activity during chemotherapy for patients with early stage breast cancer
Methods	2-arm RCT (target sample 120)
Participants	Breast cancer (adjuvant treatment)
Interventions	Exercise prescription aimed at increasing physical activity by a minimum of 10 MET hours/week. Motivational phone calls aimed at encouraging the patient to adhere to their exercise prescription
Outcomes	Physical activity (activity log and pedometer data) Fatigue (FACIT-F questionnaire)
Starting date	9 June 2014 (proposed end date: March 2017). Current status: active not recruiting (last updated 18 May 2017)
Contact information	Not provided
Notes	ClinicalTrials.gov identifier: NCT02159157 Country: United States.

NCT02454777

Trial name or title	High-intensity interval training for stage I-III breast cancer patients
Methods	2-arm RCT (target sample 60)
Participants	Breast cancer (neoadjuvant treatment)
Interventions	High intensity exercise over 30 minutes, thrice weekly for 8 weeks
Outcomes	Feasibility (attendance rate and exercise time completed) Physical fitness (VO2 peak)
Starting date	29 September 2015 (proposed end date: 29 September 2019). Current status: recruiting (last updated 17 July 2017)
Contact information	Christina Dieli-Conwright, PhD, 323-442-2180, cdieli@usc.edu
Notes	ClinicalTrials.gov identifier: NCT02454777 Country: United States

NCT02802826

Trial name or title	Studying tailored exercise prescriptions in breast cancer patients (STEPS)
Methods	2-arm RCT (target sample 100)
Participants	Breast cancer (neoadjuvant/adjuvant)
Interventions	Quote: "Tailored Exercise Prescription Participants will have a discussion on the 'My Exercise Prescription' booklet on the benefits of increasing levels of physical activity. They will be encouraged to read this in more detail and guided through its completion. The participant will receive an exercise prescription using the Pre-Intervention Assessment Tool (PIAT) and following discussion with the participant on a realistic and achievable starting point.The booklets provided will guide participants through the exercise programme which is a graduated walking-based activity intervention. Both booklets provide participants with a suggested starting point for walking distance per week based on their PIAT score as well as motivational and behaviour change strategies to encourage participation"
Outcomes	Physical activity (level of moderate-vigorous physical activity) Health-related quality of life (Euro-QOL 5D and EORTC QLQ-C30)
Starting date	July 2016 (estimated study completion date January 2018). Current status: not yet recruiting (last updated 16 June 2016)
Contact information	Contact: Stephen Kihara, +44 (0) 7730609777, s.kihara@lboro Contact: Fehmidah Munir, +44 (0)1509 228228, f.munir@lboro.ac.uk
Notes	ClinicalTrials.gov identifier: NCT02802826 Country: United Kingdom

NCT02999074

Trial name or title	Exercise interventions for breast cancer patients undergoing neoadjuvant chemotherapy (BENEFIT)
Methods	3-arm RCT (target sample 342)
Participants	Breast cancer (neoadjuvant treatment)
Interventions	Resistance exercise: The progressive resistance exercise comprises 8 machine-based exercises, each performed in 3 sets, 12 repetitions at 60%-80% of one repetition maximum (1-RM) Aerobic exercise: The aerobic exercise will be performed on a cycle ergometer (or alternatively at a treadmill, elliptical, rowing ergometer, or combination) progressing from 60% to 70% VO_2 max with increasing duration.
Outcomes	Fatigue (Fatigue Assessment Questionnaire, Validated 20-item multidimensional self-assessment questionnaire) Health-related quality of life (EORTC QLQ-C30)
Starting date	January 2016 (proposed end date: January 2020). Current status: recruiting (last updated: 21 December 2016)

NCT02999074 (*Continued*)

Contact information	Dr Martina E Schmidt, +49 6221 42 2220, email: m.schmidt@dkfz.de
Notes	ClinicalTrials.gov identifier: NCT02999074 Country: Germany

NCT03102866

Trial name or title	Aerobic and strength training exercise in improving fitness and arm health during and after radiation therapy in patients with stage II-III breast cancer
Methods	2-arm RCT (target sample 44)
Participants	Breast cancer (adjuvant treatment)
Interventions	Aerobic and strength training Quote: "Patients undergo a supervised aerobic and strength training exercise session over 40-60 minutes 3 times weekly for 6 weeks during radiation therapy and for 12 weeks after completion of radiation therapy"
Outcomes	Feasibility (number of participants who complete 70% of all exercise sessions throughout the supervised program during and after radiation therapy based on collected exercise logs) Physical fitness (6-minute walk test) Adherence (International Physical Activity Questionnaire and exercise logs) Quality of life (FACT-B+4)
Starting date	30 August 2017 (proposed end date: 31 December 2019). Current status: recruiting (last updated 6 October 2017)
Contact information	Alison Quick, MD, 614-688-7374, Alison.quick@osumc.edu
Notes	ClinicalTrials.gov: NCT03102866 Country: United States

NCT03280836

Trial name or title	Exercise program in breast cancer patients receiving neoadjuvant chemotherapy (WISER-NET)
Methods	2-arm RCT (target sample 20)
Participants	Breast cancer (neoadjuvant)
Interventions	Participants will work towards the goal of 75 or more minutes a week of moderate to vigorous exercise. Participants are provided an exercise toolkit and directed on exercise progression based on personal fitness level
Outcomes	Physical fitness (cardiopulmonary exercise test)

NCT03280836 (*Continued*)

Starting date	13 September 2017 (proposed study end date 31 December 2019). Current status: recruiting
Contact information	Kathleen M Sturgeon, 717-531-0003 ext 284676, kms99@psu
Notes	ClinicalTrials.gov identifier: NCT03280836 Country: United States

NCT03509428

Trial name or title	The Wessex Fit-4-Cancer Surgery Trial (WesFit)
Methods	2-arm RCT (target sample 1560)
Participants	Major cancer surgery (neoadjuvant treatment)
Interventions	An in-hospital transition to a community based Structured Responsive Exercise-Training Programme (SRETP) ± psychological support (delivered in community/council gyms or cancer support centres). The intervention/s will be delivered before surgery. Patients receiving neoadjuvant cancer treatments prior to surgery will receive the intervention during and after these treatments
Outcomes	Physical fitness (oxygen uptake at anaerobic threshold and oxygen uptake at peak exercise) Postoperative morbidity (patients postoperative morbidity survey will be characterised on day 3, 5, 7, and 15). On day of discharge, patient's surgical complications (if any) will be graded using the Clavien-Dindo classification of surgical complications This classification is used to assess overall hospital morbidity following surgical procedures. Patients are graded as 0 (no complications) or Grade I-V based on the level of complication, including the number of organ system involvement. Grade V is defined as death of a patient. A record of the Comprehensive Complication Index (CCI) - an update of the Clavien-Dindo classification will also be collected Physical activity (number of steps, sleep efficiency, metabolic equivalents using a triaxial accelerometer) and Godin Leisure Time and Exercise questionnaire Health-related quality of life (EQ-5D-5L an EORTC-QLQ-C30)
Starting date	26 March 2018 (proposed end date: 1 March 2021). Current status: recruiting (last updated 26 April 2018)
Contact information	Dr Sandy Jack, PhD, s.jack@soton.ac.uk
Notes	ClinicalTrials.gov identifier: NCT03509428 County: United Kingdom

BORG: BORG rating of perceived exertion

CCI: Comprehensive complication index

CRT: chemoradiotherapy
EORTC QLQ-C30: European organisation for research and treatment of cancer questionnaire
EQ-5D: standardised instrument for measuring general health status
FACIT-F: Functional assessment of chronic illness therapy - Fatigue
FACT-B+4: Functional assessment of cancer therapy - Breast questionnaire

MET: Metabolic equivalent threshold
NACRT: Neoadjuvant chemoradiotherapy
PIAT: Pre-Intervention Assessment Tool
SRETP: Structured responsive exercise programme
VO2: Oxygen uptake
VO2 max: Oxygen uptake at maximal capacity
1-RM: 1-repeition maximum

DATA AND ANALYSES

Comparison 1. Intervention versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Aerobic fitness (VO_2 max on cycle ergometer)	2	381	Mean Difference (IV, Random, 95% CI)	0.05 [-0.03, 0.13]
2 Aerobic fitness (6-minute walk test)	3	146	Mean Difference (IV, Random, 95% CI)	16.79 [-7.39, 40.96]
3 Muscle strength (upper body: grip strength)	3	419	Mean Difference (IV, Random, 95% CI)	0.73 [-0.86, 2.32]
4 HRQoL (EORTC QLQ-C30 global health status)	3	472	Mean Difference (IV, Random, 95% CI)	2.29 [-1.06, 5.65]
5 HRQoL (EORTC QLQ-C30 cognitive functioning)	3	505	Mean Difference (IV, Random, 95% CI)	3.13 [-0.55, 6.80]
6 HRQoL (EORTC QLQ-C30 social functioning)	3	505	Mean Difference (IV, Random, 95% CI)	3.62 [-0.33, 7.58]
7 HRQoL (EQ-5D utility)	2	263	Mean Difference (IV, Random, 95% CI)	0.01 [-0.05, 0.07]
8 HRQoL (SF-36 general health perceptions)	2	317	Mean Difference (IV, Random, 95% CI)	0.67 [-3.24, 4.57]
9 HRQoL (SF-36 mental component scale)	2	317	Mean Difference (IV, Random, 95% CI)	2.58 [0.16, 5.01]
10 HRQoL (SF-36 bodily pain)	2	317	Mean Difference (IV, Fixed, 95% CI)	0.06 [-3.03, 3.15]
11 Fatigue (multidimensional fatigue inventory)	3	449	Mean Difference (IV, Random, 95% CI)	-1.05 [-1.83, -0.28]
12 Fatigue (EORTC QLQ-C30)	3	506	Mean Difference (IV, Random, 95% CI)	-5.91 [-10.15, -1.68]

Analysis 1.1. Comparison 1 Intervention versus control, Outcome 1 Aerobic fitness (VO_2 max on cycle ergometer).

Review: Exercise interventions for people undergoing multimodal cancer treatment that includes surgery

Comparison: 1 Intervention versus control

Outcome: 1 Aerobic fitness (VO_2 max on cycle ergometer)

Study or subgroup	Favours usual care N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Adamsen 2009	118	1.96 (0.5)	117	1.88 (0.5)		37.1 %	0.08 [-0.05, 0.21]
May 2017	83	1.55 (0.3)	63	1.52 (0.3)		62.9 %	0.03 [-0.07, 0.13]
Total (95% CI)	**201**		**180**			**100.0 %**	**0.05 [-0.03, 0.13]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.37$, df = 1 (P = 0.54); I^2 =0.0%

Test for overall effect: Z = 1.22 (P = 0.22)

Test for subgroup differences: Not applicable

Analysis 1.2. Comparison 1 Intervention versus control, Outcome 2 Aerobic fitness (6-minute walk test).

Review: Exercise interventions for people undergoing multimodal cancer treatment that includes surgery

Comparison: 1 Intervention versus control

Outcome: 2 Aerobic fitness (6-minute walk test)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Haines 2010	27	545 (83)	30	535 (88)		29.6 %	10.00 [-34.40, 54.40]
Husebo 2014	29	644.02 (63.3)	31	628.33 (60.44)		59.4 %	15.69 [-15.67, 47.05]
Reis 2013	12	477.9 (79.2)	17	436.8 (121.4)		10.9 %	41.10 [-31.96, 114.16]
Total (95% CI)	**68**		**78**			**100.0 %**	**16.79 [-7.39, 40.96]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.52$, df = 2 (P = 0.77); I^2 =0.0%

Test for overall effect: Z = 1.36 (P = 0.17)

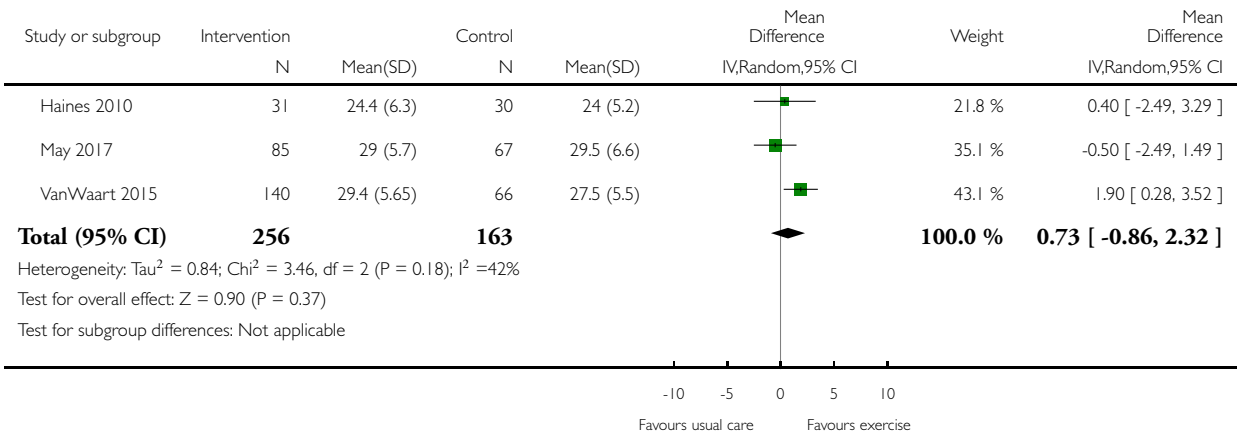
Test for subgroup differences: Not applicable

Analysis 1.3. Comparison 1 Intervention versus control, Outcome 3 Muscle strength (upper body: grip strength).

Review: Exercise interventions for people undergoing multimodal cancer treatment that includes surgery

Comparison: 1 Intervention versus control

Outcome: 3 Muscle strength (upper body: grip strength)



Analysis 1.4. Comparison 1 Intervention versus control, Outcome 4 HRQoL (EORTC QLQ-C30 global health status).

Review: Exercise interventions for people undergoing multimodal cancer treatment that includes surgery

Comparison: 1 Intervention versus control

Outcome: 4 HRQoL (EORTC QLQ-C30 global health status)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Adamsen 2009	118	67.2 (20.3)	117	63.3 (22.4)		37.6 %	3.90 [-1.57, 9.37]
Haines 2010	33	75.8 (15.2)	32	74 (15.5)		20.2 %	1.80 [-5.67, 9.27]
May 2017	93	70.4 (18.3)	79	69.3 (16.2)		42.2 %	1.10 [-4.06, 6.26]
Total (95% CI)	**244**		**228**			**100.0 %**	**2.29 [-1.06, 5.65]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.55$, df = 2 (P = 0.76); $I^2 = 0.0\%$

Test for overall effect: Z = 1.34 (P = 0.18)

Test for subgroup differences: Not applicable

Analysis 1.5. Comparison 1 Intervention versus control, Outcome 5 HRQoL (EORTC QLQ-C30 cognitive functioning).

Review: Exercise interventions for people undergoing multimodal cancer treatment that includes surgery

Comparison: 1 Intervention versus control

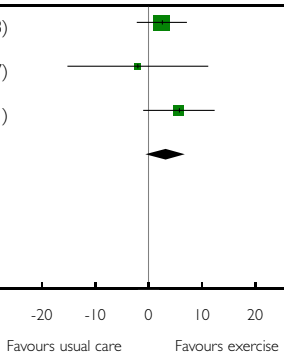
Outcome: 5 HRQoL (EORTC QLQ-C30 cognitive functioning)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Adamsen 2009	118	83.8 (16.7)	117	81.3 (19.8)		61.6 %	2.50 [-2.19, 7.19]
Haines 2010	32	76.6 (29.6)	32	78.6 (23.7)		7.8 %	-2.00 [-15.14, 11.14]
VanWaart 2015	140	75.9 (21.9)	66	70.2 (23.1)		30.6 %	5.70 [-0.95, 12.35]
Total (95% CI)	**290**		**215**			**100.0 %**	**3.13 [-0.55, 6.80]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.23$, df = 2 (P = 0.54); $I^2 = 0.0\%$

Test for overall effect: Z = 1.67 (P = 0.096)

Test for subgroup differences: Not applicable



Analysis 1.6. Comparison 1 Intervention versus control, Outcome 6 HRQoL (EORTC QLQ-C30 social functioning).

Review: Exercise interventions for people undergoing multimodal cancer treatment that includes surgery

Comparison: 1 Intervention versus control

Outcome: 6 HRQoL (EORTC QLQ-C30 social functioning)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Adamsen 2009	118	82.6 (20.5)	117	79.4 (20.8)		56.1 %	3.20 [-2.08, 8.48]
Haines 2010	32	85.4 (20.2)	32	83.9 (16.7)		19.0 %	1.50 [-7.58, 10.58]
VanWaart 2015	140	74.1 (22.2)	66	67.9 (29.1)		24.9 %	6.20 [-1.73, 14.13]
Total (95% CI)	**290**		**215**			**100.0 %**	**3.62 [-0.33, 7.58]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.64$, df = 2 (P = 0.73); $I^2 = 0.0\%$

Test for overall effect: Z = 1.80 (P = 0.072)

Test for subgroup differences: Not applicable

Analysis 1.7. Comparison 1 Intervention versus control, Outcome 7 HRQoL (EQ-5D utility).

Review: Exercise interventions for people undergoing multimodal cancer treatment that includes surgery

Comparison: 1 Intervention versus control

Outcome: 7 HRQoL (EQ-5D utility)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Haines 2010	35	0.8 (0.21)	34	0.83 (0.18)		34.1 %	-0.03 [-0.12, 0.06]
May 2017	101	0.84 (0.1)	93	0.81 (0.3)		65.9 %	0.03 [-0.03, 0.09]
Total (95% CI)	**136**		**127**			**100.0 %**	**0.01 [-0.05, 0.07]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.10$, df = 1 (P = 0.29); $I^2 = 9\%$

Test for overall effect: Z = 0.34 (P = 0.74)

Test for subgroup differences: Not applicable

Analysis 1.8. Comparison 1 Intervention versus control, Outcome 8 HRQoL (SF-36 general health perceptions).

Review: Exercise interventions for people undergoing multimodal cancer treatment that includes surgery

Comparison: 1 Intervention versus control

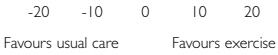
Outcome: 8 HRQoL (SF-36 general health perceptions)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Adamsen 2009	118	68.7 (19.7)	117	65.5 (22.4)		38.2 %	3.20 [-2.20, 8.60]
Chandwani 2014	39	47.1 (8.7)	43	48 (8.5)		61.8 %	-0.90 [-4.63, 2.83]
Total (95% CI)	**157**		**160**			**100.0 %**	**0.67 [-3.24, 4.57]**

Heterogeneity: $Tau^2 = 2.81$; $Chi^2 = 1.50$, df = 1 (P = 0.22); $I^2 = 33\%$

Test for overall effect: Z = 0.34 (P = 0.74)

Test for subgroup differences: Not applicable

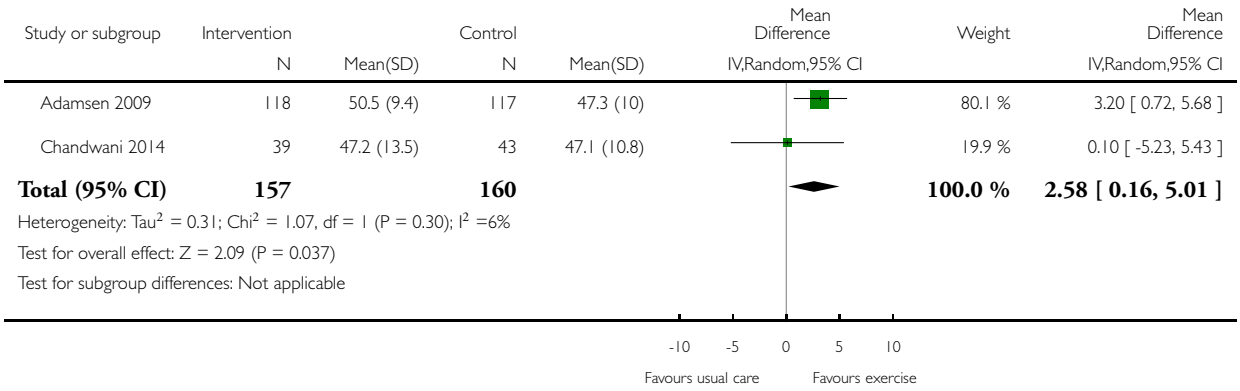


Analysis 1.9. Comparison 1 Intervention versus control, Outcome 9 HRQoL (SF-36 mental component scale).

Review: Exercise interventions for people undergoing multimodal cancer treatment that includes surgery

Comparison: 1 Intervention versus control

Outcome: 9 HRQoL (SF-36 mental component scale)

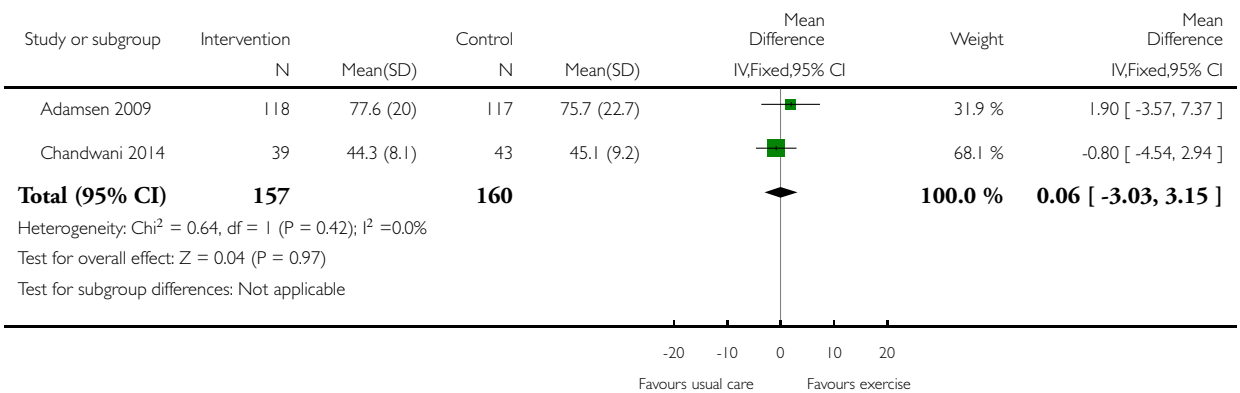


Analysis 1.10. Comparison 1 Intervention versus control, Outcome 10 HRQoL (SF-36 bodily pain).

Review: Exercise interventions for people undergoing multimodal cancer treatment that includes surgery

Comparison: 1 Intervention versus control

Outcome: 10 HRQoL (SF-36 bodily pain)



Analysis 1.11. Comparison 1 Intervention versus control, Outcome 11 Fatigue (multidimensional fatigue inventory).

Review: Exercise interventions for people undergoing multimodal cancer treatment that includes surgery

Comparison: 1 Intervention versus control

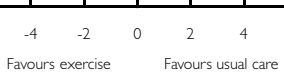
Outcome: 11 Fatigue (multidimensional fatigue inventory)

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Haines 2010	36	11.1 (4.2)	34	11.9 (4.5)		14.5 %	-0.80 [-2.84, 1.24]
May 2017	91	11.8 (4.2)	82	12.7 (3.7)		43.6 %	-0.90 [-2.08, 0.28]
VanWaart 2015	140	13.4 (3.9)	66	14.7 (4.2)		41.9 %	-1.30 [-2.50, -0.10]
Total (95% CI)	**267**		**182**			**100.0 %**	**-1.05 [-1.83, -0.28]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.29$, df = 2 (P = 0.87); $I^2 = 0.0\%$

Test for overall effect: Z = 2.65 (P = 0.0080)

Test for subgroup differences: Not applicable

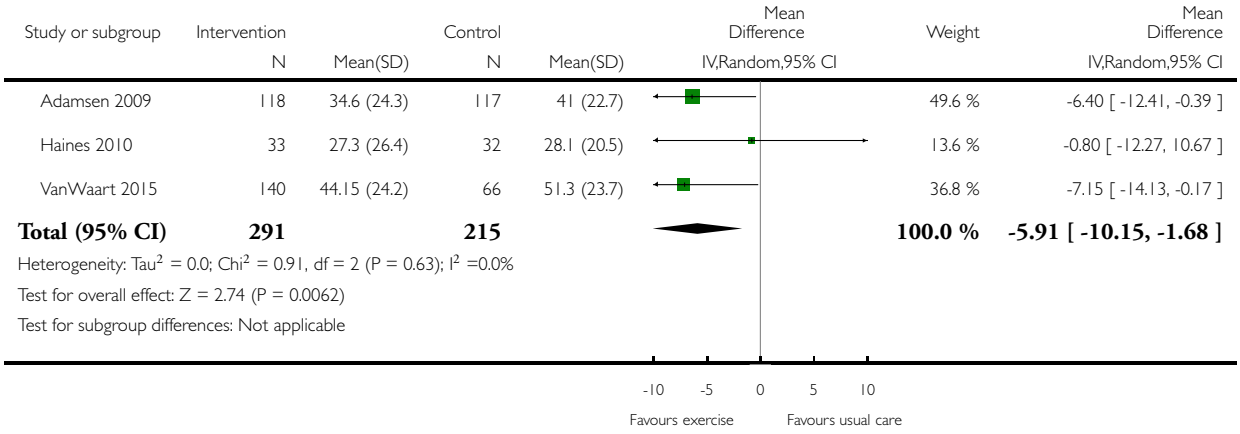


Analysis 1.12. Comparison 1 Intervention versus control, Outcome 12 Fatigue (EORTC QLQ-C30).

Review: Exercise interventions for people undergoing multimodal cancer treatment that includes surgery

Comparison: 1 Intervention versus control

Outcome: 12 Fatigue (EORTC QLQ-C30)



ADDITIONAL TABLES

Table 1. Physical fitness data from individual studies

		Exercise group		Usual care control group		
Outcome measure	**Study**	**Baseline**	**Post-intervention**	**Baseline**	**Post-intervention**	P value
Aerobic fitness						
Maximal short exercise capacity (watts)	VanWaart 2015	263.7 (49.3)[a]	239.3 (57.3)[a]	245.0 (48.9)	202.4 (66.5)	0.001
Maximal short exercise capacity (watts)	VanWaart 2015	256.1 (48.2)[b]	221.0 (63.4)[b]	245.0 (48.9)	202.4 (66.5)	0.34
Endurance timed test (mins)	VanWaart 2015	13.5 (9.2)[a]	13.7 (9.0)[a]	11.4 (8.6)	5.1 (5.4)	< 0.001
Endurance timed test (mins)	VanWaart 2015	12.3 (8.7)[b]	9.0 (9.0)[b]	11.4 (8.6)	5.1 (5.4)	< 0.001

Table 1. Physical fitness data from individual studies (*Continued*)

Step test (steps in 15 secs)	Haines 2010	15.1 (3.5)	15.2 (3.2)	15.8 (4.2)	15.8 (4.2)	0.46
Upper body strength						
Chest press (kg)	Adamsen 2009	37.9 (15.6)	45.2 (17.9)	40.2 (18.0)	39.7 (17.2)	< 0.001
Pull-down test (kg)	Adamsen 2009	39.6 (14.0)	47.2 (14.4)	42 (16.3)	42.8 (16.1)	< 0.001
Elbow flexion test (Nm)	VanWaart 2015	31.7 (12.5)[a]	32.0 (13.7)[a]	29.1 (13.0)	25.2 (12.1)	0.002
Elbow flexion test (Nm)	VanWaart 2015	30.2 (11.6)[b]	27.4 (11.9)[b]	29.1 (13.0)	25.2 (12.1)	0.22
Lower body strength						
Leg press test (kg)	Adamsen 2009	110.8 (30.5)	132.4 (42.3)	107.6 (33.3)	110.4 (36)	< 0.001
Leg press test (kg)	Haines 2010	71.1 (24.3)	81.9 (25.6)	67.4 (15.0)	80.2 (20.5)	0.71
30-sec chair stand test (times)	VanWaart 2015	19.3 (5.5)[a]	19.1 (5.0)[a]	17.7 (4.3)	16.9 (5.3)	0.11
30-sec chair stand test (times)	VanWaart 2015	18.8 (6.4)[b]	18.8 (7.0)[b]	17.7 (4.3)	16.9 (5.3)	0.14
Knee extension test (Nm)	VanWaart 2015	70.2 (18.6)[a]	71.4 (17.6)[a]	65.7 (20.8)	62.3 (22.0)	0.27
Knee extension test (Nm)	VanWaart 2015	70.3 (20.9)[b]	66.3 (20.6)[b]	65.7 (20.8)	62.3 (22.0)	0.10
Right knee extensor peak toque at 60 ^{O}/s (Nm)	May 2017	102.6 (32)	106.3 (25.9)	106 (27.3)	100.8 (25.5)	#
Right knee flexor peak torque at 60 ^{o}/s (Nm)	May 2017	58.6 (20.5)	66.2 (16.8)	59.8 (22.7)	56 (19.9)	#
Left knee extensor peak torque at 60^{o}/s (Nm)	May 2017	96.4 (31.5)	102.2 (31.5)	97.7 (28.3)	93.1 (32.6)	#

Table 1. Physical fitness data from individual studies (*Continued*)

Left knee flexor peak torque at 60 ^{o}/s (Nm)	May 2017	59.3 (19.7)	67.3 (24)	61.3 (25.3)	58 (2.2)	#
Right knee extensor peak torque at 180^{o}/s (Nm)	May 2017	54.1 (22.4)	61.3 (24.2)	58 (23)	57.9 (20)	#
Right knee flexor peak torque at 180^{o}/s (Nm)	May 2017	41.6 (20.3)	48.3 (17.9)	40.8 (20.6)	42.5 (20)	#
Left knee extensor peak torque at 180^{o}/s (Nm)	May 2017	49.1 (20.4)	53.7 (27.5)	60 (21.9)	51 (19.9)	#
Left knee flexor peak torque at 180^{o}/s (Nm)	May 2017	40.5 (19.1)	45.3 (17.6)	39.1 (21.2)	41.8 (18.4)	#

Data are presented as mean (SD). [a] Intervention group 1 (OnTrack group - a supervised programme); [b] Intervention 2 group (Onco-Move - home-based programme); # P values were not provided however authors reported that lower body muscle strength for flexion and extension of both right and left legs were significantly higher than the usual care control groups at 60o/s but not for 180o/s.

Table 2. Health-related quality of life data from individual studies

		Exercise group		Usual care control group		
Outcome measure	**Study**	**Baseline**	**Post-intervention**	**Baseline**	**Post-intervention**	P value
EORTC QLQ-C30 questionnaire subscales						
EORTC (physical functioning)	Adamsen 2009	84.7 (14.5)	89 (12.4)	84 (15.7)	86.4 (14.5)	0.09
EORTC (physical functioning)	Haines 2010	84.9 (14.8)	83.6 (15.8)	91.3 (9.6)	87.5 (10.8)	0.64
EORTC (physical functioning)	VanWaart 2015	89.4 (10.2)[a]	80.3 (14.1)[a]	84.8 (13.8)	68.1 (17.6)	< 0.001
EORTC (physical functioning)	VanWaart 2015	87 (13.4)[b]	77.8 (17.2)[b]	84.8 (13.8)	68.1 (17.6)	0.001

Table 2. Health-related quality of life data from individual studies (*Continued*)

EORTC (role functioning)	Adamsen 2009	68.7 (28.4)	74.8 (26.3)	65.6 (28.5)	68.9 (26.5)	0.2
EORTC (role functioning)	Haines 2010	84.8 (19.2)	80.3 (20.2)	86.4 (21.3)	86.5 (18.7)	0.32
EORTC (emotional functioning)	Adamsen 2009	77.6 (12.2)	81.3 (17.2)	75.7 (19.3)	80.6 (17.8)	0.9
EORTC (emotional functioning)	Haines 2010	75.4 (19)	81.7 (25.1)	84.3 (15.2)	95.4 (14.2)	0.90
EQ-5D questionnaire						
EQ-5D (VAS)	Haines 2010	72.6 (15.6)	80.4 (12.7)	77.5 (13.5)	79.3 (14.1)	0.09
SF-36 questionnaire subscales						
SF-36 (physical functioning)	Adamsen 2009	84.3 (13.7)	88.2 (13.2)	83.6 (14.8)	84.3 (16.2)	0.01
SF-36 (physical functioning)	Chandwani 2014	41.9 (8.1)	43.7 (8.7)	45.9 (7.9)	45.7 (8.6)	0.18
SF-36 (physical component scale)	Adamsen 2009	44.2 (8.4)	47.4 (6.7)	44.3 (8.3)	45.1 (8.5)	0.02
SF-36 (physical component scale)	Chandwani 2014	41.8 (8.1)	42.3 (8.1)	44.9 (9.2)	44.1 (7.9)	0.47
SF-36 (role physical)	Adamsen 2009	30.5 (35.2)	46.1 (40.2)	27.1 (35.7)	31.8 (37.6)	0.007
SF-36 (role physical)	Chandwani 2014	36.8 (9.4)	39.1 (8.7)	38.3 (10.5)	40.8 (9.9)	0.54
SF-36 (role physical)	Adamsen 2009	30.5 (35.2)	46.1 (40.2)	27.1 (35.7)	31.8 (37.6)	0.007
SF-36 (vitality)	Adamsen 2009	57.8 (20.2)	65.5 (18.1)	55.8 (21.1)	55.6 (21.6)	< 0.001
SF-36 (role emotional)	Adamsen 2009	56.1 (39)	69.6 (40.1)	58.6 (41.2)	58.7 (41.9)	0.02

Table 2. Health-related quality of life data from individual studies (*Continued*)

SF-36 (mental health)	Adamsen 2009	74 (16.3)	78.6 (15)	72 (16.7)	74.2 (16.1)	0.04
SF-36 (social functioning)	Adamsen 2009	77 (21.1)	79.7 (22.2)	75.4 (21.8)	76.5 (22)	0.4
WHOWOL questionnaire subscales						
Overall quality of life	Hwang 2008	3.06 (0.75)	3.47 (0.51)	3.30 (0.57)	3.20 (0.77)	< 0.001
Overall health	Hwang 2008	2.59 (0.87)	2.88 (0.70)	2.55 (0.69)	2.60 (0.88)	0.006
Physical	Hwang 2008	11.41 (2.03)	15.00 (2.24)	12.35 (2.30)	12.10 (2.27),	< 0.001
Psychological	Hwang 2008	11.71 (2.11)	12.71 (2.02)	12.50 (2.65)	12.25 (2.40)	0.001
Social	Hwang 2008	12.77 (1.79)	13.71 (1.65)	13.15 (2.46)	12.75 (2.20)	< 0.001
Environmental	Hwang 2008	12.12 (1.73)	11.82 (3.38)	12.45 (2.42)	12 (2.29)	0.267
FACIT-F questionnaire subscales						
Physical well-being	Reis 2013	23.8 (4.04)	25.2 (2.52)	24.9 (3.39)	24.2 (3.45)	NR
Social/family well-being	Reis 2013	24.3 (4.35)	23.2 (4.06)	23.6 (6.24)	23.2 (5.03)	NR
Emotional well-being	Reis 2013	19.2 (2.37)	20.5 (3.45)	18.9 (3.34)	20.6 (3.15)	NR
Functional well-being	Reis 2013	20.1 (4.91)	22.8 (4.57)	22.3 (5.02)	22.7 (4.9)	NR
FACT-G	Reis 2013	87.3 (12.58)	91.7 (10.96)	89.8 (12.55)	90.6 (11.06)	NR
Outcome measure not known	Choi 2012	2.69 (0.63)	3.78 (0.71)	2.87 (0.64)	3.16 (0.50)	0.004

Data are reported as mean (SD). [a] Intervention group 1 (OnTrack group - a supervised programme); [b] Intervention 2 group (Onco-Move - home-based programme); EORTC (European Organisation for Research and Treatment of Cancer); SF-36 (Short Form Health Survey); WHOQOL (World Health Organisation quality of life); FACIT-F (Functional Assessment of Chronic Illness Therapy-Fatigue); NR (P value not reported).

Table 3. Fatigue data from individual studies

		Exercise group		Usual care control group		
Outcome measure	**Study**	**Baseline**	**Post-intervention**	**Baseline**	**Post-intervention**	P value
Brief fatigue inventory questionnaire	Chandwani 2014	3.2 (0.3)	2.9 (0.3)	2.6 (0.3)	3.2 (0.4)	0.03
Schwartz cancer fatigue scale	Choi 2012	18.27 (5.82)	8.45 (3.33)	15.38 (4.35)	12.08 (4.42)	0.020
Schwartz cancer fatigue scale	Husebo 2014	10.28 (3.93)	12.01 (4.38)	11.36 (3.56)	13.13 (4.47)	NR
FACIT-F questionnaire	Reis 2013	125.8 (23.51)	136.8 (15.67)	130.8 (20.66)	132.9 (16.85)	0.05

Data are reported as mean (SD). FACIT-F (Functional Assessment of Chronic Illness Therapy-Fatigue); NR (P value only reported for the whole sample).

APPENDICES

Appendix 1. CENTRAL Search strategy

#1 MeSH descriptor: [Neoplasms] explode all trees
#2 (neoplas* or carcinoma* or adenocarcinoma* or malignan* or cancer* or tumor* or tumour*):ti
#3 #1 or #2
#4 MeSH descriptor: [Surgical Procedures, Operative] explode all trees
#5 Any MeSH descriptor with qualifier(s): [Surgery - SU]
#6 (surgery or surgical):ti
#7 #4 or #5 or #6
#8 MeSH descriptor: [Combined Modality Therapy] explode all trees
#9 (combined modality or multimodal* or multi modal*):ti
#10 Any MeSH descriptor with qualifier(s): [Drug therapy - DT]
#11 MeSH descriptor: [Antineoplastic Agents] explode all trees
#12 MeSH descriptor: [Antineoplastic Combined Chemotherapy Protocols] this term only
#13 chemotherap*:ti
#14 MeSH descriptor: [Radiotherapy] explode all trees
#15 Any MeSH descriptor with qualifier(s): [Radiotherapy - RT]
#16 radiotherapy* or irradiat* or radiat*:ti
#17 MeSH descriptor: [Immunotherapy] explode all trees
#18 immunotherap*:ti
#19 (adjuvant or neoadjuvant or neo-adjuvant) near/3 (therap):ti

#20 #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21 MeSH descriptor: [Exercise] explode all trees
#22 MeSH descriptor: [Exercise Therapy] explode all trees
#23 MeSH descriptor: [Exercise Movement Techniques] explode all trees
#24 MeSH descriptor: [Physical Fitness] this term only
#25 MeSH descriptor: [Physical Endurance] explode all trees
#26 MeSH descriptor: [Muscle Strength] explode all trees
#27 MeSH descriptor: [Muscle Fatigue] explode all trees
#28 (exercise* or movement* or stretch* or aerobic* or anaerobic*):ti
#29 ((resistance near/3 train*) or stamina or (physical near/3 fit*) or ((musc* or neuromusc*) near/3 fatigue)):ti
#30 walk* or swim* or cycl* or run* or yoga or tai chi or pilates:ti
#31 #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30
#32 #3 and #7 and #20 and #31

Appendix 2. MEDLINE Ovid Search strategy

1. exp Neoplasms/
2. (neoplas* or carcinoma* or adenocarcinoma* or malignan* or cancer* or tumor* or tumour*).ti.
3. 1 or 2
4. exp Surgical Procedures, Operative/
5. surgery.fs.
6. (surgery or surgical).ti.
7. 4 or 5 or 6
8. exp Combined Modality Therapy/
9. (combined modality or multimodal* or multi modal*).ti.
10. drug therapy.fs.
11. exp Antineoplastic Agents/
12. Antineoplastic Combined Chemotherapy Protocols/
13. chemotherap*.ti.
14. exp Radiotherapy/
15. radiotherapy.fs.
16. (radiotherap* or irradiat* or radiat*).ti.
17. exp Immunotherapy/
18. immunotherap*.ti.
19. ((adjuvant or neoadjuvant or neo-adjuvant) adj3 therap*).ti.
20. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21. exp Exercise/
22. exp Exercise Therapy/
23. exp Exercise Movement Techniques/
24. Physical Fitness/
25. exp Physical Endurance/
26. exp Muscle Strength/
27. Muscle Fatigue/
28. (exercis* or movement* or stretch* or aerobic* or anaerobic*).ti.
29. ((resistance adj3 train*) or stamina or (physical adj3 fit*) or ((musc* or neuromisc*) adj3 fatigue)).ti.
30. (walk* or swim* or cycl* or run* or yoga or tai chi or pilates).ti.
31. 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32. 3 and 7 and 20 and 31
33. randomized controlled trial.pt.
34. controlled clinical trial.pt.
35. randomized.ab.
36. placebo.ab.

37. clinical trials as topic.sh.
38. randomly.ab.
39. trial.ti.
40. 33 or 34 or 35 or 36 or 37 or 38 or 39
41. 32 and 40
Key:
mp = title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier

Appendix 3. Embase Ovid Search Strategy

1. exp neoplasm/
2. (neoplas* or carcinoma* or adenocarcinoma* or malignan* or cancer* or tumor* or tumour*).ti.
3. 1 or 2
4. exp surgery/
5. su.fs.
6. (surgery or surgical).ti.
7. 4 or 5 or 6
8. multimodality cancer therapy/
9. (combined modality or multimodal* or multi modal*).ti.
10. dt.fs.
11. exp chemotherapy/
12. exp antineoplastic agent/
13. chemotherap*.ti.
14. exp radiotherapy/
15. rt.fs.
16. (radiotherap* or irradiat* or radiat*).ti.
17. exp immunotherapy/
18. immunotherap*.ti.
19. ((adjuvant or neoadjuvant or neo-adjuvant) adj3 therap*).ti.
20. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21. exp exercise/
22. exp kinesiotherapy/
23. fitness/
24. endurance/
25. muscle strength/
26. muscle fatigue/
27. (exercis* or movement* or stretch* or aerobic* or anaerobic*).ti.
28. ((resistance adj3 train*) or stamina or (physical adj3 fit*) or ((musc* or neuromusc*) adj3 fatigue)).ti.
29. (walk* or swim* or cycl* or run* or yoga or tai chi or pilates).ti.
30. 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31. 3 and 7 and 20 and 30
32. crossover procedure/
33. double-blind procedure/
34. randomized controlled trial/
35. single-blind procedure/
36. random*.mp.
37. factorial*.mp.
38. (crossover* or cross over* or cross-over*).mp.
39. placebo*.mp.
40. (double* adj blind*).mp.
41. (singl* adj blind*).mp.

42. assign*.mp.
43. allocat*.mp.
44. volunteer*.mp.
45. 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44
46. 31 and 45
Key:
mp = title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword
ti = title
fs = floating subheading

Appendix 4. Sports Discus Search Strategy

1. expNeoplasm
2. Canc*.tw.
3. Neoplasm*.tw.
4. expTumor
5. Tumo*.tw.
6. expCarcinoma
7. Carcin*.tw.
8. expMalignant
9. expOncology
10. Oncol*tw.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. expNeoadjuvant
13. Neoadjuvant*.tw.
14. expChemo
15. Chemo*.tw.
16. expRadiotherapy
17. expCancer treatment
18. 12 or 13 or 14 or 15 or 16 or 17
19. expExercise
20. Exercise*.tw.
21. expFitness
22. Fit*.tw.
23. expOxygen consumption
24. expAerobic
25. Aerobic*.tw.
26. Anaerobic
27. Anaerobic*.tw.
28. 19 or 20 or 21 or 21 or 22 or 23 or 24 or 25 or 26 or 27
29. Surgery
30. Surg*.tw.
31. Surgical (including Anatomy, drainage, mortality, patient, science, stress, wound, ward all terms)
32. 29 or 30 or 31
34. Morb*.tw.
35. Mort*.tw.
36. Recurrence*.tw.
37. Outcom*.tw.
38. 34 or 35 or 36 or 37

WHAT'S NEW

Date	Event	Description
10 December 2018	Amended	Protocol information added to 'Other published versions of this review'

CONTRIBUTIONS OF AUTHORS

Study conception and design: Lisa Loughney, Malcolm West, Graham Kemp, Michael Grocott, and Sandy Jack

Acquisition of data: Lisa Loughney and Malcolm West

Analysis and interpretation of data: Lisa Loughney and Malcom West

Drafting of manuscript: Lisa Loughney

Critical revision: Lisa Loughney, Malcom West, Graham Kemp, Michael Grocott, Sandy Jack

DECLARATIONS OF INTEREST

Lisa Loughney: None known

Malcolm West: None known

Graham Kemp: None known

Michael Grocott: None known

Sandy Jack: None known

Michael Grocott: received honoraria for speaking, for travel expenses, or both from Edwards Lifescience, Fresenius-Kabi, BOC Medical (Linde Group), Ely-Lilly Critical Care, and Cortex GmBH. He has also received research grants from the National Institute of Health Research, Association of Anaesthetists of Great Britain and Ireland, Sir Halley Stuart Trust, and Francis and Augustus Newman Foundation. He leads the Xtreme-Everest hypoxia research consortium, which has received unrestricted research grant funding from BOC Medical (Alinde Group), Ely-Lilly Critical Care, Smiths Medical, Deltex Medical, London Clinic, and Rolex. None of these activities are related to the work under consideration in this review.

SOURCES OF SUPPORT

Internal sources

- None to declare, Other.

Not applicable

External sources

- There were no external sources of support in terms of funding for the review, Other.

Not applicable

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We made the following changes between the protocol and review:

- Safety is now a single secondary outcome and feasibility (adherence and compliance) has been omitted as an outcome. Adherence is now reported in the Characteristics of included studies tables and compliance is reported in incomplete data in the 'Risk of bias' tables.
- We added additional study details to the data extraction section.
- We reported data as means (MDs) with standard deviations (SDs) and not as standardised mean differences (SMDs).
- We did not conduct subgroup analyses according to: cancer type (solid and haematological tumours); cancer treatment (neoadjuvant, adjuvant chemotherapy, adjuvant radiotherapy, immunotherapy); exercise intervention characteristics (frequency, intensity, timing, type); participant characteristics (gender and age), due to the small number of studies measuring the same outcomes.